Epidemiology – Genetics – Immunology

PP 001

Incidence of type 1 diabetes in children and young adults in Varmia and Mazury Region, Poland, in years 1994–2003

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Aims: To overview total as well as age and sex specific incidence rates (IR) of Type 1 diabetes (T1DM) in persons 0–29 years old, and to compare IR of childhood onset T1DM in the group 0–14 years old to the older age group (15–29 years old) during the period 1994–2003, in a well-defined province of Varmia and Mazury (V&M), Poland.
Methods: New cases of T1DM were independently reported by the local general and pediatric departments to the Polish Diabetes Registry as well as by the Endocrinology and Diabetology Department in Olsztyn, prospectively according to EURODIAB ACE. Completeness of ascertainment was calculated by the capture–recapture methods.
Results: In the study period from January 01, 1994 to December 31, 2003, 331 persons (157 women and 174 men) were registered. The average IR T1DM per 100 000 persons/year in V&M Province was 9,21 (95%CI: 8,4–10,1). In the age group 0–14 total IR was 10.9 (95%CI: 9.6–12.2) and 7.7 (95%CI: 6.7–8.8) for the 15–29 age group. The increase of IR in the whole group from 5.1 (95%CI: 3.1–7.2) in 1994 to 11.3 (95%CI: 8.2–14.4) in 2003 was observed. In the group 0–14 the growing tendency of IR was observed, from 4.6 to 17.2, particularly in females from 3.2 to 19.9. In the group 15–29 IR varied between 5.8 (in 1994) to 13.6 (in 1997). Sex differences during the whole period were not statistically significant: IR for women 8.9 (95%CI: 7.5–10.3) and IR for men 9.5 (95%CI: 8.1–10.9). Significantly higher IR was observed in urban areas – 10.1 (95%CI: 8.7–11.4) than in rural areas – IR 8.0 (95%CI: 6.6–9.3). The estimated completeness of the ascertainment was 94% (95%CI: 89,6–98,1) for children and 87,9% (95%CI: 85,2–89,9) for youths and young adults.
Conclusions: Our study shows that the IR T1DM in V&M Province is growing. It also shows that it is higher in childhood (age 0–14) than in the older group (age 15–29). The higher IR T1DM in urban areas than in rural areas was observed. The reason for this is probably related to westernisation effect.

PP 002

High height and weight gain from early childhood up to the time of diagnosis in children with type 1 diabetes

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Introduction: The Accelerator Hypothesis regards increased insulin demand as the common basis for Type 1 and Type 2 diabetes, and weight increase as the trigger of Type 1. The Beta Cell Stress Hypothesis includes in addition other factors causing insulin resistance. To test these hypothesis we wanted to evaluate the height and weight gain from early childhood up to the time of diagnosis of Type 1 diabetes in children with diabetes.
Methodology: Growth charts were received from child welfare clinics and school nurses of the children who developed Type 1 during August 1995–August 2000 in the south-east part of Sweden (probands) and from age and sex matched healthy controls. The height and weight measurements have been read as standard deviation score (SDS).
Results: The children who later developed diabetes had the same weight and height at birth as the control children. Both the gain in height and weight was significantly greater in probands than in controls from birth up to 7 years of age ($p < 0.01$, height and $p < 0.05$, weight). No difference between gender was seen regarding height while the girls were responsible for the difference regarding the weight. Children who developed diabetes already between 0–5 years of age gained significantly more in weight between birth and 3 years of age ($p < 0.01$) than controls, while children diagnosed in age group 6–10 years gained significantly more in length between birth and 5 years of age ($p < 0.03$). The weight and height gain from 1–2 years before diagnosis up to the time of diagnosis did not differ between probands and controls.
Conclusion: Rapid growth early in childhood is a risk factor for Type 1 diabetes.

PP 003

Rates of type 1 diabetes in children continue to rise over 25 years in Yorkshire, UK

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Introduction: To determine whether the incidence of childhood Type 1 diabetes in Yorkshire, UK continues to rise and in which age groups and to investigate the influence of socioeconomic status, population density and ethnicity on incidence trends.
Methodology: Details of 3,176 children aged under 15 years were extracted from the population-based Yorkshire Register of Diabetes in Children and Young Adults, diagnosed between 1978–2003. Annual mid-year population estimates were used to calculate age-standardised incidence rates per 10^5/yr. Rates were examined separately by 5-year age group and sex. Trends in incidence were determined using log-linear regression. Small area-based measures of deprivation and population density, using UK census derived indices assigned via the postcode at diagnosis, were calculated in order to compare incidence trends over time. The proportion of patients categorised as Asian or not was compared across the cohort.
Results: A significant rise in incidence rates was present for all ages combined and within each age group (0–14: 2.7%/yr $p < 0.001$, 0–4: 3.2%/yr $p < 0.001$, 5–9: 2.7%/yr $p = 0.001$, 10–14: 2.6%/yr $p < 0.001$). The rate of increase appeared to level off after 1999, and there was evidence of a consistent cyclical pattern in incidence. Male incidence trends largely mirrored those for females throughout the 25-year period ($p = 0.33$). The relative proportion of Asians with diabetes increased from 3% in 1978 to 7% during the most recent years (Mann–Whitney $p = 0.0004$), despite the background proportional Asian population remaining stable over this time period. No significant differences were seen in the overall incidence rates or in the temporal trends by deprivation ($p = 0.42$) or population density ($p = 0.71$).
Conclusion: There has been a statistically significant steady rise in the incidence of childhood Type 1 diabetes in Yorkshire over the last 25 years. This increase in incidence appears to have levelled off over the last 5 years as seen in some Scandinavian countries, although the periodicity indicates a recurring environmental factor may be influencing the onset of disease in young people. The sharp increase in the proportion of Asians with diabetes warrants careful monitoring

particularly with the increasing prevalence of obesity in this ethnic minority group.

PP 004

The swedish childhood diabetes registry, 0–18 years. Experiences with HbA1C from the first four years

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SWEDIABKIDS (Swedish Childhood Diabetes Registry, 0–18 years), analysis data from all visits to pediatric diabetes out-patient clinics since 2000.

Aim: To investigate if the mean HbA1c level improved during the first 4 years of this quality control program, and to estimate if some of the registered variation in HbA1c levels between clinics can be explained by variation in methodology.

Methodology: Data from 2579 children (2000) up to 4470 (2003) were analysed; corresponding to 15000 visits in 2003 in 29 out-patient clinics. HbA1c values from periods when insulin need was >0.5 U/kg were used to calculate a yearly mean HbA1c for each patient. All HbA1c values measured in Sweden are standardized to the Mono S level (1.0–0.7% units lower than NGSP-level), and the performances of the laboratories are monitored through monthly EQA schemes. The inter-laboratory coefficient of variation (CV) and the yearly mean deviation from the target value in the surveys are calculated for each clinic.

Results: The range for clinic mean HbA1c (Mono S) decreased from 8.5–6.7% in 2000 to 8.0–6.7% in 2003. The 4 highest and 2 lowest clinic means deviated significantly from the over-all mean for 2003. The mean CV in the EQA schemes during 2003 was 3.6% (corresponding to 2.9 CV% if data are expressed in NGSP units). A maximum of 6–18% of the variation in mean HbA1c between clinics might be explained by methodological variation. The 4 clinics with highest mean patient HbA1c in 2000 showed a steady decline over the study period and reached in 2003 almost the mean HbA1c value for all clinics. No statistically significant improvement was found among the other clinics. With exception for the 4 clinics above, no clinic mean HbA1c changed with more than 0.5%.

Conclusion: The variation in yearly mean HbA1c between clinics could only to a small part be explained by variation in methodology.

PP 005

Both socioeconomic status and urban residence are associated with increased incidence of type 1 diabetes in western Australia

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Introduction: Geographic variation in the incidence of Type 1 diabetes (T1DM) has been shown to occur both between, and within countries. There are inconsistent findings on the relationship between socioeconomic factors and the incidence of T1DM. As Princess Margaret Hospital is the only paediatric referral centre in Western Australia (WA), case ascertainment levels of >99% can be achieved. This study aimed to analyse the incidence of T1DM in 0–14 year olds in WA, from 1985 to 2002, by region and socioeconomic status.

Methodology: Primary case ascertainment was from the prospective population-based WA Diabetes Register and secondary case ascertainment was from the WA Hospital Morbidity Data System. The case ascertainment rate was calculated using the capture–recapture method. Address at diagnosis was used to categorise cases into metropolitan, rural and remote areas according to standard definitions, and into 5 socioeconomic groups based on the Socioeconomic Index for Area indices published by the Australian Bureau of Statistics. Poisson regression modelling was used to analyse incidence rates and trends, by area and socioeconomic status.

Results: From 1985 to 2002 there were 1144 new cases of T1DM. Case ascertainment was estimated at 99.8% complete. The mean annual age-standardised incidence was 18.3/100,000 person years (95%CI: 17.1–19.5) in metropolitan, 14.4/100,000 (95%CI: 12.4–16.5) in rural and 8.0/100,000 (95%CI: 5.8–10.2) in remote areas. The incidence was significantly higher in metropolitan compared to rural areas (Incidence rate ratio (IRR) 1.27, $p = 0.001$) and in rural compared to remote areas (IRR 1.80, $p < 0.001$). The incidence in the highest socioeconomic group was 72% greater than the lowest socioeconomic group (IRR 1.72, $p < 0.001$). The differences in incidence by socioeconomic status and region were independent of each other.

Conclusion: Higher socioeconomic status and residence in metropolitan areas are independently associated with an increased risk of T1DM in Australian children.

PP 006

Epidemiology of type 1 diabetes mellitus in Montenegrin children: 1993–2002

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Introduction: The incidence rates of type 1 diabetes mellitus show rapid increases in many parts the word. In Montenegro (The Balkans, Mediterranean area) type 1 diabetes mellitus is growing health problem.

Aim: To determine dynamics of change in the incidence ratio of the diabetes mellitus in Montenegrin children aged 0–14 in period 1993–2002.

Methodology: 166 diabetic children with onset of type 1 diabetes mellitus before the age 14 in the period 1993–2002 were taken in account (obtained from type 1 diabetes registry). The data were processed regarding the general incidence, the incidence based on age groups, the gender and seasonal variation. We compared the results with those obtained in previous years.

Results: During the period 1993–2002, 166 new cases of type 1 diabetes in children in Montenegro are reported. The incidence of type 1 diabetes is in rising from 6,4 in period 1983–1992 to 10,7 in 1993–2002. The group of the youngest children (0–4 years) had the most intensive increase in incidence ratio from 3,5 (1983–1992) to 7,7 (1993–2002). The highest incidence is observed among children aged 10–14: 8,8 in period 1983–1992, and 13,4 in 1993–2002. There was no significant difference in the incidence ratio between girls and boys. The majority of patients were diagnosed during winter (November–December).

Conclusion: The incidence ratio type 1 diabetes mellitus in Montenegrin children is increasing, especially in the youngest group (0–4 years).

PP 007

Steadily high incidence of childhood type 1 diabetes in NSW, Australia

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Introduction: The incidence of childhood type 1 diabetes (T1DM) has been increasing in many western countries for more than a decade, with a concomitant rise in type 2 diabetes over this period. A significant rise in T1DM in children < 15 years was observed from 1990–96 in NSW, where one third of Australians reside. The incidence in <5 year olds doubled over this time. The aim of the current analysis is to further investigate these epidemiological trends.

Methodology: Incident cases of T1DM were ascertained prospectively from 1990. Secondary ascertainment was from the National Diabetes Supply Scheme until 1999, and from the National Diabetes Register from 2000. Age and sex standardised incidence rates per 10^6 were calculated using the direct method. Poisson regression models were used to analyse trends in incidence, using age-group, sex, calendar year and their interaction terms in the models.
Results: Mean annual incidence over the study period was 20.9 per 10^6 compared with 17.8 from 1990–96. The incidence in girls was 20.7 and boys 21.1 (NS). Peak incidence was 36.3 in males aged 10–14 years in 1998. Incidence increased by 3.8% per year (95% CI 2.37–5.21), with the greatest rise in 0–4 year olds (4.1% per year).

Mean annual incidence (95% CI) of T1DM in NSW

Period	0–4 years	5–9 years	10–14 years	Total (0–14 years)
1990–1996	10.9 (8.0–14.5)	17.8 (14.1–22.4)	24.9 (20.3–30.1)	17.8 (15.6–20.3)
1997–2002	13.5 (10.3–17.4)	20.2 (16.3–25.0)	28.7 (24.0–34.2)	20.9 (18.5–23.5)

Conclusion: The incidence of T1DM has increased significantly in NSW since 1990. Rates have remained steady, however, at around 21 per 10^6 since the mid 1990s, whilst type 2 diabetes has continued to rise. The increase in the toddler age-group, in particular, has significant implications for education and management, for families and the health care team.

PP 008

Association of HLA-DMA, DMB alleles with clinical status heterogeneity of type 1 diabetes in Chinese

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Introduction: HLA-DMA and DMB are non-classical genes whose product (DM molecules) play an important role in antigen presentation. Our present study was designed to investigate the relationship between human leucocyte antigen–DMA, DMB and clinical status heterogeneity of type 1 diabetes.
Methodology: A total of 80 children (male 36, female 44) with type 1 diabetes were selected as research subjects. Diagnosis of type 1 diabetes was made according to WHO criteria. The range of age at onset of type 1 diabetes were 2.5–14 years old. 91 healthy adult blood donors were selected as normal controls. polymerase chain reaction and dot blot hybridization techniques were used to classify DMA and DMB alleles. Patients with type 1 diabetes were classified into different groups according to different clinical status including sex, age of onset, ketosis onset situation on diagnosis, remained function of β cell, etc. Then distribution of DM susceptive alleles and heterodimer in different clinic groups were studied.
Results: The frequencies of DMA*0103 and DMB*0103 alleles in patients were significantly increased (50% vs. 8%, 42.9% vs. 21.8% respectively), these two alleles confer susceptibility to type 1 diabetes in Chinese. The frequencies of DMA*0103/DMB*0102, DMA*0103/DMB*0103 and DMA*0103/DMB*0101 heterodimers were also increased in the patients. The above heterodimers confer predisposition to type 1 diabetes. Both DMB*0103 allele and DM susceptive heterodimers are related to islet β cell function on diagnosis. The patients with DMB*0103 allele or DM susceptive heterodimers were significantly increased in the patients with lower c-peptide level on diagnosis (55.6% vs. 29.4%; 58.3% vs. 34.4% respectively). DM heterodimer are also related to onset age and ketosis-onset- situations of the patients. The patients carrying DM susceptive heterodimers have higher probability to suffer type 1 diabetes before 10 years and have the predisposition to ketosis or ketoacidosis on diagnosis.
Conclusion: HLA-class II non-classical alleles-DMA and DMB play an important role in pathogenesis of type 1 diabetes, and clinical status heterogeneity of type 1 diabetes are related to genetic mechanism.

PP 009

Examining similarities in the geographical occurrence of childhood type 1 diabetes and acute lymphoblastic leukaemia

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Introduction: The causes of childhood type 1 diabetes (T1D) and acute lymphoblastic leukaemia (ALL) remain largely unknown, although the two conditions share some common epidemiological features supporting an environmental aetiology, potentially involving infectious agents. We have shown that the incidence of both diseases is correlated at the international level and we aimed to test whether there was evidence of cross-space-time clustering between cases of childhood T1D and ALL in the north of England, UK.
Methodology: Data on the incidence of childhood (ages 0–14) T1D and ALL were extracted from two population-based disease registers covering the Yorkshire Region, diagnosed between 1978 and 2000. The Region covers a childhood population of 700,000 people and an area of 12,000 km^2 reflecting a mix or urban and rural communities. Each child's postcode at diagnosis was validated and geo-located to a grid-reference. Knox tests for space-time interactions were applied between cases in different disease groups, with fixed thresholds defined as being close in space (<5 km) and close in time (<1 year apart) to determine whether more pairs of children with T1D and ALL occurred in close proximity than would be expected by chance. Tests were repeated replacing geographical distance with distance to the N^{th}-nearest neighbour (NN) to adjust for varying population density. N was chosen such that the mean distance was 5 km, and was equal to 36. A measure of the strength of interaction (S) between conditions was derived by calculating [(O-E)/E x100%] for each pair of disease counts which were close in space and time.
Results: 2721 cases of T1D and 516 cases of ALL were identified. There was no evidence for cross-space-time clustering between diseases. Using the Knox geographical distance test, S = 1.2% (p = 0.25) and using the NN threshold version of the Knox test, S =–0.9% (p = 0.64).
Conclusion: This study does not provide further evidence of the similarities in the descriptive epidemiology of T1D and ALL in children, although further analyses are planned using more sophisticated methods.

PP 010

Type-1 diabetes in children – socio-economic and rural–urban gradients.

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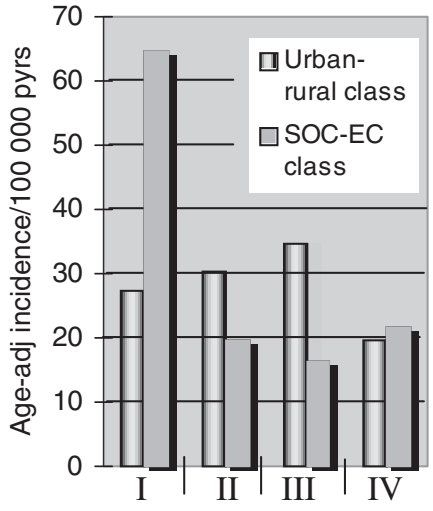
Introduction: Sweden has the second highest incidence of diabetes after Finland. Recent time-space studies in five counties in south-east Sweden has shown geographical variations. Searching for determinants and co-variates in environmental exposures, life-style and genetics is therefore essential to uncover potential etiological mechanisms and triggers.
Methodology: 1900 children diagnosed with Type 1 diabetes between 0–16 year of age during a 25 years period in south-east Sweden were included and allocated x- and y-co-ordinates in the national grid by matching to a population- and a property registry for residencies using

a unique personal identification number. The resulting file containing demographic and clinical data were then geocoded in a digital map. Population and socio-economic data aggregated in 82000 200-meter squares covering the study area were geocoded likewise using the co-ordinates of the left lower corner. Data were analysed by geographic information technology (ArcGIS 8.3 and MapInfo v.7.0). By overlay technique cases and background population were defined for urban area polygons of different population size, density and socio-economic attributes. Socio-economic gradients in disease incidence were investigated separately for family income, education and overcrowdness and for a deprivation index based on z-scores for the summarised variables.



Results: There was an urban–rural trend with increasing incidence in semi-rural areas and lowest in rural heartland. Areas with high incidence had larger families (≥7) compared with small (≤3) (OR = 1.94), and a higher average support from social welfare system (OR = 1.72). The deprivation score showed a higher incidence in wealthy areas than in lower classes.

Conclusion: Population density and relative socio-economic deprivation influences incidence of type-1 diabetes in children and adolescents.

PP 011

Why girls are born lighter than boys: the gender insulin hypothesis

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Introduction: Girls are born lighter than boys. The consistency of this observation across different populations is striking, suggesting that it may have fundamental significance, particularly for conditions linked with lower birth weight, such as diabetes. Previous hypotheses relating low birth weight to subsequent diabetes have addressed differences in insulin resistance within the sexes, but not between them. We hypothesised that gender-specific genes affecting insulin sensitivity account for the gender difference in birth weight – the genetically more insulin resistant female fetus is less responsive to insulin and is therefore smaller.

Methodology: Using data from the EarlyBird Study, we tested the fetal insulin hypothesis by gender, correcting for paternal BMI. We examined differences in insulin resistance (HOMA-IR) between girls and boys at five years, adjusting for a wide range of variables with which insulin resistance correlates, and between their mothers and fathers, adjusting for waist circumference. We examined the relationship between insulin resistance and waist circumference in both sexes.

Results: We found an inverse relationship between paternal insulin resistance and birth weight in girls ($r = -0.20$, $p = 0.053$, $n = 96$), consistent with the fetal insulin hypothesis, but a direct relationship in boys ($r = 0.18$, $p = 0.045$, $n = 117$), challenging it. We found that girls at five years are substantially (~33%, $p < 0.001$) more insulin resistant than boys, even after adjustment, and that mothers are some 25% ($p < 0.001$) more insulin resistant than fathers after adjustment for waist circumference. The gradient of the relationship between (log) insulin resistance and waist circumference is the same in males and females (0.027, $p > 0.5$), but their displacement substantial (females higher, $p < 0.01$).

Conclusion: These data are consistent with a gender-specific genetic contribution to insulin resistance, and we propose that females are intrinsically (genetically) more insulin resistant than males. These genes also explain why reports of type 2 diabetes in young populations show a female preponderance.

PP 012

An education and support program for siblings of a child with type 1 diabetes

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Siblings of children with chronic illness are at increased risk of psychological morbidity. Chronic illness can shift the family balance and focus of concern, which may be detrimental to sibling relationships. Preventative programs are vital to meet the needs of siblings who may have difficulty adjusting to new family roles. An education and psychological support program has been developed for children aged 8–10 years with a sibling with type 1 diabetes. The program aims to reduce isolation, enhance self-esteem, share experiences, provide diabetes information and establish coping skills. Two sibling programs were conducted, with 22 participants in total. Parental pre questionnaires for both groups, and post questionnaires for Group 1, included the Achenbach Child Behaviour Checklist and a standardised measure of vicarious futurity. Formal evaluation as well as subjective information from siblings was collected to understand more about their concerns and for future program development. Pre-program concerns identified by the parents using the Achenbach included: sibling isolation, anxiety, low self-esteem, anger difficulties, and social skill deficits. Similar worries were raised by the siblings. Questionnaire results revealed that 85% of siblings scored within the normal range of functioning and 85% of the parents had high hope for their child's future. Ten percent of the children fell into the clinical range of functioning and parents had concerns about their child's hope for the future. There were no significant differences between pre and post measures for Group 1, this may be due to the small numbers in the group. This program is an innovative way of addressing the identified problems and in this format was rated as positive and beneficial by siblings.

PP 013

Is there a relationship of beta cell failure with GADA and 1A–2A levels at onset of type 1 diabetes

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Introduction: Albania is included in the European map as a low incidence country for the type 1 diabetes ($3/10^5$). A recent study correlated this with the high frequency of protective allele DQB1*0301 and low impact of the susceptible DQB1*302. The aim of actual study was to

determine the role of GADA and IA-2A as marker of autoimmunity and the relationship with beta cell failure.
Methods: During the years 2003, 69 new diabetics (aged 1.5–45 years), clinically classified as type 1 diabetes, were tested for GADA, IA-2A and C-peptide, measured with RIA.
Results: At diagnosis 65.2% (n = 45) of patients were positive for GADA and 49.2% (n = 34) positive for IA-2A. 54 (78.2%) were positive for at least one of the antibodies and 36% (n = 25) for both. We found $GADA^+$ more frequent in female 70.3% than in male 61.9%, and $IA\text{-}2A^+$ lower in patient older than 20 years; 25% vs. 54%. Low C-Peptide level (<0.26 mmol/L) was found 58% in the group positive only for one antibody (mv 0.37 nmol/L), 48% in positive for both GADA and IA-2A (mv 0.30 nmol/L), and 33% in negative antibodies group (mv 0.38 nmol/L).
Statistically there was no significant differences in C-peptide level between positive and negative antibodies group ($\chi^2 = 2.37$ $p > 0.1$). In the group positive for both antibodies C-peptide value was lower than in other groups (0.30 nmol/L), but without significant statistical differences with the one positive group ($\chi^2 = 0.62$ $p > 0.1$).
Conclusion: GADA is capable to determinate more cases than IA-2A at diagnosis (68% vs. 49.2%). GADA is more frequent in female, while IA-2A is more frequent in cases under 20. Measurements of two antibodies increased the determination of positive cases in 78.2%. These antibodies are truly markers of autoimmune diabetes but beta cell failure is not specifically related with them at the moment of diagnosis.

PP 014

Human beta cells expand by proliferation in a dedifferentiated state

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Introduction: Pancreatic beta cell mass can increase remarkably in response to metabolic demands, although the proliferative capacity of differentiated beta cells is very limited. Neogenesis of beta cells from tissue stem cells has been considered to be an important mechanism. However, recent transgenic mouse experiments have suggested that stem cells would not contribute to the beta cell pool after early development. To clarify these issues, we have studied the replication and neogenesis of human beta cells in vitro using isolated islets and ductal cells.
Methodology: Human islets or duct-cell enriched fractions were cultured and induced to differentiate as described by us previously (Gao et al. Diabetes 52:2007–2015, 2003). Transitional cell types of mixed ductal-endocrine phenotype were identified by double immunofluorescence based on CK19 and chromogranin A (ChrA) immunoreactivity. Cell-type specific proliferation was assessed by BrdU labelling. Magnetic cell separation (MACS) based on NCAM antibody was used to eliminate pre-existing endocrine cells prior to culture.
Results: As we have reported before, long-term culture of mixed cell populations followed by a differentiation phase including Matrigel overlay and serum-free culture resulted in the differentiation of islet cells from a proliferating duct-like precursor cell. At least part of these precursor cells were derived through 'dedifferentiation' of the islet cells during early phase of the culture, since up to 9% of all endocrine cells were $CK19/ChrA^+$ at 24 h of culture. No such cells were detected in the original islets. Elimination of pre-existing endocrine ($NCAM^+$) islet cells by MACS resulted in the loss of endocrine differentiation from the remaining duct-cell enriched cultures, suggesting that the pre-existing endocrine cells were the source of precursor cells.
Conclusion: These studies are consistent with the idea that pancreatic tissue stem cells do not contribute to the human beta cell mass. Instead, it appears that the beta cell mass can increase through transient dedifferentiation into a proliferating duct-cell like phenotype.

PP 015

Neonatal screening for genetic risk of type 1 diabetes: parental understanding of the risk and anxiety caused by emergence of islet cell Autoantibodies (ICA) during the follow-up

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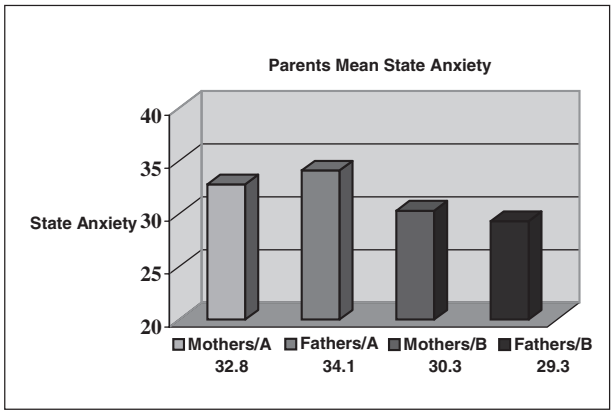
Introduction: In Type 1 Diabetes (T1D) Prediction and Prevention Project (DIPP) child's genetic T1D risk is measured at birth, and those carrying increased risk are recruited to follow-up with visits at 3- to 6-month intervals. Serum ICA are analyzed at each visit, and if positive, other autoantibodies are also measured in all samples collected from that child previously and later. We now studied parents' understanding of the child's risk to develop T1D, their anxiety after learning that the child had developed ICA and their satisfaction with participation to the study.
Methodology: Analytical methods were two-way analysis of variance, Tukey's test and Kruskall-Wallis ANOVA. Level of state anxiety was analyzed using State-Trait Anxiety Inventory for adults (STAI) Manual. Open questions were analyzed using content analysis. Group A (45 parents) had recently received the information about child's ICA positivity. Group B (30 parents) had received the information a year earlier.
Results: Parents in group A (20/45 = 44%) knew better than parents in group B (9/30 = 30%) their child's real risk to develop T1D. In group A 17 parents (17/45 = 38%) and in group B 19 parents (19/30 = 63%) underestimated their child's risk. Mothers in group A thought often about child's risk, while fathers in group B thought about child's risk less often. The mothers in group A and B combined thought about child's risk more than fathers in group A and B combined (p = 0.026). Almost all mothers (40/42 = 95%) and all fathers (34/34 = 100%) were very satisfied with participation to study.



Parents' anxiety levels show low State Anxiety Scores. The state anxiety between mothers and fathers or groups A and B were not different.
Conclusion: Our findings suggest that the frequent follow-up and information of child's seroconversion to ICA positivity in the DIPP-project causes only mild to moderate anxiety in the families. Parents' understanding of child's risk were rather inaccurate, hence, means to clarify new and simpler information about child's risk are needed.

PP 016

The frequency of autoantibodies positive (IAA, ICA, GADA) in type 1 diabetes children in Guangdong China

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Aims: The most of type 1 diabetes (T1DM) in children was considered to be an autoimmune disease associated with the presence of different types of autoantibodies. Our study was to test if it was true in Guangdong, China.
Methods: 34 new-onset (the course of disease was less than 4 months) T1DM children were involved in the study, 12 boys and 22 girls, aged 7.1 ± 3.6 (7~12) years, the serum C-peptide less than 0.5 ng/ml, without over weight or obesity before onset of the disease, no one had acanthosis nigricans, all come from Guangdong China. The serum GADA, ICA and IAA were measured in all cases and 30 healthy age-matched children by ELISA. GADA, ICA and IAA ELISA Box were produced by Bimetric.
Result

The results of serum autoantibodies

	T1DM (N = 34)		Normal (N = 30)		P
	+ (%)	–	+ (%)	–	
GADA	15 (44.1%)	19	7 (23.3%)	23	0.08
ICA	6 (17.6%)	28	1 (3.3%)	29	0.06
IAA	12 (35.3%)	22	3 (10.0%)	27	0.01

The frequency of IAA positive was significant higher in T1DM patients than in normal controls ($P < 0.05$), The frequency of GADA and ICA positive were a little higher in T1DM patients than in normal controls, but no statistics differences between two groups ($P > 0.05$, respectively).
Conclusions: The frequency of autoantibodies positive was low in T1DM children in Guangdong China, meant that the most of T1DM in Guangdong China maybe idiopathic.

PP 017

Type 1 diabetes and Fibrocalculous diabetes are more common than previously recognized in young onset cases from Bangladesh

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Introduction: Diabetes is increasing in younger age groups, a problem in Bangladesh subjects where type 1 diabetes (T1D) is uncommon. It has been previously shown that N34S *SPINK* variant identifies 1/3 of subjects with fibrocalculous diabetes (FCPD). Anti-GAD and IA-2ic antibodies and SPINK genotype were used to determine the causes of diabetes in subjects with an age of onset below 30 years (YDM).
Methodology: 314 subjects with YDM (known FCPD/T1D excluded), 41 with FCPD and 280 controls (fasting glucose level <7 mmol) were studied. Anti-GAD and IA-2ic antibodies were determined by radioimmuno-precipitation method, C-peptide by ELISA and the *SPINK* variant by a PCR-RFLP.
Results C-peptides were low in YDM (0.29 ± 0.26 nmol/l) and FCPD (0.17 ± 0.16 nmol/l) versus controls (0.43 ± 0.19; $p < 0.0001$). GAD and IA-2ic antibodies in YDM and FCPD were detected more frequently than in controls ($p = 0.001$), 8% of YDM and 14.6% of FCPD were positive for both antigens. YDM GAD positive subjects compared to GAD negative patients had a younger age of onset ($p = 0.001$), a lower C-peptide ($p < 0.001$) and a lower BMI ($p < 0.001$). 6% controls compared to 11.8% YDM ($p = 0.025$) and 36.6% FCPD ($p = 0.001$) were *SPINK* variant positive.
Conclusion: Autoimmunity and subclinical FCPD are common in young onset diabetes in Bangladesh.

PP 018

Antisulfatide antibodies in children with pre-type 1 diabetes

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Introduction: Some children with pre-type 1 diabetes have autoantibodies against sulfatide, a lipid molecule expressed e.g. in beta cells. Our aim was to evaluate how well antisulfatide antibodies (ASA) correlate with the conventional diabetes associated antibodies against islet cells (ICA), insulin (IAA), glutamic acid decarboxylase (GADA) and IA-2 protein (IA-2A).
Methodology: Serum samples (n = 106) were collected from children (n = 99) carrying HLA DQB1-conferred risk alleles for T1D and participating in the Type 1 Diabetes Prediction and Prevention Project (DIPP). ASA, ICA, IAA, GADA and IA-2A were analysed in all samples collected. Thirty-eight samples from 31 children contained one or more conventional diabetes associated autoantibodies, and the remaining 68 samples were autoantibody negative.
Results: The presence of conventional diabetes associated autoantibodies showed no correlation with the presence of ASA in serum samples. The sensitivity and specifity of ASA to discover whether the samples were positive for diabetes-associated autoantibodies were 47% and 49%, respectively. Three and half years after the samples for ASA analysis were collected, 7 study children had developed T1D. All of them had been positive for conventional diabetes associated autoantibodies before developing clinical T1D, but only three of them had been positive for ASA.
Conclusion: Antisulfatide antibodies are poor markers of pre-T1D in children and their value in predicting which children will develop clinical T1D is limited if any.

PP 019

Incidence of type 1 diabetes in children of South Asian and white or other ethnic backgrounds in Leicestershire, UK: 1989–2003

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Aims and objectives: To compare with new census data the incidence of type I diabetes (TIDM) in children of South Asian (SA) and white or other (WO) ethnic backgrounds in Leicestershire, UK.
Methods: All Leicestershire resident children aged <15 years with newly diagnosed TIDM over the 15 year period 1989–2003 were included in the study (incident cohort). Children living in Leicestershire but diagnosed previously were excluded (prevalent cases). Ethnicity was assigned as SA (Indian, Pakistani, Bangladeshi) or WO according to names. 1991 and 2001 census were used to define population data. Crude and age specific incidence rates (95% confidence interval) for the SA and WO ethnic groups were estimated for three 5 year periods; 1998–1993, 1994–1998 and 1999–2003.
Results: 498 children fulfilled the criteria for inclusion in the study, comprising 71(14%) classified SA and 427 (86%) WO. The overall crude incidence rate for SA for 1989–93, 1994–98 and 1999–2003 were 17.2 (10.5–26.5), 19.7 (12.8–28.8) and 18.9 (12.2–27.9) per 10^5 person years respectively which are not statistically significantly different from the WO group rates which were 16.3 (13.5–19.5), 19.2

(16.2–22.6) and 21.9 (18.6–25.5) per 10^5 person years. There was a trend towards higher incidence rates in the older age groups. Using the 1989–93 period as the standard, standardised incidence ratios (SIR) were 117 (76–170) and 112 (73–165) for 1994–98 and 1999–2003 respectively for SA, compared with 114 (96–135) and 130 (111–152) for the WO group.

Conclusion: The incidence of TIDM in Leicestershire children is still increasing. Incidence rates for TIDM among SA children in Leicestershire are similar to the WO group, in contrast to lower rates reported for SA living South Asian countries. This similarity, as previously reported, suggests that environmental factors continue to exert an influence on the genetic predisposition to the disease aetiology.

PP 020

The assessment of chosen genetic risk factors of DMT1 among sick children and their healthy siblings

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Introduction: The studies of different populations with DMT1 confirm that the highest risk is connected with the HLA region. But not all people with predisposing haplotype suffer from DMT1. The immunological reaction of the organism is under control of cytokine genes. Are they factors responsible for the onset of DMT1?

The aim of the study was to assess of chosen genetic risk factors: allele locus DRB1, DQB1 and polymorphisms of cytokine genes: TNF-α (308 A/G), Il-10 (1082 A/G, 819 C/T, 592 A/C), Il-6 (174 C/G) and IFN-γ (874 T/A) in children with newly diagnosed DMT1 and their healthy siblings.

Methodology: 87 children (aged 1,55–18,22) with DMT1 were followed up. The second examined group were siblings (78 children, aged 0,69–19,99). The samples for HLA genes and cytokine genes were obtained (PCR-SSP and PCR-SSO). For statistical analysis 44 pairs ill child-healthy child were chosen to compare with control group (85 people).

Results: The haplotype DRB1*04/DQB1*03 was observed in 57 (65,5%) children with DMT1 and in 35 (44,8%) siblings. The haplotype DRB1*03/DQB1*02 was present in 54 (62%) children with DMT1 and in 37 (47,4%) siblings. The highest risk of DMT1 in our population is connected with alleles: DRB1*0401 (OR = 5,1; CI: 2,7–9,57), DRB1*0301 (OR = 2,72; CI: 1,48–5,01), DQB1*0201 (OR = 4,04; CI: 2,17–7,52) and DQB1*0302 (OR = 5,08; CI: 2,54–10,14). The analysis didn't show significant differences for Il-10, Il-6 and IFN-γ polymorphisms between all groups. Only allele TNF-α: A was noted more often in children with DMT1 (36,76% vs. 18,1% in control group, p = 0,039) and in their siblings (28,4%).

Conclusion: Children with DMT1 and their siblings present similar risk factors of DMT1. The estimated cytokine genes are not responsible for the onset of DMT1.

PP 021

The distributions of HLA-DQ, DR alleles in type 1 diabetes children in Guangdong China

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Aims: To explore the distributions of HLA-DR, DQ alleles in T1DM children of Guangdong area and its relationship with diabetes.

Methods: 47 T1DM children were involved in the study, 20 boys and 27 girls, aged 6.7 ± 3.7 years (9 months~13 years), all come from Guangdong China, no one was over weight or obesity or had acanthosis nigricans before onset of the disease, serum C-peptide were all less than 0.5 ng/ml at onset. HLA-DQA1, DQB1 and DRB1 on Lymphocyte were determined by PCR-SSP in all cases and 60 healthy adults.

Result

Results of HLA-DQA1 alleles

DQA1	T1DM (n = 47)	Normal (n = 60)	OR	P
0501	29 (61.7%)	15 (25.0%)	4.83	0.000*
0301	19 (40.4%)	11 (18.3%)	3.02	0.012*
0302	13 (27.7%)	14 (23.3%)	1.26	0.61
0201	3 (6.4%)	3 (5.0%)	1.30	1.00a
0102/3	25 (53.2%)	19 (31.7%)	2.45	0.025*
0103	7 (14.9%)	7 (11.7%)	1.33	0.62
0101/2/4	35 (74.5%)	15 (25.0%)	8.75	0.000*

Results of HLA-DQB1 alleles

DQB1	T1DM (n = 47)	Normal (n = 60)	OR	P
0201	5 (10.63%)	3 (5.0%)	2.26	0.47a
0301	7 (14.89%)	23 (38.3%)	0.28	0.007*
0302	5 (10.63%)	3 (5.0%)	2.26	0.47a
0303	13 (27.66%)	3 (5.0%)	7.27	0.001*
0401	10 (21.28%)	3 (5.0%)	5.14	0.011*
0402	12 (25.53%)	4 (6.67%)	4.8	0.007*
0602	3 (6.38%)	1 (1.67%)	4.02	0.32a

Result of HLA-DRB1 alleles

DRB1	T1DM (n = 47)	Normal (n = 60)	OR	P
01	11 (23.40%)	8 (13.3%)	1.99	0.18
15	9 (19.15%)	11 (18.3%)	1.06	0.91
03	9 (19.15%)	3 (5.0%)	4.50	0.021*
04	23 (48.94%)	5 (8.33%)	10.54	0.000*
09	16 (34.04%)	7 (11.7%)	3.91	0.005*
12	16 (34.04%)	6 (10.0%)	4.65	0.002*

*means significant difference comparing with normal.

Conclusions: The distributions of HLA-DQA1, DQB1 and DRB1 alleles in T1DM children in Guangdong area were a little different from the other area in China. HLA-DQA1*0501, 0301, 01, DQB1*0303, 0401, 0402, DRB1*03, 04, 09 and 12 might be risk factors for T1DM in Guangdong area children, whereas DQB1*0301 allele be not.

PP 022

The influence of social-economical postcommunist transformation for T1DM incidence

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In postcommunistic countries the highest dynamic of increase T1DM incidence has been noted in last 15 yrs. This period of time coincides with their social and economical transformations. The aim of the study was to analyze the influence of some parameters, which can determine the level of hygiene, health care and economic status of examined population on the incidence ratio of T1 DM in children.

Methodology: Incidence of T1DM in children aged up to 15 yrs (in age groups: 0–4; 5–9; 10–14) was estimated accordingly to EURODIAB criteria, between 1989–2002 in Upper Silesia region. For estimation of the level of hygiene, health care and economic status the following parameters were chosen: number of salmonellas, taeniasis, diarrhea, and diarrhea in children aged 0–2 yrs, alimentary toxicosis and neonatal mortality, average women and men life expectancy, accessibility of the water-supply and sewage systems and the unemployment rate in this period of time. Statistics: Spearman test and linear regression model.

Results: A dramatic increase in incidence ratio of T1DM children was observed (1989 – 4,72/10^5; 2002 – 15,20/10^5). T1DM was diagnosed in 1046 children. The statistical significance of negative correlation to incidence ratio of T1DM was found for salmonellosis and taeniasis

($p < 0.01$) in all age groups. Statistically significant correlation was also observed for accessibility of water supply and sewage system ($p < 0.001$). The parameters of health care, decreasing ratio of neonatal mortality, increasing life expectancy of women and men correlated significantly with the increase of T1DM incidence ratio ($p < 0.001$). Economic status described by the unemployment rate did not influence of incidence ratio of T1DM.

Conclusion: Higher status of hygiene and health care of population seems to increase its susceptibility to T1DM.

PP 023

Function and autoimmunity of thyroid and adrenal glands in children and adolescents with diabetes mellitus type 1

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Association of diabetes mellitus type 1 (DM-1) with other endocrine disease is well known. The aim of the present study is to examine the function and autoimmunity of thyroid and adrenal glands in these patients. 93 children and adolescents with DM-1, duration 0.08–14.2 yrs, 52 boys and 41 girls, mean age 12.8 ± 3.1 yrs (4.5–17.4 yrs) have been studied. Goiter was found in 56 patients (60.9%; I A degree in 40–43.5%, I B – in 13–14.3%, II – in 3–3.3%), thyroid dysfunction – in 10 children (10.8% – 2 with Graves and 8 with Subclinical Hypothyroidism-SH). Antithyroglobulin (ATA) and antimicrosomal antibodies (AMA) with positive titer (≥1 : 80) were found respectively in 34 and 43 children and elevated TGSI – in one (6.3%). Thyroid ultrasound examination showed picture typical or suspected for autoimmune thyroiditis (AT) in 16 children (57.1%) and typical for Graves (G) – in one (3.6%). Autoimmune Thyroid Disease (ATD) was diagnosed in 36 children with DM-1 (38.7%-AT: G = 34 : 2; in 7 children AT was without goiter-atrophic variant). The diurnal cortisol rhythm in three children with DM-1 and antiadrenal abs (to 17 OH and 21 OH fractions) – in 24 children were normal. Children and adolescents with DM-1 have increased thyroid dysfunction (mainly SH), thyroid antibodies formation and ATD. The adrenal function and antibodies in these patients was not changed. Thyroid function and autoimmunity should be checked in all children and adolescents with DM-1 at diagnosis of diabetes and every half a year thereafter.

PP 024

HLA screening for type 1 diabetes at birth in the general population in Italy and implementation of a primary prevention trial with vitamin D and cow's milk hydrolysate (the Prevefin Trial)

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Introduction: The Italian national 'Prevefin' trial has been implemented with the purpose to validate the short-term efficacy of a primary prevention strategy (vitamin D supplementation and beta casein-free diet) for T1DM in high genetic risk subjects (defined as HLA DRB1 03/DRB1 04.DQB1 0302 in absence of the protection allele DRB1 0403).

Methodology: High risk subjects from the general population are randomly assigned at birth to one of the two groups of treatment (group A: Vitamin D, 500 IU daily, and diet with a cows milk hydrolysate for the first 12 months; group B: Vitamin D and free diet for the first 12 months) followed up for the appearance of islet cell autoantibodies.

Results: We sampled cord blood from 9409 Caucasian subjects born in 11 Centers of Continental Italy and screened them for type 1 associated HLA class II markers. The enrolment started in February 2001. 73 newborns (0.8%) were at 'high risk', a low figure which can explain why the incidence of T1DM is low in continental Italy. For the trial 2 families were lost at recall, 12 parents did not give written consent; 1 baby is waiting for randomisation and the drop-outs are 16. Therefore 42 babies are now in long-term follow up; 17 in group A and 25 in group B. So far 6 babies (3 in group A, 3 in group B) have developed autoantibodies: 3 babies (1 transiently) developed GADA and 3 IAA (1 transiently, 2 not confirmed yet).

Conclusion: These preliminary data show that it is possible to perform a population-based screening for T1DM, associated to a primary prevention in the Italian population.

PP 025

Vitamin D receptor gene polymorphism and susceptibility to type 1 diabetes

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Introduction: Recent studies have clarified the molecular basis of vitamin D immunomodulatory activity and have postulated that this hormone could play an important role on the pathogenesis of type 1 diabetes (T1DM). In this contest the relationship between polymorphism of vitamin D receptor (VDR) gene and the development of T1DM was postulated and some studies, performed on other European populations, confirmed this hypothesis. Our study was intended to investigate this relationship in our T1DM patients.

Methodology: We compared polymorphism of VDR gene in a group of T1DM patients (group A) and in a group of normal subjects (group B). The group A consisted of 31 patients followed at our Genova Centre (21 males, mean age 12.4 years) and group B consisted of 36 blood donors (24 males, mean age 33 years). VDR genotyping was performed using PCR and Bsm I, Apa I and Taq I restriction enzymes, in order to identify alleles A, a, B, b, T, t. VDR gene polymorphisms were compared between patients and controls using the chi square test.

Results: Our study did not confirm any significant relationship between the VDR gene and T1DM susceptibility, except a significantly higher frequency of the genotype AaBbTt in controls than in diabetic patients. Moreover we observed that the frequency of the genotypes AaBbTT and AABbTt was higher in group A patients than in Group B subjects, but not significantly.

Conclusion: Further studies on larger series of T1DM patients and controls are necessary in order to confirm that polymorphism of VDR gene is important in the pathogenesis of T1DM.

PP 026

High frequency of exon-3 deleted polymorphism of the growth hormone receptor gene (GHRd3) in type 1 diabetics from chile

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Introduction: Type 1 diabetes is a multifactorial autoimmune disease characterized by the destruction of β cells with both environmental (virus or diet) and genetic factors contributing to the development of the disease. Both, wild type (GHRwt) and the exon 3 deletion isoform (GHRd3) has been identified and both are expressed in liver, pancreas, stomach and small intestine. A high expression of mRNA of GHR gene

in mucosal gut suggest the possible role on digestive and immune functions. To date the functional importance of the GHR domain encoded by exon 3 is unknown.

Aim: We investigate the putative effect of the allelic variant GHRd3 on cytokine profile in type 1 diabetic children.

Subjects and Methods: A control population (n = 150) and recent diagnosis type 1 diabetic children (n = 111, age: 8.7 ± 3.6 years) were analysed for height, weight, IL-1β, IL-2, IL-4, TGFβ1 and INFγ cytokines profile. GHRd3 polymorphism was determined by means of multiplex PCR.

Results: The allele frequency for d3 allele was 32.8% in type 1 diabetics and 35.1 % in controls. No statistical significant difference was observed in Type 1 diabetics or controls regarding to GHRd3 polymorphism and height or weigh. Among type 1 diabetic children, the d3 polymorphism was associated with a significant high levels of IL-1β ($p < 0.05$).

Table 1. GHRd3 carriers and cytokine level in type 1 diabetes (mean value and range)

GHRd3	IL-1β (pg/ml)	IL-2 (pg/ml)	IL-4 (pg/ml)	TGFβ1 (ng/ml)	INFγ (pg/ml)
f1/f1 (n = 68)	8.9 (2.7–192.2)	20.8 (3.2–90.3)	9.8 (7.2–32.6)	1.2 (0.3–4.2)	22.4 (7.6–50.8)
d3 carriers (n = 43)	15.5* (5.0–87.0)	17.5 (3.0–59.8)	8.9 (7.0–18.5)	1.4 (0.5–2.8)	21.3 (8.7–33.4)

Conclusion: A high frequency of d3 isoform was found in Chilean population. In type 1 diabetic children, the carries of d3 isoform shown higher levels of IL-1β compared with non carriers. The regulatory importance of this isoform on expression of pro-inflammatory cytokines need to be elucidated.

PP 027

Vitamin D receptor polymorphism and susceptibility to type 1 diabetes in Chilean subjects: A case–parent study

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Several reports have found a relationship between polymorphisms of the vitamin D receptor gene (VDR) and development of type 1 diabetes.

Aim: We examined the association of three VDR polymorphism in 59 Chilean case–parents trios. Genotyping for Bsm1, Apa1 and Taq1 polymorphism were performed. Transmission/disequilibrium tests were used to assess gene-disease associations through the evaluation of allelic transmission to affected offspring.

Results: Non-significant increased transmissions of B allele (probability of transmission = 52.5%, p-value = 0.69), A allele (probability of transmission = 58.4%, p-value = 0.17) and T allele (probability of transmission = 52.0%, p-value = 0.77) were estimated. Haplotype-based analyses also showed non-significant preferential transmissions (global p value = 0.52).

	Bsm1 (b allele)		Apa1 (a allele)		Taq1 (t allele)	
Transmitted/non transmitted	28/59		27/65		23/48	
p-value	0.69		0.17		0.77	
Haplotypes	**bat**	**bAt**	**BAt**	**bAT**	**BAT**	**Bat**
p value	0.50	0.26	0.61	0.42	0.85	0.45
p value (global)	0.52					

Conclusion: The present study does not suggest a significant contribution of VDR alleles in the etiology of type 1 diabetes of Chilean cases.

PP 028

TCRVB repertoire abnormality in type 1 diabetic Japanese patients

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Introduction: Type 1 DM is autoimmune disease against pancreatic β cells characterized by the presence of insulitis with T cell infiltration and pancreas-related autoantibodies. Recently the presence of T cells which are reactive to enterovirus has been found in type 1 DM. We analyzed TCR repertoire of circulating $CD4^+$ and $CD8^+$ T cells from patients with type 1 DM of onset at childhood.

Methodology: Frequencies of 21 TCRVβ-chain$^+$ cells in $CD4^+$ and $CD8^+$ T cells from 36 type 1 DM patients were analyzed by 3-color flow-cytometry. Spetratype of complementary determined region 3 (CDR3) in sorted $CD4^+$ and $CD8^+$ T cell populations was analyzed by Gene Scan methods based on PCR reaction using 25 TCRVβ specific primers. In selected cases with TCRVβ showing mono-, or oligoclonal expansion, the amino acid sequences of CDR3 were determined in 10–33 clones.

Results: We found the apparent increases of particular TCRVβ-chains$^+$ frequencies in $CD8^+$ T cells from 8 cases in 25 autoantibody-positive patients, but only one case within 11 autoantibody-negative patients. $CD8^+$ T cells with TCRVβ chains with increased frequencies showed effector/killer phenotypes with $CD62L^-$, $CD28^-$, $CD27^-$, $CD244^+$, and $CD56^+$. Abnormal increase of TCRVβ in $CD4^+$ T cells was not found in all cases. Spectratype analysis showed the mono-, or oligoclonal skewed peaks in 10 TCVVβ from $CD8^+$ T cells in 7 patients and 4 TCRVβ from $CD4^+$ T cells in 3 patients. Amino acid sequences of CDR3 showing the skewed patterns were quite restricted and 60–92% of clones from each TCRVβ were identical in selected 6 TCRVB.

Conclusion: Our results indicated that particular T cell clones, which were mainly $CD8^+$ T cells, expanded in type 1 DM patients and might involve in the pathogenesis of β cell destruction although the specificity of target antigen of expanded $CD8^+$ T cell clones was unknown.

PP 029

Rare etiology of childhood diabetes in one large hungarian family: MODY2, T1DM, T2DM in the same family

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Genetically MODY is defined as an autosomal dominant form of non-insulin requiring, non-ketotic type of diabetes, with onset before age 25. A group of heterogeneous disorder, each is a single-gen abnormality. To date 6 genes were linked to MODY in various families. A certain MODY genotype describes a certain clinical phenotype. The authors describe an interesting family with glucokinase deficiency. To date 43 members of the family were tested and 17 were found to have the MODY2 "hungarian" new mutation. The clinical features of the family and those members of the family suffering from MODY2 mutation do not follow the clinical description of the literature. Concerning the grandparents (1st generation): MODY2 and T2DM is present with full clinical spectrum of type 2 diabetes. Concerning the parents (2nd gen-

eration): the authors found MODY2, T2DM and GDM. Concerning the children (3rd generation): beside the beta-cell dysfunction (MODY2) we found presence of autoantibodies in 2 children, what indicates that also type 1 diabetes is present. To date the clinical form of diabetes in the children's generation is: diabetes without insulin-resistance and without insulinopenia. The beta-cell dysfunction and consequently the glucose-abnormality are deteriorating- more rapidly than it is described in the literature. This can be explained with the presence of T2DM in the parents' generation and in the family. Another line of the family-tree fulfils the diagnostic criteria of MODY: DM with autosomal dominant inheritance, but on the test genetically they are not MODY2. Maybe they suffer from another type of MODY? According to the family tree the genes of different types of diabetes is present in the children's generation making the clinical decision and therapeutic choice difficult. Whether oral antihyperglycemic agent or insulin should be used for treatment? When a disorder is inherited, family members can be screened. This affords an opportunity for prevention. Understanding the genetic basis of diabetes can foster the development of novel and more effective therapies. Our exciting case of this big family represents the wide etiology of diabetes-syndrome.

PP 030
Peculiarities of cellular and humoral immunity in children and adolescents with type 1 diabetes mellitus

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Introduction: There are the inconsistent data about a role cellular and humoral immunity in pathogenesis of type 1 diabetes mellitus. The aim of this research was to study features of the immune status and of the activity of metabolic enzymes in lymphocytes of blood in children with diabetes type 1.
Methodology: Cellular and humoral immunity parameters were studied in 94 patients with type 1 diabetes mellitus aged 6–18 years (the mean age was 11.6 ± 0.3 yrs) and 104 controls the same age. The patients were divided into 3 groups with different duration of diabetes: up to I year, 1–5 years, and more than 5 years. The metabolic control of diabetes we estimated on levels of glycemia and HbA1c. Population and subpopulation composition of peripheral blood lymphocytes wav studied by indirect immunofluorescence. Serum concentrations of the main immunoglobulin classes were measured by radial immunodiffusion. The activity of NAD-dependent dehydrogenases investigated by the bioluminescence method.
Results: 88% of the diabetes patients had HbA1c levels higher than 10%. The average HbA1c was 12.3%. At the initial stage of diabetes the immunoreactivity status in children and adolescents manifested by depression of T-cellular component of the immune system and activation of humoral immunity, this depression progressing with the disease duration. The concentration $CD16^+$ cells was increased in all patients, irrespective of diabetes duration. The content of $HLA\text{-}DR^+$ lymphocytes was increased at the stage of initial diabetes and decreased to the norm later. No definite patterns in changes of serum immunoglobulins A and M concentrations could be distinguished during the observed period of disease.
Conclusion: This study has shown, that there are the suppression of T-cellular immunity and the activation of humoral immunity in the initial stage of diabetes type 1.

PP 031
Increasing incidence of childhood-onset type 1 diabetes in Estonia

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Introduction: In 1991–1998 the incidence of childhood-onset Type I diabetes in Estonia was 12.2 with highest incidence of 17.0 in age group 10–14 years (Podar et al, Diabetologia 2001). The aim of the study was to investigate the incidence of Type I diabetes in Estonia in 1999–2003 and compare the results with data from 1991–1998.
Methods: Population-based incidence data were collected from 2 centres where all children with Type 1 diabetes in Estonia are seen after the diagnosis and thereafter at least once a year.
Results: 181 new cases of Type 1 diabetes were diagnosed among the children aged 0–14.9 years between 1999 and 2003. The incidence for that period was 14.9 (95%-confidence intervals 12.84–17.27), which is significantly ($p < 0.05$) higher than 12.2 in 1991–1998. There was an increasing trend in the incidence over the study period: 1999 – 11.1, 2000 – 16.8, 2001 – 12.4, 2002 – 16.3, 2003 – 18.7. The incidence in the 5–9 year age group was significantly higher than in the 10–14 year group (19.4 vs. 11.9, $p < 0.01$). However, the biggest rise in the incidence occurred in the 0–4 year age group, where the incidence increased by 73% from 8.4 in 1991–1998 to 14.5. There was a regional variation with highest incidence in capital Tallinn and its region – 21.0 and the lowest in the Western regions and on islands – 13.6.
Conclusions: the incidence of childhood-onset Type I diabetes in Estonia has increased by 21% over the last 6–7 years, particularly in the age group 0–4. Diabetes is now the most common in the age group of 5–9 years.

Diabetes care

PP 032
24-Hours telephone hotline for young patients with diabetes

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Introduction: To improve metabolic control and minimize the number of severe hypoglycaemic events and ketoacidosis we introduced a telephone hotline service in 2000. The hotline could be contacted from 4 pm to 8 am on weekdays and 24 hours on holydays.
Methodology: In 2004 we analysed the calls from a 3-months period, and conducted a questionnaire survey concerning the family's use and satisfaction with the hotline.
Results: There were 465 calls, on average 4 calls on weekdays and 7 on holydays. The calls came from 146 families. Mean age of the patients was 9.9 (±3.9) yrs, 9.2% < 4 yrs and mean diabetes duration 1.4 (±2.3) yrs. 89.3% of the calls were registered in the evenings or nights. Mean time consumption of the calls was 6.2 (range 1–20) minutes. 70.9% of the calls included insulin adjustments, 6.4% hypoglycaemia, 14.3% illness with high BG, 8.3% other causes. There were 7 admittances, 4 from ketoacidosis and 3 from gastroenteritis. In the study period questionnaires were handed out to 270 families. 204 (75.5%) returned the questionnaires. 198 (97%) of the patients were aware of the hotline and 147 (72%) had used it. Of these families 98.6% were satisfied with the advice given, and 100% wanted the hotline to continue. 43.1% wrote positive remarks concerning their experiences. In the period 2000–2004 mean HbA_{1c} of our patients decreased from

8.5–8.2% ($p < 0.05$). The number of severe hypoglycaemia decreased from 7.5–4.0/100 patient year (NS) and ketoacidosis from 0.9–0.3/100 patient year (NS).
Conclusion: Telephone hotline is an excellent tool to provide continuous patient support outside the opening hours of the diabetes clinic. The hotline helps to improve metabolic control and maintain severe hypoglycaemia and ketoacidosis at a low level. At the same time there is a high patient satisfaction.

PP 033
The results of diabetes management in children and adolescents in Małopolska region in the years 1987–2003

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Introduction: The management of children and adolescents with type 1 diabetes should be directed towards the achievement of the best possible results with no deterioration of their quality of life. The aim of the study was to evaluate the results of long-term diabetes control in children's and adolescents from Małopolska region attending diabetes clinic in the years 1987–2003. Patients: children and adolescents aged 8 months to 22 years with diabetes duration from 6 months to 18 years. The number of patients evaluated in each year increased from 230 in 1987 to 566 in 2003.
Methods: The quality of glycemic control was estimated by the results of HbA1c measurement performed 4–6 times a year. The methods employed were: affinity chromatography (Pierce) from 1987 to 1995 and HPLC thereafter. The results obtained with the former method were corrected to be comparable to HPLC results.
Results: The mean HbA1c improved significantly during the analyzed period from 12.0 ± 2.55% to 7.5 ± 1.19% ($p < 0.001$). This significant improvement was observed to the same extent in boys and girls and in all age groups. But mean HbA1c was significantly higher in girls than in boys and increased with age of patients. The significantly better HbA1c was achieved by patients with different diabetes duration. At the same period of time significantly increased the percentage of children with the best HbA1c results i.e. <7% (from 0.4% in 1897 to 35.5% in 2003) and decreased the proportion of patients with the worst control i.e. mean HbA1c >9% (from 93% in 1987 to 9.2% in 2003). The possible causes of the improvement of diabetes control in our patients were: the arrangement of multidisciplinary team of the health care professionals providing comprehensive and continuous education to diabetics and their families, the advances in self blood glucose monitoring, introduction of intensive insulin therapy and continuous subcutaneous insulin infusion.

PP 034
Annual review of children and adolescents with diabetes mellitus at Birdem

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A total of 993 children and adolescents with Diabetes Mellitus are enrolled in the Paediatric out patient department. Although patients were followed up regularly, formal 'Annual Review' was started from January 2001 according to the WHO guideline. Annual review of 48 (4.8%) patients were performed over a 1 year period from January 2001 to January 2002. Twenty-five were girls and 23 were boys. The majority i.e. 23 (47.9%) were malnourished and had no pancreatic calculi; they have been termed 'Malnutrition Modulated Diabetes Mellitus'. Fourteen patients (29.2%) had Type 1 DM. 11 patients (22.9%) were malnourished and had pancreatic calculi. Thirty-two patients (66.6%) were aware of complications of diabetes mellitus, dental and foot care, benefits of regular exercise as well as monitoring and adjusting the doses of insulin. Thirteen patients (27%) had no knowledge about hypoglycaemia. Eight patients (16.65%) hid their illness from relatives, neighbours and friends and they were girls. Thirty-seven patients (77%) performed urine tests at home. We found stunting (height for age-2SD) in fourteen patients (29.1%). All patients were on insulin; the dosage ranged between 0.6–1.7 u/kg. We categorized the level of HbA1c as good (6–8%), fair control (8–10%) and poor control (<10%). Twenty patients (41.6%) were poorly controlled, 12 patients (25%) were moderately controlled and 14 were well-controlled (29.1%). Eight complained of burning extremities suggestive of peripheral neuropathy. Fifteen patients (31.2%) were admitted in the hospital for the control of diabetes, but only one (2%) was admitted with ketoacidosis after one year of diagnosis and treatment.
Conclusion: The annual review has given us an insight into the patients' knowledge about Diabetes as well the areas which need to be reinforced.

PP 035
Changes in the adiponectin levels in children with type 1 diabetes

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Introduction: In the pathogenesis of type 1 diabetes (T1D), near to insulin secretion deficiency as a result of chronic β-cells destruction, the other disorders e.g. in adipose cells are also observed. One of the most important adipocyte-expressed cytokine in human serum is adiponectin (adipoQ). The aim of this study was to determine an association between adiponectin serum level and clinical characteristics of type 1 diabetes in children.
Methodology: For this purpose 129 type 1 diabetic patients (50 female and 79 male, mean age = 9.7 ± 4.1 years) and 50 healthy children as a control group (18 female and 32 male, mean age = 11.4 ± 4.7 years) were examined. The levels of adipoQ were measured by radioimmunoassay at the onset and in 6^{th}, 24^{th}, 36^{th}, 48^{th} month after diagnosis. Among the clinical features: insulin requirement (U/kg/24h), HbA1c levels, z-score as BMI normalized by age and sex, fasting glycaemia and clinical remission were considered.
Results: The adiponectin level decreased during the T1D: at the onset –19.0 (12.1–28.7) μg/ml, in 6 month –16.7 (quartiles: 9.9–22.5) μg/ml, after 24 months –14.3 (8.5–20.8) μg/ml, after 36 months –10.8 (8.5–15.4) μg/ml and after 48 months –9.6 (7.1–12.4) μg/ml ($p < 0.001$). Moreover, a correlation between adipoQ levels at the onset and in the 6^{th} month of the disease duration ($r = 0.25$, $p < 0.03$) was found. The adiponectin level in the 6^{th} month of diabetes was negatively correlated with age at the onset ($r = –0.23$, $p < 0.008$). In the 48^{th} month of the disease duration the adiponectin level was statistically lower in the patients than in the control group (10.45 ± 7.42 μg/ml vs. 15.47 ± 5.3 μg/ml, $p < 0.007$). No differences in adiponectin level were found as gender and other clinical parameters were concerned.
Conclusion: Concluding, it was difference in adiponectin level between type 1 diabetic patients and healthy children. The level of adiponectin decreased during the type 1 diabetes.
Acknowledgement: Supported by Polish State Committee for Scientific Research grant No. 3P05E 04923.

PP 036
Deterioration of glycemic control during puberty in patients with type-1 diabetes: impact of gender and time of diabetes onset

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Introduction: Management of diabetes during puberty is a great challenge for diabetes care professionals and patients. Hormonal changes leading to insulin resistance and psychosocial developmental transition from childhood to adulthood may complicate diabetes treatment and impair glycemic control.
Methodology: We analyzed clinical and metabolic data of 1,310 patients (697 boys, 613 girls) treated for type-1 diabetes (mean age at onset 8.8 ± 4.1 years) at a single center. Since 1980, HbA1c was measured at every visit by microcolumn method (Panchem), by HPLC (Biorad Diamat, since 1988) or by DCA2000 (Bayer, since 2002). Results of the primary methods were converted to DCA2000 results. Patients had 4.2 ± 1.7 measurements per year. A total of 7,203 years of follow-up was available for analysis. Remission was defined as diabetes duration with daily insulin requirements less than 0.5 IU per kg body weight.
Results: During childhood, annual HbA1c values were nearly constant. However, HbA1c sharply increased during puberty, particularly from the age of 11 to 12 years ($p < 0.001$). This was more pronounced in girls than in boys ($p < 0.05$, Fig. 1,2) as well as in patients with diabetes onset before the age of 12 years ($p < 0.001$, Fig. 3). Glycemic control during puberty remained more unfavorable in patients with diabetes onset before age of 12 even after adjustment for the honeymoon effect ($p < 0.01$).
Conclusion: Deteriorating metabolic control during puberty is a phenomenon due to several physiological and/or psychological influences. However, adolescents with longstanding diabetes experience seem to need more support during this period than those with diabetes onset in adolescence.

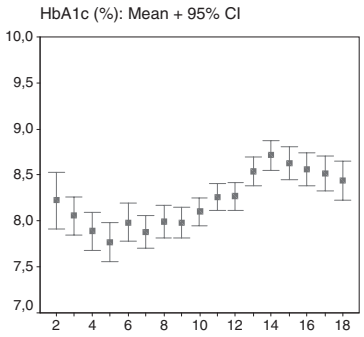

Fig. 1: Boys Age (yrs)

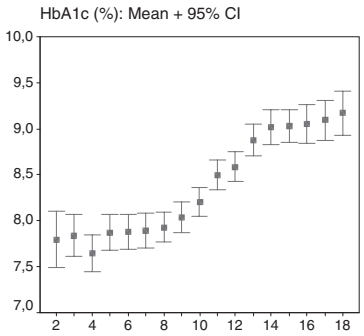

Fig. 2: Girls Age (yrs)

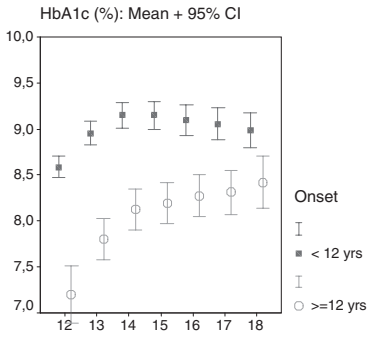

Fig. 3: Total Age (yrs)

PP 037
Endogenous GLP-1 levels in association with beta-cell function during the first 12 months after diagnosis

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Background and aims: To investigate endogenous incretion hormones GLP-1 and GIP and residual beta cell function during the first 12 months after diagnosis.
Methods: Clinical data, genetic and immunological samples were collected from 246 children and adolescents below 16 years with newly diagnosed type-1 diabetes. Stimulated C-peptide (Boost) test was performed at 1, 6, 12 months after diagnosis – capillary glucose measured at time 0; venous C-peptide GLP-1, GIP and glucose at 90 min.
Results: GLP-1 increased significantly from 1 and 6 to 12 months (21.7 ± 0.9; 22.6 ± 0.9; and 24.9 ± 0.9 pM, mean ± SEM, $p < 0.001$, repeated measurements model, corrected for age) and GIP (23.1 ± 1.3; 27.0 ± 1.4; and 28.3 ± 1.3 pM, mean ± SEM, $p < 0.01$) whilst residual beta-cell function decreased. Multiple regression models with C-peptide at 1, 6 and 12 months as a function of stimulated GLP-1, glucose levels, sex and age show that at 1 month after diagnosis GLP-1 has more important correlation with stimulated C-peptide levels (coefficient to GLP-1: 0.27, SE 0.10, $p < 0.01$) than glucose (coefficient to glucose: –0.03, SE 0.02, $p = 0.06$) (corresponding GIP n.s.). However, the importance of GLP-1 on C-peptide is lost at 6 months and 12 months, and is now negatively correlated with C-peptide, when most children are no longer in remission. Instead, glucose is the important correlate at 6 and 12 months (coefficients to glucose: –0.04 and –0.07, $p < 0.01$ and $p < 0.0001$).
Conclusion: The inverse relationship between stimulated GLP-1 and C-peptide could indicate an enteroinsulinar feedback mechanism whereby a compensatory increase in stimulated GLP-1 release occurs in association with the progressively failing beta-cell function. The significance of this is uncertain.

PP 038
Evaluation of osteoporosis in children with type I diabetes mellitus

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Introduction: To analyze whether bone mineral density (BMD) and bone metabolic markers are influenced by long-term metabolic control and duration of disease in children with long-standing type 1 diabetes mellitus.
Methods: Thirty six children (age 9.02 ± 2,7 years, duration of diabetes 3,9 ± 2,0 years) were studied. BMD (z score) was measured by using dual-energy X-ray absorptiometry (DEXA) in the lumbar spine (L1, L4). Bone turnover was evaluated by the biochemical markers of

bone formation [bone specific alkaline phosphatase (BSAPase)] and resorption [telopeptytes of type 1 collagen- (CTx)]. Linear (Pearson) correlations between lumbar BMD z score or CTx excretion- BSAPase and age and long-term metabolic (Hb A1c whole duration) control, duration were sought.
Results: The mean BMD z score was –1.14 ± 0.75 and CTx excretion, BSAPase was not increased in diabetic cases. A negative advanced correlation was found between z score, height (r – 0.44; $p < 0.01$) and duration of diabetes (r – 0.63; $p < 0.01$), HbA_{1c} (r – 0.39; $p < 0.01$). A negative intermediated correlation was found between z score and weight (r – 0.40; $p < 0.05$).
Conclusions: At last years pediatric patients at Type 1 diabetes mellitus appear to constitute a population at risk of osteoporosis in adulthood. Optimization of metabolic control in growing diabetic children may prevent osteoporosis in later life, for long term follow up that children, BMD should be used for osteopenia.

PP 039
Goal setting as a tool for focused dietary management in UK children with type 1 diabetes

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Introduction: A dietary intervention was designed to reduce total fat intake in a group of children and adolescents with type 1 diabetes. The intervention involved an individual assessment of the child's intake and a personalised programme targeting high fat food choices. A behavioural approach to goal setting was used as part of the intervention.
Methodology: Eighty-two children completed a three-day food diary before and one-year after the dietary intervention. The nutrient analysis and the food choices that contributed to total fat intake were fed-back to the children and families and formed the basis of the intervention. Three dietary goals, which would potentially reduce total fat, were self-selected by each child. The approach to goal setting can be described by the acronym 'SMART': Specific, measurable, achievable, relevant to the goal of treatment and time specific (agreed time-frame).
Results: The most popular dietary goals chosen by the children were: reduce the consumption of crisps (fried potato snack food); change to lower fat biscuits; change to a low fat butter or margarine, preferably monounsaturated. There was a statistically significant reduction in crisp consumption, polyunsaturated and soft margarine. The increase in monounsaturated margarine was statistically significant. Thirty-eight (46%) of study participants reported they had achieved all three dietary goals, compared with groups achieving only two or one goal. The group achieving all three goals reduced total fat intake from 36.3% to 34.2% (% total energy). This reduction of 2.1% was greater than the other groups who reported achieving fewer goals and the difference between the groups was statistically significant.
Conclusion: The 'SMART' approach to self-selected dietary goals appears to have been an effective tool in this dietary intervention designed to lower total fat intake. Identifying goals provided a focused approach to changing individual foods with an opportunity to measure the changes objectively over time.

PP 040
Metabolic control in summer camps for children with T1D in Slovenia

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Introduction: Summer camps are an important educational program for children with T1D. The first Slovenian summer camp was held in 1967. Every year since, 120 children from throughout Slovenia attended the camp for 14 days. We compared HbA1c in two summer camps in years 1998 and 2003.
Methodology: 118 children aged 7–16 years (mean 12.3), representing almost 50% of all children with T1D in this age group in Slovenia, attended each summer camp. HbA1c was analyzed with the DCA2000$^+$ analyzer.
Results: The HbA1c values are summarized in the table. The drop in HbA1c was statistically significant ($p < 0.01$). In the year 2003, 62 children (52%) were using CSII. The HbA1c from children who attended the camp did not differ from the HbA1c of their peers who did not attend the camp in the same year.
Conclusion: The significant drop in HbA1c in the last five years in a representative group of school children with T1D was mainly due to improved educational program (strict carbo counting and strict use of correction boluses), and introduction of CSII as a routine treatment modality.

Table: HbA1c values in children with T1D attending the summer camps in 1998 and 2003

Patients (n = 118)	HbA1c (%) in 1998 Normal < 6.2	HbA1c (%) in 2003 Normal < 6.2
All	8.16 ± 1.53	7.27 ± 0.79
MDI	8.16 ± 1.53	7.33 ± 0.87 (n = 56)
CSII	None	7.23 ± 0.74 (n = 62; 52%)
Attending both camps (n = 35)	8.49 ± 1.17	7.23 ± 0.62
Not attending the summer camp (n = 50)	8.18 ± 1.77	N.D.

PP 041
Health-related and diabetes-related quality of life (QOL) in children and adolescents with type 1 and type 2 diabetes

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Background and Aim: The main aims of diabetic care in children and adolescents are to achieve optimal glycemic control and normal psycho-social development. It is global problems in increase incidence of juvenile onset of type 2 diabetes. It is quite appropriate to evaluate QOL of type 1 and type 2 diabetic children as well family burden related to diabetes.
Subjects and Methods: 645 diabetics aged 9 to 22 and their parents were enrolled in this study. The proportion of type 1 and type diabetics were 484 and 132, mean ages were 15.3 ± 3.4 and 15.5 ± 2.9 years and mean duration of diabetes were 7.8 ± 4.7 and 3.5 ± 2.7 years respectively. QOL questionnaire for children and parent were distributed and recovered.
Results: Mean HbAic levels in type 1 diabetes was 8.0 ± 2.2% which was significantly higher than that of type 2 diabetes (7.2 ± 4.8%). Health-related QOL score in younger age group (less than 15 years) and elderly age group (more than 16 years) of type 1 and type 2 diabetes were 134.5 ± 196: 126.7 ± 18.5, 134.6 ± 21.3: 128.1 ± 18.7 respectively and type 1 diabetic children were significantly higher than that of type 2 diabetes in both age groups ($p < 0.05$). Diabetes-related QOL score was not significantly different between two groups except Satisfaction with life score is slightly higher in type 2 diabetes ($p = 0.047$). Parent diabetes QOL score was not significantly different between two groups ($p = 0.528$). However, Family burden related diabetes, particularly family burden related Diabetes care was significantly higher in type 1 than type 2 diabetes (12.4 ± 7.0: 7.7 ± 4.1 ($t = 6.74$, $p < 0.001$)).

Conclusion: This is a first nation-wide survey of QOL in diabetic children and their parents. Health-related QOL was higher in type 1 diabetics than healthy school children proved that diabetic children were supported from school, society and family, however lower in type 2 diabetics suggested the existence of psychosocial background for development of the disease.

PP 042

Childhood diabetes in finland: evaluation of the quality of treatment

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Introduction: As a part of the national Finnish Diabetes Prevention and Treatment Development Program, quality criteria for treatment of childhood diabetes were determined. They were chosen to describe the outcome as well as the process and organization of treatment. To clarify the Finnish health care organizations capability to collect data for quality analysis, a structured questionnaire study was performed.
Methodology: In February 2004, a postal questionnaire consisting of 38 aspects was posted to all health care organizations in the field of paediatric diabetes treatment in Finland (N = 33). The organizations were asked to reply even if the data were not available.
Results: Altogether 24 organizations returned the questionnaire. All but one of them could report the total number of their patients (3373). 22 were able to report the number in different age groups (age 0–4 years: 5.9%, age 5–9 years: 27.4%, age 10–14 years: 43.3%, age 15–19 years: 23.4%). A small minority of the patients (22 patients) were diagnosed with other than Type I diabetes. The HbA1c data were available from 18 organizations. The proportion of patients with HbA1c less than 8.0% in different age groups were 0–4 years: 39.9%, 5–9 years: 33.1%, 10–14 years: 23.0%, 15–19 years: 16.8%. Fifteen organizations did report the data regarding insulin infusion regimens. In many questions, like data concerning serious hypoglycaemic events or ketoacidosis the organizations capability to report their data was poor. Most data was received from organizations that kept a separate register over the data. Almost equal amount of data was received from units that have an electronic patient journal.
Conclusion: This study demonstrates the fact that the vast majority on children with diabetes are not in good metabolic control. Unfortunately, as shown in this study, methods for measuring and developing the quality of treatment both at the organizational and at the national level are less than optimal. To improve that, implementation of the electronic patient registers should be encouraged, with the demand that the data collected in each organization should be nationally comparable.

PP 043

Insulin resistance in adolescents with T1DM

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Background: Insulin resistance contributes to the deterioration in glycaemic control that occurs during adolescence in T1DM.
Aim: 1) to describe the clinical features of adolescents with poorly controlled diabetes. 2) to describe the factors associated with insulin resistance in this population. *Methodology*: We describe the factors affecting glycaemic control among 275 patients with T1DM aged 10–18 years attending the diabetes clinic at Sydney Children's Hospital. Data were obtained from our clinic database and from the baseline characteristics of a group (n = 30) participating in an ongoing clinical trial. The subjects in the clinical trial were selected based on insulin dose (>1.1 units/kg/day). Of these, 7 had insulin stimulated glucose uptake measured by a euglycaemic hyperinsulinaemic clamp.
Results: Of the 275 subjects identified from the clinic database, 59% had a HbA1c above 8%. Those with a higher HbA1c were on higher doses of insulin per kg ($r = 0.36$, $p < 0.001$). Insulin dose increased with age and duration of diabetes. Among the 30 patients participating in the clinical trial, the prevalence of overweight (17%) and obese (7%) was similar to that of non-diabetic adolescents in Australia. The median insulin stimulated glucose uptake was 247 mg/m^2/minute (range 22–324). Neither BMI, pubertal stage, HbA1c, insulin dose per kg, insulin dose per carbohydrate exchange nor night-time insulin dose were significantly associated with insulin stimulated glucose uptake.
Conclusion: The use of insulin dose per kg may not reliably predict the severity of insulin resistance in adolescents with T1DM.

PP 044

Selected environmental risk factors probably related to type 1 diabetes in Varmia&Mazury Region (V&M), Poland

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Background: The increasing incidence rate (IR) of Type 1 diabetes (T1DM) in Central and East Europe is partly explained by influence of environmental factors.
Aim: To analyse selected environmental risk factors related to T1DM in V&M.
Methods: We collected the new cases of T1DM between 1994–2004 using methods EURODIAB ACE. IR/100 000/year according to sex group, place of living (urban vs. rural area) and birth before and after Chernobyl accident were calculated. Additionally we assessed the influence of birth weight, educational level of mothers, breast feeding, exposure to cow milk protein, season of onset of T1DM, frequency of viral infections, vaccinations against viral diseases, the mean level of cadmium content in deer's organs, biochemistry and pH of drinking water on IRT1DM.
Results: 331 patients in age 0–40 year 157 female, and 174 men T1DM had 37,1% mothers with elementary education, 23.5% had birth weight less than 3000 g, 51.86% were fed with breast more than 3 months, 53.36% were exposed to cows milk protein. Significantly higher IRT1DM was observed among persons born after Chernobyl accident from 5.1 (95% CI: 5.5–5.8) to 21.6 (95% CI: 21.3–21.9) with significant trend in IRT1DM. Statistically significantly higher IRT1DM was observed in urban area: 10.1 (95% CI: 8.7–11.4) than rural area: 8.0 (95%: 6.6–9.3)/100 000 persons. Higher numbers of new cases T1DM were observed in autumn and winter. We also observed increase of IR depending on mumps epidemic in 1995, 1998, 2001 year with peak IR 11.7, 10.6, 10.1/100 000 respectively. The highest mean cadmium concentration (3.351 mg/kg body weight) was found in kidneys of deer in the investigated area comparing to Poland. No correlation of T1DM with sex, pollution after Chernobyl accident, vaccinations and biochemistry and pH of drinking water was observed.
Conclusions: The following environmental risk factors probably related in etiology T1DM in V&M Region: nutrition (milk cow exposition), viral infection (mumps), seasonal factors, westernization effect and environmental pollution (cadmium).

PP 045

Recovery from permanent neonatal diabetes

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Introduction: We recently described that 2/3 cases with permanent neonatal diabetes are caused by 6 novel mutations in the ATP-sensitive KIR6.2 gene (NEJM 2004,350,1838–49). Kir6.2 is associated with the sulfonurea receptor (SUR) and we supposed mild mutations may be

amenable to SUR therapy. A 2 year old patient indeed came off insulin at 2 × 2.5 mgr/day glibencamide for 3 months now, hba1c 6.5% with virtual normoglycemia. We will show that avoidance of hypoglycemia is dependent of the SUR dose. KIR6.2 is also expressed in the CNS and in skeletal muscle. On insulin therapy (0.6 EH/Kg BW) for 2 years, he had a motordelay of 14 months and a developmental delay of 8 months. Since SUR treatment his milestones improved, however not fully (yet). This is the second patient coming off insulin. These patients are important models for SUR-agonists.

PP 046

Communication improves non-attendance in a young adult clinic

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Introduction: Non-attendance at clinic visits and poor diabetes control is common in young adults. Many just forget to come to the clinic. The proliferation of mobile phones and the use of text messaging allows ready communication with these young people wherever they are.
Methods: A commercially available computer and mobile phone based texting program has been utilised to automatically contact the 115 young people aged 17–25 yr attending the Young Adult Diabetes Clinic in Southampton, 14 days before and again 1 day prior to their hospital clinic appointment. In addition they have been reminded to post in a blood sample for HbA1c determination prior to the clinic visit.
Results: At present we have 60% of the young people's mobile phone numbers. Following the introduction of texting in 2004, non-attendance has fallen from a peak of 44% to 2%, only one person having not attended, compared with 14% of those not texted. In addition since texting the percentage sending in an HbA1c sample has risen from 40 to 75%.
Conclusions: Personal contact with young people by text messaging increases clinic attendance, allows a change of appointment where appropriate and also prompts them to send a blood sample for HbA1c which would then be available at their visit.

PP 047

Improving diabetes control in young people: nothing venture nothing gain

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There has been an acceptance that diabetes control in young people (YP) deteriorates during adolescence although control differs between Specialist Centres. Two studies, the DCCT and that from Copenhagen, have shown significant improved and sustained control at this age following a change in practice. This approach has been used in Southampton in the age group 14–17 yrs.
Methods: Following an audit of care for all those young people aged 14–17 yrs, a multidisciplinary change in provision of diabetes care was agreed, concentrating on outpatient management, education, increased clinic, home and school visits, 24 hr emergency telephone contact and frequent telephone review of control and insulin dosage. In addition a multiple insulin regime, including Glargine, was used and the avoidance of fat pads was targeted.
Results: From 2000 to 2003 mean HbA1c values in the 76 young people fell from 9.6% to 8.8% then 8.5%. The same trend as for those aged 0–13 yr. Clinic, home visits and out of hours telephone calls all increased. Many who used MII and improved their control, continued with frequent Blood Glucose monitoring and expressed a feeling of improved well being. Those YP most difficult to improve frequently had major family problems.
Conclusion: Deterioration of diabetes control at adolescence is not inevitable and a targeted and personalised approach can match the progress of the DCCT. Personalised care and MII, using Glargine, offers greater empowerment with more frequent monitoring. Fat pads and leaking insulin pens are a major source of problems to be targeted. The change has involved a cost of 2 extra clinics per month and a change of work emphasis away from ward to clinic and community care. The pattern of delivery of care may largely explain the published differences between Specialist Centres.

PP 048

'Diaborexia' not anorexia: eating disorders in adolescents with type 1 diabetes are related to emotional problems and not primarily to weight and shape concerns

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Introduction: Subclinical eating disorders are increasingly recognised in adolescents with type 1 diabetes. It is unclear whether this reflects weight and shape concerns, or relates to adjustment to diabetes. Examination of subscale scores in eating disorders measures may allow us to identify differences in the pattern of distress in diabetes compared with primary eating disorders.
Methodology: We collected questionnaire data from 63 adolescents with type 1 diabetes (duration ≥12 months) aged 10–17 years (mean 13.0; 58% female). Mean duration of diabetes 5.9 years; HbA1c range 9–15%. Eating disorder symptomatology was assessed by completion of the Eating Disorder Inventory-2 (EDI2). Raw scores were calculated for subscales: (1) Drive for Thinness, (2) Bulimia, (3) Bodily Dissatisfaction, (4) Ineffectiveness, (5) Perfectionism, (6) Interpersonal Distrust, (7) Interoceptive Awareness, (8) Maturity Fears, (9) Asceticism, (10) Impulse Regulation and (11) Social Insecurity. Raw scores were compared with normative profiles. Psychological distress was assessing using the Strengths and Difficulties Questionnaire (SDQ).
Results: 10% of subjects had profiles consistent with a clinical eating disorder. However, the profile of subscale scores was similar to the general population for all subscales except Interpersonal Distrust (20% had scores within the eating disorder range), Maturity Fears (50% within eating disorder range) and Impulse Regulation (25% in eating disorder range). Weight, shape and food related subscale scores were similar to normative profiles. Psychological distress was positively associated with Bodily Dissatisfaction, Ineffectiveness, Interoceptive Awareness, Interpersonal Distrust, Maturity Fears and Social Insecurity.
Conclusion: While 10% of adolescents with T1D had EDI2 scores suggestive of eating disorder, profiles suggested problems were related to fears of maturity, difficulty trusting others and issues with impulse control rather than with weight, shape and food per se. This suggests that subclinical eating disorders in diabetes ('diaborexia') may relate to emotional distress rather than weight and shape concerns.

PP 049

A multi centre randomised controlled trial (RCT) delivering motivational interviewing (MI) with adolescents with insulin dependent diabetes mellitus (IDDM)

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Introduction: Teenagers with IDDM experience problems with self care and there are few effective behavioural interventions. Motivational Interviewing (MI) is a counselling approach which promotes behaviour

change in adult patients seen in healthcare settings. A pilot study with teenagers with diabetes indicated that MI may lead to improvements in HbA1C and patients perception of diabetes.
Method: We aimed to recruit 80 participants from five diabetes clinics within South Wales, to examine the impact of a year long intervention versus individualised counselling support in adolescents with IDDM. Measures of mean glycosylated haemoglobin (HbA1c) and a range of psychosocial variables were taken at baseline and at 6 and 12 months during the intervention. In order to compare the two groups, a repeated measures analysis of covariance was performed with HbA1c measurements at 6 and 12 months with the baseline measurement treated as covariate.
Results: Eighty subject were randomised into the study (43 MI group, 37 control). However, 7% (n = 3) of the MI group and 24% (n = 9) of control subjects declined to enter into the study. Sixty eight subjects were therefore recruited (n = 40 MI group, and n = 28 controls) with a mean age of 15.3 and a gender ratio of 33 : 35 (M : F). There were no differences between the two groups demographics at baseline, although the MI group did have a greater dropout rate than the control group (10 vs. 3 – not significant). The MI group showed better control and reduced their HbA1c over the study period but this was not significantly different (p = 0.072). Psychosocial outcome measures and 24 months follow up data will also be analysed, and the findings and implications of this data will be available to present a later date.
Conclusion: Although the study produced an overall negative effect finding, there is some support for the clinical usefulness of MI in teenagers with IDDM.

PP 050

Enabling young people to participate in their own diabetes care through the internet: *Betterdiabetes.Com*

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Introduction: Adolescents with diabetes have traditionally been a challenging group of patients to care for – frequently resisting attempts to engage them in their own health care. Part of the challenge in this area relates to finding an acceptable mode of communication between adolescents and their diabetes care teams. These difficulties are accentuated when adolescents live in remote communities, such as those in regional Australia. High use and acceptance of the internet by adolescents has been well-documented. The stereotypic nature of diabetes care (3 monthly visits with HbA1C, blood glucose monitoring, repertoire of insulin regimes, etc) means that much of diabetes care data is amenable to presentation in an internet-based forum.
Methodology: Betterdiabetes.com is an internet-based, interactive model of health care between patient and health care provider. The strategy employed allows patients to have their own Personalised Patient Record (PPR) which is updated by data downloads from clinic visits. The PPR allows patients to view their longitudinal HbA1C, height, weight and BMI data. In addition to regular clinic visits, patients are able to download blood glucose meter results to their PPR and send these via the internet to their diabetes health care team for comment and management suggestions. Health care team members have access to most recent clinic details and are able to formulate responses with all the relevant information to hand. Responses are returned via the internet and archived for medicolegal purposes.
Results: We have been utilizing Better.diabetes.com for 1 year in a tertiary hospital clinic of 1200 patients. Of those patients estimated to have internet access at home the uptake/usage rate is 65%.
Conclusion: Betterdiabetes.com is a strategy that relies upon the convergence of internet-friendly features of diabetes care characteristics and adolescent mores and to engage diabetic adolescents in their own health care.

PP 051

Establishment of an ambulatory stabilisation program for children and adolescents with newly diagnosed type 1 diabetes mellitus: the first year's experience

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Introduction: Ambulatory stabilisation of children and adolescents with newly diagnosed type 1 diabetes mellitus (T1DM) may lead to lower hospital bed occupancy, less disruption to family life and a decreased risk of hospital acquired infections such as gastroenteritis. In 2003 Monash Medical Centre (MMC) was the first centre in Victoria, Australia, to establish an ambulatory stabilisation program.
Methodology: Staff recruitment commenced in October 2002 with the first admissions to the program in late April 2003. Requirement for admission, admission duration, readmissions for gastroenteritis were recorded prospectively. A satisfaction survey was conducted to determine family's confidence and coping in the initial stages after diagnosis.
Results: In the twelve months prior to full clinical service commencement, 52 newly diagnosed patients were managed at MMC (100% admitted; mean length of stay 5.0 days). In the twelve months since full clinical services of the ambulatory stabilisation program began 56 newly diagnosed patients have been managed at MMC (61% admitted; mean length of stay 3.1 days) of whom 22 (39%) have undergone ambulatory stabilisation, rather than having an inpatient admission resulting in a total reduction of overall mean length of stay to 1.9 days. Episodes of gastroenteritis requiring readmission have also fallen in the same time period. Over the first 6 months of the program, the satisfaction survey showed that families were very confident with diabetes management following the ambulatory stabilisation process with greater than 85% of respondents feeling moderately to very confident in managing hypoglycaemia, insulin administration, diet and self monitoring.
Conclusion: Ambulatory stabilisation of children and adolescents with T1DM is achievable in the paediatric setting, with good acceptance by patients and their families and is accompanied by reduced length of stay and reduced readmission rate.

PP 052

Glycaemic range, variation and metabolic control in pre-pubertal children with type 1 diabetes

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Introduction: Little is known about the true frequency of marked glycaemic fluctuations and the degree of glycaemic variation in pre-pubertal children with type 1 diabetes. The aim of this study was to describe the metabolic control and glycaemic variation of a cohort of pre-pubertal children with established type 1 diabetes using continuous glucose monitoring.
Methods: Children aged 5–10 years with diabetes for greater than 2 years were recruited from the Royal Children's Hospital, Melbourne, and wore the continuous glucose monitor (CGMS) over a 72–96 hour period. Clinical information collected on each child included auxology, HbA1c, duration of diabetes and insulin dosage. Each CGMS trace was qualitatively and quantitatively analysed using mean glucose values, percent time in glycaemic ranges, mean of daily differences (MODD) and continuous overlapping net glycaemic action (CONGA).
Results: Fifty-two children (21 male, 31 female) participated with a mean CGMS glucose level of 10.9 mmol/l (Range 6.9–17.7 mmol/l) per

trace. Mean percentage time spent within respective glucose categories was 3.1% (<2.6 mmol/l), 5.4% (<4.0 mmol/l), 51.3% (4.0–12.0 mmol/l) and 40.2% (>12 mmol/l) with low glucose readings occurring mostly between 24:00–08:00 hrs ($p = 0.001$). The group mean MODD value was 1.8 and mean CONGA was 3.2. Mean CGMS glucose values were positively associated with HbA1C ($p = 0.002$). Relative total daily insulin dose was positively associated with CONGA ($p = 0.04$). Patients with the least amount of low glucose readings had a lower mean CONGA value ($p = 0.03$).

Conclusions: Mean CGMS readings correlated well with HbA1C within this cohort. Nocturnal low glucose values are relatively common and associated with patterns of less stable glycaemic control. Intra-day variation in glucose levels (CONGA) are positively associated with relative insulin dosage and inversely associated with time spent in the low glucose range. CGMS data provides novel measures of glycaemic control in pre-pubertal diabetic children.

PP 053

Health related quality of life is independent of glycaemic variation in a prepubertal cohort of children with type 1 diabetes mellitus

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Introduction: Type 1 diabetes has been found to have a significant negative impact upon health related quality of life (HRQOL). The purpose of the study was to ascertain whether HRQOL was associated with measures of metabolic control such as glycaemic variation and episodes of hypoglycaemia derived from continuous glucose monitoring.

Methods: Forty-one children with type 1 diabetes from the Royal Children's Hospital, Melbourne wore the continuous glucose monitor over a 72–96 hour period. Data cleaning and analysis was carried out using Stata. Glycaemic outcomes included mean blood glucose (MBG), mean of daily differences (MODD), percentage time hypoglycaemic (CGMS <4.0 mmol/L), normoglycaemic (4.0–12.0 mmol/L) and hyperglycaemic (>12.0 mmol/L) and continuous overall net glycaemic action (CONGA). Each parent completed the child health questionnaire (CHQ-PF50). Summary scales of physical and psychosocial health were calibrated using normal Australian population data. Pearson's calculation assessed correlations between glycaemic and health outcomes.

Results: The continuous glucose monitor was worn for a median of 69.6 hours (range 38.1–96.8 hours). Mean blood glucose was 10.7 mmol/L (range 7.5–15.1 mmol/L). Mean of daily differences was –0.35 (range –4.7 to +3.8). Percentage time spent in the low, normal and high glycaemic ranges was 7.6%, 53.1% and 39.3% respectively. The mean of the continuous overall net glycaemic action (CONGA) for the cohort was 2.94 (range 1.86–4.22).

Mean physical scale score for the cohort was 44.5 (range 8.1–55.6). Mean psychosocial scale was 39.6 (range 27.9–53.9). No correlation was found between the outcomes of the CHQ and CGMS measures.

Conclusions: Parents' negative perceptions of their diabetic children's HRQOL do not appear to be related to measured short-term markers of glycaemic control and may be biased by their own underlying fears of either short or long-term outcomes.

PP 054

Do children with type 1 diabetes miss more school than their sibs or nondiabetic peers?

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Objectives: i) to determine whether children with type 1 diabetes (DM) miss more school than their non-DM siblings and peers; and ii) to identify factors associated with school absenteeism.

Study Design: School absenteeism for the 2001–2002 academic year was obtained for 78 DM, 38 sibs and 118269 age-matched peers in Toronto, Canada. Questionnaires and hospital records were reviewed to evaluate child-, family- and diabetes-related factors associated with school absenteeism in the DM group.

Results: DM children missed slightly, but significantly more school than both their nonDM sibs ($p < 0.001$) and peers ($p < 0.0005$). Multiple regression analysis revealed that school absenteeism in DM group was associated with parental attitudes to school attendance ($p < 0.002$); poorer metabolic control (<0.006); shorter duration of DM (<0.006), and lack of aggressive behaviour ($p < 0.02$).

Conclusion: With currently available management strategies, children with DM should be expected to have near normal school attendance and this goal should be strongly encouraged by parents and health professionals. Poor metabolic control and shorter disease duration are diabetes-specific barriers, while parental attitudes to school attendance was the major family-related contributor to school attendance or absenteeism.

PP 055

School visits and management of type 1 diabetes: parent–teacher outcomes

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Each year in New South Wales approximately 280 children (0–15 years) develop type 1 diabetes. Research has shown that parents and their child with diabetes encounter problems with management at school. Schools have a duty of care to provide a safe environment for all students, including those with diabetes. There is a need for staff to be equipped with sufficient information about diabetes to ensure the safety of those students. An International Diabetes Federation information package is available to schools, however an evaluation has indicated the need for further intervention to meet parental concerns. To address this need, Diabetes Australia-NSW provides a school visit program. To evaluate outcomes of the program, pre and post questionnaires were administered to parents and teachers to determine perceptions and subjective evaluation of diabetes management at school. The questionnaire was administered to thirty-six schools and parents from March 2003 to May 2004. Twenty-three teachers and sixteen parents completed the questionnaire. Prior to the school visit, sixty-five percent (65%) of schools indicated that there were issues regarding management with hypoglycaemia (87%), staff awareness (73%), testing (60%) and food (60%) being the highest rated concerns. Eighty-one percent (81%) of parents identified issues regarding diabetes management at school, including staff awareness (85%), hypoglycaemia (69%) and physical activity (46%). Following the school visit, teachers reported a significant increase in the schools confidence in managing diabetes ($p < 0.001$), attitude to the seriousness of diabetes ($p < 0.001$), understanding of management ($p < 0.001$) and physical activity ($p < 0.001$). Parents reported a significant improvement the schools management of their child ($p < 0.001$) and teachers attitude towards diabetes ($p < 0.001$). The results of this evaluation indicate that the school visit program improves the management of the child with diabetes at school.

PP 056

Educating families from ethnic minorities in diabetes

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Introduction: Ethnic minorities may constitute vulnerable groups within Western health services. A previous study found that immigrants' ability to master severe chronic diseases could be affected by

barriers such as different culture and health/illness beliefs, communication problems and limited educational background.
Methodology: An educational programme was performed, including the development of adapted educational material, guidelines for health professionals and subsequent re-education of children, adolescents and parents from 37 immigrant families. Evaluation comprised family questionnaires, comments from other experts and data on diabetes: HbA_{1c}, number of severe hypoglycaemia (unconsciousness and/or convulsions) and ketoacidosis.
Results: The immigrant families still did not seem to fit properly into the adapted educational program. However, the study demonstrated that it was possible to improve health outcome. During the intervention knowledge of diabetes management increased from 9.6 to 11.0 correct answers out of 12, but with considerable differences between the families. HbA_{1c} decreased during the intervention from 9.2 ± 1.4% to 8.6 ± 1.0% ($p = 0.01$), but was gradually increasing during follow-up. There was a non-significant increase in the number of severe hypoglycaemic events, which did not relate to low or decreased HbA_{1c} values.
Conclusions: The study found that education of immigrant families could be improved by the development of adapted educational programs/material and by extended use of professional interpreters. Education should be based on basic knowledge of the immigrants' background and performed in a simple and precise way, including a personal approach to the individual families. New projects including immigrants as active participants in developing appropriate programs and material are encouraged.

PP 057

Social consumption of alcohol in adolescents with type 1 diabetes is associated with increased glycaemic variation but not hypoglycaemia

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Introduction: Adolescents with type 1 diabetes frequently engage in risk-taking behaviours such as heavy use of alcohol in social settings. The aim of this study was to investigate on how alcohol consumption may influence glycaemic variability in a group of ambulant adolescents.
Methods: Fourteen (5 male) patients who were over 16 years of age and who were known to regularly drink alcohol were recruited from the diabetes clinic at the Royal Children's Hospital. Continuous glucose monitoring system (CGMS) was attached on a weekend when alcohol consumption was planned for one night only. The twelve-hour period from 1800 hours to 0600 hours for the night with alcohol consumption ('study time') was compared for each patient with the same period with non-alcohol consumption ('control time') 24 hours either before or after the alcohol study night. Each subject was used as its own control. Glycaemic outcomes calculated from continuous glucose monitoring included mean blood glucose (MBG), mean of daily differences (MODD), percentage time spent in hypoglycaemia (CGMS <4.0 mmol/L), normoglycaemic (CGMS 4.0–12.0 mmol/L) and hyperglycaemia (>12.0 mmol/L) and CONGA (continuous overall net glycaemic action). We adopted standard quality criteria for the CGMS traces: traces are valid only if reporting a validating metre reading eight hourly.
Results: Mean number of alcoholic drinks (mixed spirits, beer and wine) consumed on the study night was 9.0 for males and 6.3 for females. There was no difference in percentage of time in hyper and normoglycemia in both the study time and control time. During control time there was a higher percentage of time with low glucose levels hypoglycaemia compared with the study time ($p < 0.05$). There was an increased level of glycaemic variation during the study time when compared with the control time ($p = 0.006$).
Conclusions: In an uncontrolled, social context, moderately heavy alcohol consumption appears to be associated with increased glycaemic variation but not with a hypoglycaemia.

PP 058

Reliability of determination of HbA1c in blood on filter paper

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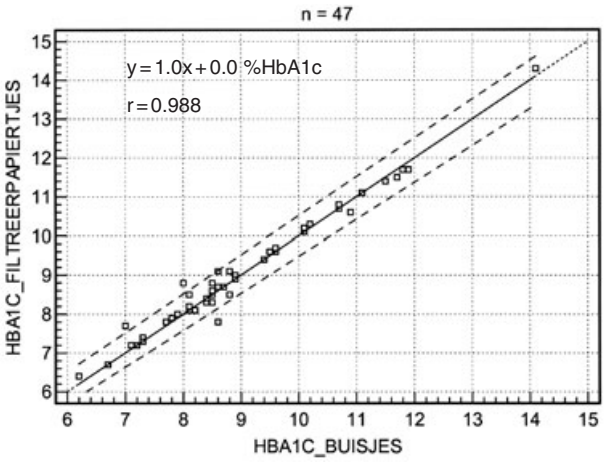
Introduction: HbA1c measurement has been used as a marker for long-term glycemic control in diabetic patients. Blood taken at home by the patient and send on filter paper for HbA1c determination is a simple and patient-friendly method. A study was performed to test the reliability of this method.
Methodology: We included 48 children in the study. Simultaneously 0.5 cc blood was collected in an EDTA-tube and some blood was applied on a filter paper. Blood on the filter paper was taken home by the patients and send to the laboratory of our hospital. Analysis was performed on the filter paper on the day of arrival. Haemoglobin was eluted from the filter paper by placing it in a polystyrene tube and adding 1 cc solution containing distillate water/EDTA/Triton-X 0.1%, sodium-azide 0.1%. After vortex mixing for 1 hour the diluted haemolysate is used. Analysis were performed in the diluted haemolysate and EDTA-tube by a high-performance liquid chromatography system (automated Glycohemoglobin analyser type A1c2.2). The results of both methods were compared.
Results: 48 of the 49 samples on filter paper arrived at the laboratory. Hb-chromatography of 1 sample could not be interpreted. Filter papers were analysed 1 day (34%), 2 days (38%), 3 days (19%), 5 days (2%), 6 days (4%) and 7 days (2%) after collecting blood. There is a close correlation between HbA1c values obtained from blood in a EDTA-tube and from blood on a filter paper (see figure).
%HbA1c-filter paper = 1.0 × %HbA1c − EDTA-tube + 0.0% HbA1c ($r = 0.988$, $n = 47$)
Conclusion: 1. determination of HbA1c in blood on filter paper is a reliable method 2. collecting blood on filter paper is a simple and patient-friendly method that can be done easily at home without visiting the laboratory.



PP 059

Improvememt of Hba1c Standardization in Collaboration Study Japan: The Provision for Intrenationally Unified Number of Hba1c

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Introduction: To standardize HbA1c data in the DCCT, the primary lab was set by an assay ystem with using Bio-Rex70 HPLC, now the number succeeded by NGSP. In the Japan Diabetes Society, JDS, the HbA1c number has been set by Reference Calibrators, Lot1s succeeded by Lot2s. The IFCC has offered a standardizing system of HbA1c measurement based on peptide mapping. We aim to unify the HbA1c number of data from each institute by our sub-calibrators according to Lot1s/ Lot2s and accumulate our data valid for tracing to each IFCC, JDS or NGSP number, including data in IDF/WPR projects.
Methodology: In our group data of certain specimens from each institute were corrected to our unified HbA1c data by our sub-calibrators in central lab, SRL. Absolute relative differences, ARD, were calculated between the unified data and those in each institute. Since Lot2s have additional numbers tentatively approved by IFCC and NGSP, we examined whether patients' data by the NGSP certified Bio-Rad system in IDF/WPR projects become compatible with those by SRL, each corrected with Lot2s.
Results: With marked improvement in nation-wide coefficient variation of test samples these 10 years, our mean ARD has become ≤ 3%. As reported by the JDS committee, patients' data by SRL showed nearly 0.3% less than NGSP number by Bio-Rad in IDF/WPR projects. The data by Bio-Rad became almost equivalent to the concordant SRL number by each correction with Lot2s, except in the low reference ranges.
Conclusion: Master equations between each standardizing system are ready to start based on peptide mapping. However, we need full knowledge regarding the globally unified number and its name of what we measure as a definite "HbA1c", since a premature change in number will induce confusions as seen in the past in Sweden. Meanwhile we recommend the use of common calibrators such as Lot2s to trace the results to each number.

PP 060

The utility of point-of-care HbA_{1c} and glucose measurements for diagnosing and monitoring diabetes in a remote indigenous Australian community

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Introduction: Diabetes is a significant health problem for contemporary Aboriginal society, particularly in rural and remote Australia where pathology testing services required for diagnosing and monitoring diabetes may be limited. On-site point-of-care (POC) pathology testing offers a potential solution to this difficulty.
Methodology: As part of a community based project, 152 residents (11–76 yr) of a remote Australian Aboriginal Community were screened. Assessment included medical history, physical examination, and fasting POC capillary glucose (Glucose201, Hemocue, Medipac Scientific). Capillary POC HbA_{1c} (DCA 2000+, Bayer, Australia) and venous blood were collected if capillary glucose ≥ 5.0 mmol/l (n = 88). Diabetes prevalence was determined using WHO criteria.
Results: Despite repeated requests for overnight fasting, 56% admitted to have ingested calories on the screening morning. The correlation coefficient r between the POC and laboratory results was 0.98 for glucose and 0.99 for HbA1c. The bias (mean difference) between the POC and laboratory methods was 0.36 mmol/L for glucose (P = 0.007), and 0.002 for HbA1c (P = 0.95, ns). Diabetes prevalence was found to be 33% in adults (36 of 112) and 0% in children. Sensitivity and specificity for diabetes were 77% and 100% using a 7% POC HbA_{1c} cut-off, 71% and 94% using a 7 mmol/l plasma glucose cut-off (ADA criterion), and 97% and 76% using a 6.1% POC HbA_{1c} cut-off.
Conclusion: POC capillary HbA1c, in particular, appears to offer an accurate, reliable, robust, cost-effective, and community-friendly way of diagnosing and monitoring diabetes in remote clinical settings, where people often present unfasted.

PP 061

Hyperglycaemia in type 1 diabetes: the patient's perspective

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Introduction: Although parents and patients often report adverse effects of acute hyperglycaemia on mood or on intellectual and fine-motor performance, this remains to be established.
Methods: Parents and children with Type 1 diabetes (n = 400) were asked via questionnaire about their perception on the effects of hyperglycaemia. Subjects were also asked about their sporting and musical activities and whether they considered hyperglycaemia affected their performance in these activities.
Results: Answers were received for 368 children (92%); mean age was 12.5 years (range 3.7 to 19.8 years). Blood glucose levels between 15–18 mmol/l, were reported by 68% to affect thinking performance, by 75% to affect mood and emotions and by 57% to affect coordination. The symptoms most commonly associated with hyperglycaemia were (in decreasing order): Irritable (64%), short-tempered (60%), moody (56%) Unreasonable (43%), aggressive (37%), hyperactive (31%), sad/depressed (27%) confused (23%), clumsy (18%). Homework was thought to be affected by hyperglycaemia in 34%, sport in 22%, musical instrument playing in 25%. There was no significant relationship between the HbA1c of the subjects and their answers. Those in whom behaviour or the way they were feeling prompted BGL measurement every day had a significantly higher HbA1c level (9.0%, SD 0.2%) than those who only measured BGL, based on behaviour or feeling, twice or less per week (8.3%, SD 0.2%) ($p < 0.01$).
Conclusions: The effects of hyperglycaemia on immediate performance is of concern to children and parents. Hyperglycaemia (15–18 mmol/l) appears to influence emotion and behaviour more than intellectual and fine-motor performance. Despite this, the few studies on this topic have concentrated intellectual aspects, with discrepant results.

PP 062

Continuous overall net glycaemic action – a novel measurement of glycaemic variation in continuous glucose monitoring

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Introduction: Various methodologies have been proposed for analysis of continuous glucose measurements. These methods have mainly focussed on the proportion of low or high glucose readings in a controlled post-prandial environment and have not attempted to analyse other dimensions of the data obtained or reflect every-day, ambulant diabetes control. The purpose of this study was to review of the available methodologies and develop a new measure for glycaemic variation.
Methods: Ten children with type 1 diabetes from the Royal Children's Hospital, Melbourne and 5 healthy adult volunteer controls were

studied. Mean blood glucose and mean of daily differences (MODD) were used to assess the degree to which the CGMS trace was representative of 3 month glycaemic pattern. Percentage times in low, normal and high glucose ranges were used to assess the risk of marked glycaemic excursion. Continuous overall net glycaemic action (CONGA), a novel method developed by the authors, was used to assess intra-day glycaemic variability.

Results: The healthy controls had lower values for mean blood glucose, MODD, CONGA. Diabetic patients had higher percentages of time spent in high and low glucose ranges. All patients with diabetes had CONGA values greater than or equal to 1.7, whereas all the healthy controls had CONGA values equal to or below 1.2.

Conclusions: We advocate an approach to the analysis of CGMS data that is based upon a hierarchy of relevant clinical questions alluding to the representative nature of the data, the risk of glycaemic excursions and the degree of glycaemic variation. Integrated use of these algorithms distinguishes between various patterns of diabetic and non-diabetic glycaemic control.

PP 063

Evaluating a diabetes prediction tool with continuous glucose monitoring

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Introduction: Diabetes self-management involves a difficult balancing act between insulin, food and exercise, largely relying on 'trial and error'. The challenge is to develop innovative, validated prediction tools to empower patients to make appropriate adjustments to optimise glycaemic control. 'Librae' is a computerised diabetes simulator tool in diary format and has been developed as a predictive tool for patients, reducing the 'trial and error' approach by allowing them to simulate and experiment with dietary or insulin adjustments on a 'body-double'. We have evaluated the predictive ability of 'Librae' using a Medtronic™ Continuous Blood Glucose Monitoring System (CGMS).

Methodology: Patients with Type 1 Diabetes were invited to use 'Librae' for one week and were then fitted with a CGMS for 72 hours. The predictive ability of 'Librae' was then compared with concurrent data obtained from the CGMS over the 72-hour period. 11 patients piloted 'Librae', mean age 14.8 years (range 7.48–21.1) with average duration of diagnosis 3.3 years (range 0.1–7.7) on a variety of insulin regimens (2 twice-daily pre-mixed insulin, 5 basal-bolus and 4 pump therapy) with a mean HbA1c of 8.3% (range 6.4–11.8).

Results: 7960 paired glucose readings were obtained from the 11 patients. 'Librae' exhibited a slight underestimation of the measured CGMS values, the error having a positive mean of 0.35 mmol/l (95% CI 0.22–0.48 mmol/l). However, a scatter graph of error against CGMS reveals that 'Librae' tends to under-estimate at high measured glucose values and over-estimate at low measured glucose values.

Conclusion: The 'Librae' data correlated well with the CGMS data overall. This validation study provides a large data set to further improve the mathematical model. 'Librae' may provide a tool to empower patients to make appropriate adjustments to their diabetes routine and optimise their glycaemic control.

PP 064

Evaluation of growth in a series of children and adolescence with type 1 diabetes mellitus

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Introduction: Through most important criteria for evaluating the status of health in children, is growth pattern. Diabetes is commonest Endocrine and metabolism disorder of children and adolescence with important complications. Our goal is to investigate the growth status of diabetic children and adolescence.

Methodology: Growth data collected in a longitudinal/cross sectional way between 2000 and 2002 in 131 diabetic subjects (52 males, 79 females) were available for analysis of height and weight. The individual growth carve of each patient was compared to growth standards. P values <0.05 were considered statistically significant.

Results: The result shows a significant difference between height and weight of two groups (p = 0/05). In addition, there is a significant difference between height and weight velocity in both boys and girls test group and control group (p = 0.05). This study also shows that there is more abnormality in height and weight growth rate in children who had diabetes before 5 years old in compare to those who had after this age (p = 0.05). In children who had complications of diabetes, the abnormalities of growth were more than those without complications. This study also shows that using NPH and regular insulin 2 times a day, would be effective in reducing the abnormalities in compare with those who had used NPH insulin one or two per day.

Conclusion: As diabetes is a chronic disease and also a systemic disorder, it can decrease velocity of height and weight growth rate in children and adolescence so control of children focusing on different criteria of diabetes and its complications, can be preventive.

PP 065

To study the prevalence of autoimmune thyroiditis and thyroid dysfunction in Indian children with type 1 diabetes

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Introduction: Autoimmune thyroiditis and thyroid dysfunction are known to be associated with Type 1 diabetes mellitus (T1DM) in children and adolescents. Higher prevalence has been observed at a later age especially in girls, in most studies. Untreated hypothyroidism affects their growth and has adverse metabolic effects. In view of this we screened Indian children and adolescents with T1DM for evidence of thyroid autoimmunity and/or thyroid dysfunction.

Methodology: 60 children with T1DM were screened for thyroid dysfunction by checking levels of Free T_4 and TSH. Of these 50 children were screened for thyroid autoimmunity by determining the Thyroid Peroxidase (TPO) and Thyroglobulin (TGA) antibodies.

Results: Prevalence of thyroid autoimmunity and hypothyroidism in males(M) and females(F) in different age groups is summarized below:

Age in years	TGA		TPO		Hypothyrouidism	
	M	F	M	F	M	F
0–4.9	1/5 (20%)	1/3 (33.3%)	2/5 (40%)	1/3 (33.3%)	0/7	1/7 (14.%)
5–9.9	0/5	1/12 (8.3%)	1/5 (20%)	3/12 (25%)	0/21	1/21 (4.8%)
10–14.9	2/10 (20%)	2/11 (18.2%)	3/10 (30%)	3/11 (27%)	1/25 (4%)	2/25 (8%)
15–20	0/2	0/2	0/2	0/2	0/7	0/7
0–20	3/22 (13.6%)	4/28 (14.3%)	6/22 (27.2%)	7/28 (25%)	1/60 (1.7%)	4/60 (6.7%)
Total	7/50 (14%)		13/50 (26%)		5/60 (8.3%)	

26% subjects had at least 1 positive antibody; the prevalence of TPO being higher than TGA and there was no significant difference between females and males. The overall prevalence of hypothyroidism was 8.3%, being higher in females. Subjects with hypothyroidism had at least 1 positive antibody. Prevalence of thyroid autoimmunity and hypothyroidism was higher in children less than 5 years compared to other studies.

Conclusions: Thyroid autoimmunity and hypothyroidism may present early in young children with T1DM and males are also at a high risk for developing thyroid autoimmunity. Hence screening for thyroid autoimmunity and hypothyroidism should be started at a young age in both sexes.

PP 066

Development of a protocol for screening children and adolescents with type 1 diabetes for coeliac disease

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Introduction: Increased prevalence of coeliac disease (CD) in patients with Type 1 Diabetes is well established, prevalence varying from 1–10.4%. Children may present with poor growth, poor diabetes control, iron or vitamin deficiency or gastrointestinal symptoms. A literature review noted that some children and adolescents with Type 1 Diabetes have asymptomatic or 'silent' CD and undetected CD may lead to severe complications. It was therefore determined that there was enough evidence to warrant screening for CD in our diabetic clinic population.
Methodology: All patients with newly diagnosed Type 1 Diabetes have IgA anti-endomysial antibodies (EMA) or more recently tissue trans glutaminase (tTg) measured 6–12 months post diagnosis. Those with negative results are re-screened every second year. Patients with positive antibodies attend a clinic appointment to discuss results and implications with the diabetes team (consultant, educator, dietitian and social worker). It is recommended that all patients with strongly positive antibodies undergo a biopsy. If the biopsy is positive for CD then the patient is allocated another appointment for diet therapy, education and social work review.
Results: We currently have 35 patients with CD (3.7% of our population). Of these, 88% are compliant with the gluten free diet (GFD).
Conclusion: The team recognises that the double diagnosis may be overwhelming to some patients and their families. Social work support is considered essential to aid with coping strategies. The team also accepts and respects that some patients and families, will choose reduced gluten intake or a normal diet with a clear understanding of the risks. The team will aim to offer on-going support should they choose to follow a GFD in the future. These patients will be monitored for possible complications of CD. Having now implemented our protocol we propose to assess the psychosocial impact and effect on diabetes control of screening for CD.

PP 067

Neither diabetes antibodies at the onset of diabetes mellitus type 1 nor DQB1 alleles can distinguish a risk group to follow for celiac disease

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Introduction: Between 4–10% of the patients with diabetes mellitus type 1 (IDDM) develop celiac disease (CD). The majority of these children have an undiagnosed CD at the onset of IDDM or develop it within some years. These children have often atypical symptoms, which are recognised by a gluten free diet. Repeated screening for CD is therefore a common procedure in children with IDDM. The aim of this study was to investigate if there are any differences in frequency of autoimmune markers and the HLAB1 02 allele between the groups of children which had CD before IDDM (group A), the children with undiagnosed CD at the onset (group B), the children which developed CD (group C) and the patients which do not developed CD (group D).
Methodology: 303 children with IDDM were screened for antibodies to endomysium autoantibodies (EMA), insulinautoantibodies (IAA), glutamate decarboxylase and islet cell autoantibodies (GAD and IA-2ab) at the onset of diabetes. Yearly screening in five years was performed with EMA in all children to detect CD.
Results: Altogether 19/303 (6%) of the children with IDDM had CD, whereas four were in Group A (1%), seven (2.3%) in group B and eight in Group C (2.7%). HLA DQB1 02 was presented in 100% (4/4), 73% (5/7) and 75% (6/8) in Group A, B and C respectively and in 53% in Group D (p = ns). 57% of the children in Group D had at least three antibodies for diabetes at the onset of IDDM compared to 25% (1/4) in Group A, 73% (5/7) in Group B and 75% (6/8) in Group C (p = ns).

PP 068

To study the prevalence of positive screening for celiac disease in type 1 diabetes

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Introduction: The association of Celiac Disease (CD) and Type 1 diabetes (T1DM) in children has been documented. Reported prevalence of CD in children with T1DM varies from 0.97–16.4%. Antiendomyselial and antitissue transglutaminase (tTG) antibodies have the best sensitivity and specificity for CD screening. Small intestinal biopsy is necessary to confirm the diagnosis of CD. A summary of 26 screening studies on 7272 children with T1DM revealed that 371 (5.1%) children had a positive antibody screen. 295 subjects were biopsied and 250 (3.4%) tested positive. Undiagnosed CD can result in poor growth and diabetes control and may increase the risk of lymphomas. These subjects may be asymptomatic. Hence we studied the prevalence of positive tTG and CD in Indian children with T1DM.
Methodology: 46 children from the age of 0–19 years with T1DM were screened for tTG. Small intestine biopsy was done to confirm the diagnosis of CD.
Results: Time of screening and results are summarised below:

Time of screening (years after diagnosis of diabetes)	Number screened	Positive tTG antibody	Number biopsied	Positive biopsy
0–0.9	20	1 (5%)	0	0
1–4.9	17	6 (35.3%)	4	2
5–9.9	4	1 (25%)	0	0
>10	5	0	0	0
Total	46	8/46 (17.4%)	4/46 (8.7%)	2/46 (4.35%)

17.4% subjects had positive tTG antibodies. 4.35% subjects had confirmed CD. 50% did not undergo biopsy, so their status is unknown. Only 50% subjects with positive antibodies were symptomatic. Peak incidence of positive tTG antibody was 1–5 years after diagnosis, although the previous antibody status of these subjects is not known.
Conclusion: The prevalence of positive antibody screening for CD in our population with T1DM is higher, but prevalence of confirmed CD is comparable to that reported from other parts of the world. Routine screening with antibodies in these subjects, even if they are asymptomatic, within 5 years of diagnosis must be done.

PP 069

Coeliac disease in children and adolescents with type 1 diabetes – a retrospective analysis of 10 years of a screening program

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Introduction: Patients with type 1 diabetes mellitus (T1DM) have an increased prevalence of coeliac disease (CD) which may be associated with increased morbidity. The Paediatric Diabetes Unit at Monash Medical Centre, Victoria has undertaken routine screening of children

with T1DM for CD since 1993. This paper reviews the results of screening over a ten year period.
Methodology: Patients are screened at diagnosis using anti-gliadin and endomysial antibodies, and total IgA, then 2–5 yearly if initially negative, earlier if there is clinical suspicion of CD. Patients with positive screening tests are referred for gastroscopy and biopsy, and then commenced on a gluten free diet (GFD) if the diagnosis is confirmed.
Results: Over 10 years, 42 patients have been diagnosed with CD (30 females, 12 males, ratio 2.5 : 1) giving a prevalence of 6.5%. Nine patients were excluded from analysis due to transfer or diagnosis within the past 6 months. Of the remaining 33 patients, 23 (70%) were considered compliant with a GFD based on antibody data. The 'compliant' group were slightly older than the 'non-compliant' group (mean age 17.8 vs. 14.0 years, NS). There was no difference between the two groups in total duration of DM or duration of DM at time of diagnosis of CD (9.6 vs. 9.3 years, and 3.6 vs. 3.4 years respectively). The compliant group had a significantly lower mean HbA1c (8.7% vs. 9.6%, p = 0.05).
Conclusion: This study confirms a high prevalence of CD in patients with T1DM and a good compliance rate with GFD. The compliant patients had a significantly lower mean HbA1c. Further studies are underway to determine whether there are factors which directly cause poor compliance with both CD and DM management, or whether there are factors operating as a consequence of the untreated CD adding to the difficulties in achieving better glycaemic control.

PP 070

Cystic fibrosis (CF), continuous glucose monitoring (CGMS) and CF-related diabetes

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The oral glucose tolerance test (OGTT) remains the gold standard for diagnosing CF-related diabetes (CFRD). CGMS is a tool that is potentially useful for diagnosing CFRD.
Methodology: 2-hour OGTT (1.75 gm/kg) and CGMS was performed on all subjects. None were on oral steroids or growth hormone. OGTT was classified according to CF consensus guidelines: Normal <7.8, impaired 7.8–11.1 & CFRD >11.1 mmol/l. CGMS as normal glucose excursions (NGE): none >7.8, impaired (IGE) 7.8–11.1, & diabetic (DGE) >11.1 mmol/l. 19 subjects were evaluated, mean age 14 ± 2 years; 7/19 male, all with homozygous ΔF508 mutations. Mean FEV1 was 58.9 ± 20, height SD score −1.2 ± 1.3, BMI SD score −0.64 ± 0.8. 6 subjects had G-tube feeding.
Results: On OGTT, fasting glucose was 5.6 ± 0.9 mmol/l and HbA1c 6.3 ± 0.8%; 7 had CFRD and 6 had impaired. On CGMS 8 had DGE and 7 IGE, 2 with IGT were normal of CGMS. Sensitivity and specificity of CGMS for diagnosing CFRD was 90 and 100% respectively. Hba_1c correlated with both mean glucose on CGMS and OGTT fasting glucose ($r^2 = 0.42$, $P < 0.01$ and $r^2 = 0.25$, $P < 0.05$ respectively) and was significantly higher in those with CFRD/IGT vs. Normal (6.7 vs. 5.7, $p < 0.05$, respectively). BMI SD & height SD scores were lower in the CFRD/IGT vs. Normal (both $P < 0.5$ respectively). 4 G-Tube fed subjects had IGT, which on CGMS was aggravated by the period of supplemental feeding; all had rapid weight gain with pre-G-tube feed insulin.
Conclusions: In these CF patients, CGMS is as good as OGTT in detecting CFRD, and was especially useful in evaluating the glycemic effects of supplemental feeds, erratic large meals and in those with borderline or questionable results on OGTT.

Insulin treatment – CSII

PP 071

Improvement of Hba1c is associated with normalization of insulin-like growth factor–I and is dependent on sufficient dosing of insulin glargine in adolescent T1DM

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Introduction: Insulin glargine has the advantage of delivering insulin more steadily, particular during the late night. Adolescents with T1DM are IGF-I deficient and this results in hypersecretion of GH, which is associated with insulin resistance. In addition to its direct glucose lowering effects, Glargine may improve glycemic control by improving GH receptor function, normalizing IGF-I effects on glucose uptake and decreasing GH induced insulin resistance.
Methodology: Twelve adolescent T1DM patients (8 females/4 males, Tanner stage 2–3) were studied before and during 12 weeks of intensified treatment with glargine. Before start of Glargine patients were on MIT with NPH as basal insulin.
Results: The mean IGF-I level was markedly subnormal (−1.8 ± 0.4 SDS; 6 patients ≤ −2 SDS) before insulin glargine, but increased 50% to −0.8 ± 0.3 SDS after 4 weeks of treatment and this was sustained throughout the 12 weeks study period (−0.6 ± 0.3 SDS at 12 weeks). The change in IGF-I concentrations was mirrored by changes in HbA1c. HbA1c improved from 8.3 ± 0.6% to 7.0 ± 0.3% at 4 weeks and 7.3 ± 0.3% at 12 weeks. The improvement of HbA1C was significantly correlated with the increase in IGF-I at 4, 6 and 12 weeks ($p < 0.01$). The mean total insulin requirement was decreased to 91 ± 6% at 6 weeks of treatment. Interestingly, the change in IGF-I was positively correlated with the change in total insulin dose.
Conclusion: We suggest that normalization of subnormal IGF-I concentrations in adolescents with T1DM may be one important mechanism involved in the improvement of HbA1C. Furthermore, normalization of IGF-I requires that the total insulin dose is not excessively reduced. Whether normalization of IGF-I may reduce long term diabetic complications awaits future studies.

PP 072

Insulin glargine treatment from start improves metabolic control during the first year in children with T1DM

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Introduction: Insulin Glargine (Glargine) is thought to offer sustained insulin delivery for up to 24 hours. This may improve night-time insulin deficiency and improve GH generation of IGF-I in patients with T1DM.

In accordance, we have recently found rapid normalization of the GH-IGF-axis in adolescents with T1DM stated on Glargine.
Methodology: Metabolic control and total insulin requirements were analysed every 3 months during the first year in consecutive cases of T1DM children started on Glargine (n = 49) or children of similar age started on NPH insulin (n = 49). All children received MIT with direct acting analogs and NPH twice daily or Glargine once daily.
Results: There were no differences between groups regarding age or metabolic status at diagnosis. In the Glargine group the mean HbA1c was lower at 3 months from start of treatment (5,6 ± 0,87% vs. 6.2 ± 0,85%, p < 0,001) and at 6 months (5,6 ± 1,2% vs. 6,6 ± 1,0%; p < 0,001). In patients followed for 12 months the mean HbA1C was still significantly lower in the Glargine group (6,0% ± 1,43; n = 32 vs. 7,2% ± 1,17; n = 49; p < 0,001). The total insulin doses were similar (0.5 U/kg) at nadir in both groups. Interestingly, the mean total insulin doses at 12 months were 0,6 ± 0,2 U/kg BW^{-24h} in the Glargine group (vs. 0,85 ± 0,3 U/kg BW^{-24h}; p < 0,001).
Conclusion: Metabolic control was significantly better during the first year on Glargine in children with T1DM. Furthermore, this was obtained with a lower mean insulin requirement at 12 months. The results could be explained by preservation of endogenous insulin secretion and/or normalisation of the GH-IGF-axis resulting from sustained insulin delivery with Glargine. A prospective study is needed to explore the mechanisms.

PP 073

Metabolic control in children and adolescents with type 1 diabetes mellitus during 12 months of insulin glargin (Lantus) treatment

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Introduction: To determine efficacy and safety of insulin glargin (Lantus) during 1-year of treatment.
Methodology: 12-months non-randomized study with the accurate monitoring of patients during the first 6 months and HbA1c control after 1 year of treatment. 50 patients with DM type 1 (6–18 yrs, 12.8 ± 3.3, duration of diabetes – 0.6–16 yrs, 4.9 ± 3.9) had multiple daily insulin injections, basal insulin – NPH. Before switching to Lantus 8% of patients had 3 injections of NPH, 88% – 2 injections, 4% – one. 22% of patients had additional injection of short-acting insulin early in the morning. The starting dose of insulin glargin at bedtime was 80% from NPH.
Results: 49 patients completed the study (1 patients withdrew his consent). Fasting glycemia levels at baseline, after 3 and 6 months were –10,8 ± 2,4; 8,6 ± 2,5 and 8,5 ± 2,5 mmol/L (p = 0,06); glycemia at 6 a.m. –10.9 ± 4.1, 8.4 ± 2.7, 8.8 ± 3.1 (p < 0.05), mean HbA1c levels were 9,1 ± 1,5%, 9,3 ± 1,8% and 8,4 ± 1,5% (p = 0.009 vs. baseline) respectively, HbA1c after 1 year was 8.8 ± 1.9 (n = 43). Allocation of patients according to HbA1c before treatment: HbA1c < 7.6%–18.4% of patients, HbA1c 7.6–10.0%–53% of patients, HbA1c > 10%–28.6% of patients, after 6 months: 32.7%–53.0%–14.3% respectively, after 12 months: 18.6%–53.5%–27.9%. Episodes of severe hypoglycemia were not registered. The incidence of nocturnal hypoglycemia tended to decrease. Insulin antibodies titer decreased insignificantly after 6 months.
Conclusion: The study results confirmed a possibility of significant improvement of glycemia control in pediatric DM1 without increase in hypoglycemic episodes, insulin's antibodies, insulin requirements and BMI. Once-daily use of insulin Lantus caused reduction of HbA1c level (after 6 months), fasting glycemia (after 3 months), tendency to decrease of nocturnal hypoglycemia and number of insulin injections.

PP 074

Recent status of insulin therapy for preschool-age Japanese children with type 1 diabetes

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Introduction: Incidence of type 1 diabetes is low in Japan and there are few preschool-age patients even in most pediatric diabetes centers. The aim of this study was to evaluate the recent status of insulin therapy for preschool-age Japanese children with type 1 diabetes.
Methods: One-hundred-forty-two patients who had been diagnosed at less than 5 years of age within the past 10 years (1993–2002) at 36 hospitals were registered in this study. The methods of daily insulin therapy and episodes of severe hypoglycemia during the preschool period were investigated.
Results: Eighty-six (61%) children were treated with a pen-type device and 56 (39%) were treated with a syringe-type device. The once-a-day insulin regimen was used for 2, a twice-a-day regimen for 104, a three-times-a-day for 28 and a four-times-a-day for 8. Fifty-eight (41%) children were injected with insulin with the dose adjusted by less than 1U notch. Episodes of severe hypoglycemia were recorded in nearly half of the subjects, and one-fourth of the subjects had repeated episodes. There was no significant difference in the type of device and injection time between children with and without severe hypoglycemia. One-hundred-eleven of their parents were questioned regarding the degree of psychosocial stress experienced during the care of their children. Most parents worried about the glycosylated hemoglobin value at each hospital visit. They were next very afraid of nocturnal severe hypoglycemia, independent of any actual experience.
Conclusion: These results suggest that although insulin therapy can involve various methods, the important point is to simultaneously provide good glycemic control and prevent severe hypoglycemia, especially during this age.

PP 075

Role of insulin secretion and insulin resistance in clinical course of type 1 diabetes mellitus in children and adolescents

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Introduction: Frequent incidence of insulin resistance in type 1 diabetic children may cause new interest in the role of insulin resistance in development and clinical course of disease. Aim of this study was to estimate the role of insulin secretion and insulin resistance in clinical course of type 1 DM in children and adolescents.
Methodology: 155 patients with type 1 DM (85 male) aged 7,3–19,6 years (mean – 13,5 ± 3,5 lat) were included into study. The patients were divided in three groups according to duration of DM: group 1 (N = 56) – 6 month, group 2 (N = 52) – 2 years and group 3 (N = 47) – 3–5 years. Insulin secretion was estimated in glucagon test (radioimmunoassay). Euglycemic-hyperinsulinemic clamp was performed to assess insulin resistance. Glucose disposal rate (index M) determined during the last 30 min of the test estimated insulin resistance. HbA1 was examined by HPLC.
Results: In type 1 DM children C-peptide-0′ level was 0,18 ± 0,19 pmol/l (in group 1; 2; 3 – 0,28; 0,14; 0,11 pmol/l respectively, p < 0,001), and C-peptide-6′ was 0,28 ± 0,24 pmol/l (in group 1; 2; 3 – 0,46; 0,20; 0,16 pmol/l respectively, p < 0,001), The index M ranged from 2,89 to 17,39 mg/kg/min, mean – 7,57 ± 2,64 (in group 1; 2; 3 – 8,12; 7,39; 7,11 pmol/l respectively, NS). The insulin daily dose was

0,77 ± 0,31 U/kg, HbA1c – 7,11 ± 1,17%. There was significant relationship between insulin secretion and insulin resistance and daily insulin dose (multiple regression R = 0,52; R^2 = 0,28; p < 0,001). This correlation was observed in group 1 and 2. The slight relationship between HbA1c and insulin secretion was found (C-peptide-0′ r = –0,28, p = 0,001, C-peptide-6′ r = –0,18, p = 0,006).
Conclusion: In type 1 diabetic children and adolescents insulin daily dose depends on residual insulin secretion and insulin resistance. The metabolic control only slightly depends on insulin secretion.

PP 076

Does experimental learning and own practise with insulin pump reduce the barriers to insulin pump treatment among the health care professionals?

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Introduction: Our aim is to offer the best treatment to the children and adolescents with diabetes. Insulin pump is not used as an equal possibility of treatment in all paediatric clinics in Finland. One reason for few insulin pumps is a lack of faith and even fear towards insulin pumps. The aim of this study is to assess does an intensive course with experimental learning and own practise with an insulin pump help to reduce barriers to insulin pump treatment among the paediatricians and diabetes nurse specialists.
Methodology: 23 paediatricians and nurses participated in the three-day course. They practised using pumps in everyday life by living as a person with diabetes during two days. In beginning and in the end of the course they were interviewed and they also answered a questionnaire concerning the barriers and fears towards the insulin pump treatment.
Results: In the beginning of a course the participants feared the most:
1. The technique of an insulin pump 35%
2. The adjustment of insulin in special occasions (sick-days, sauna, swimming) 26%
3. Own ability to give education when starting the insulin pump treatment 26%

In end of the course 70% (n = 16) of the participants answered that they don't have any barriers or fears any more.
During the course the most important learning experiences were:
1. Learning the technique of an insulin pump 70%
2. Own experiment of using insulin pump 61%
– simplicity of using the pump in different situations
– 'you can live normal life with an insulin pump'
3. Ideas how to start insulin pump treatment and educate persons with diabetes

Conclusion: Participating in a course and even better together with the whole diabetes team reduced psychological barriers to start the insulin pump treatment very effectively. Living two days as a person with diabetes gave a lot of new ideas and helped them to plan the educational sessions for the clinic. In the future more courses are needed for the paediatricians and diabetes nurse specialists who already have experience with insulin pumps.

PP 077

A novel method of selecting the initial insulin dose in children and adolescents starting on the insulin pump

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Introduction: Current calculations for choosing the initial CSII insulin dose were developed in adult settings. These calculations are based on the patients pervious insulin dose. They do not take into account that fabrication of BGLs and insulin omission is common in children and adolescents. We used these adult calculations in five patients started on insulin pump therapy. The patients had frequent hypoglycaemic episodes during the first 48 hours of treatment. After stabilisation, the patients insulin requirements were similar. We decided that a set dose of insulin based on age was more appropriate.
Methodology: Two tables were developed, one for inpatients and one for outpatients. These tables were adjusted over the following 10 patients. 25 patients were started using these charts.
Results: Hypoglycaemia was uncommon and glycaemic control has been good in the first 48 hours in all but 3 patients. These 3 patients were adolescent females with marked insulin resistance (one due to steroid immunosuppressive therapy) and required basal rates over 2 units/hour, meal boluses of 3 units/exchange and corrections of 1.5 units/mmol over 8.
Conclusion: We believe that patients need to have positive perceptions of pump therapy. These perceptions are moulded very early in the patients contact with the pump. Therefore, it is very important to avoid adverse events (such a hypoglycaemia) when therapy is initiated. We have found that set dose charts are superior to calculations in determining an initial starting dose, which then results in a positive experience for the patient and their families.

PP 078

Dietary management of children and adolescents on insulin pump therapy – improved control can be achieved without strict carbohydrate counting

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Introduction: The nutritional management of people on CSII is based on counting grams of carbohydrate. New pump technologies involve entry of grams of carbohydrate to calculate meal boluses. However, there is no evidence that this level of accuracy in carbohydrate estimation is necessary to achieve good glycaemic control. Children and adolescents on CSII are often responsible for their own meal bolus calculations. Current studies indicate missed mealtime boluses are a major cause of sub-optimal control in youths on CSII. The difficulties involved in carbohydrate counting may contribute to non-compliance. We used a simplified dietary approach to see if good glycaemic control could be achieved without carbohydrate counting.
Methods: Patients commencing on CSII were taught carbohydrate quantification to 15 gm and average carbohydrate values of takeaway meals and snacks. Food models, food photos and cup measures were used for dietary instruction. Adolescents were not required to weigh food or keep detailed food records. Patients who were unable to do the calculations were managed with pre-programmed meal boluses.
Results: 30 patients were commenced on CSII. The average decrease in HbA1c was 1.0% (p < 0.01) at 12 months post-pump commencement. Variables such as number of severe hypoglycaemic events and change in BMI Z scores compare favourably to other programmes where more precise carbohydrate counting was taught.
Conclusion: We have found that children on CSII can achieve good glycaemic control without carbohydrate counting. Carbohydrate counting is difficult and is beyond the capabilities of many children. Using food models and average values for take-away foods is a practical method of teaching approximate carbohydrate quantification.

PP 079

The SPIN programme–development of a straightforward approach to insulin pump therapy

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Introduction: The use of insulin pump therapy is increasing. It is now regarded as an effective and safe alternative for children and adolescents with Type I Diabetes. However, many of the published protocols for the use of pump therapy are highly selective on the basis of patient compliance, motivation and learning ability. We have developed a Straightforward Program for Insulin pump Newcomers (the SPIN Programme). The main elements of this program are a simplified approach to insulin pump therapy initiation and education.
Methods: Key components of SPIN include simplified education, insulin regimes, insulin adjustment, dietary instruction, meal bolus calculations and the use of pre-set boluses for patients who had difficulty giving boluses independently. No patient who requested CSII was refused. Patients with 'bad' past histories were not discouraged from CSII.
Results: 30 patients were commenced on CSII using the SPIN program. The average decrease in HbA1c was 1% (P = 0.01). There have been no adverse outcomes (severe hypoglycaemia or DKA). Two patients with histories of recurrent DKA decreased their HbA1c by 3% or more. Focus groups of children and their carers revealed high levels of satisfaction with the SPIN program.
Conclusion: The results from this program compare favourably to other more prescriptive programs. We have been able to increase accessibility of insulin pump therapy and it's benefits to groups such as adolescents with poor glycaemic control and toddlers/pre-schoolers. We feel that strict patient selection discriminates against a group of patients who may gain significant benefits from this form of therapy.

PP 080

The use of insulin dilution to adjust the insulin dose in young children on the insulin pump

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Introduction: It is difficult to achieve good glycaemic control in young children. Insulin pumps offer this group the flexibility that is needed to allow for their day-to-day variation in oral intake, exercise and growth. Currently described methods of CSII insulin dose adjustment are problematic in this group because of the small insulin doses used. For example, if the basal insulin rate is increased from 0.2 units/hour to 0.3 units/hour (an increase of 50%) then hypoglycaemia may occur. Children's growth patterns and change in insulin requirement means they need small changes (5–10%) in insulin dosage. A new method of insulin adjustment is needed for young children.
Method: Parents were given vials of insulin and vials of diluent. The child was started on 1 : 1 (insulin : diluent) or 1 : 2 dilution and the basal, meal and correction boluses were established by the normal methods. Subsequent insulin adjustment was done by parents changing the insulin dilution (e.g. 1.1 : 0.9 rather than 1 : 1). Patients were followed for 12 months.
Results: Four patients were enrolled (2y male, two 3 yo females and a 5 yo female). Average decrease in HbA1c after starting the pump was 1.25% (P = 0.01). There was no deterioration in control over a 12 month period. Hypoglycaemia has been rare and there have been no grade 3/4 events.
Conclusion: Parents have been comfortable changing the dilution without medical supervision. HbA1c improvements have been maintained without adverse events. Insulin dilution allows for subtle insulin dose adjustment in young children on insulin pump therapy.

PP 081

Does the indwelling catheter length affect patient preference when used for pumps or multiple injections?

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Introduction: Indwelling catheters are used by many children and adolescents for insulin pump therapy. They are also used as injection aids for multiple injections. Our aim was to evaluate the length and device design of catheters used for pumps (Comfort, Unomedical, Denmark) and injections (Insuflon, Unomedical, Denmark).
Methodology: 16 children and adolescents aged 9–20 years completed the pump study and 19 aged 4–15 the injection study. Their diabetes duration was 9.6 ± 4.9 years and 3.7 ± 3.1, respectively. They compared 5 insertions with the current catheter length of 17 mm with 5 insertions of a shorter 13 mm catheter. Insuflon users also scored injection pain on a 10 cm facial VAS scale.
Results: 67% of pump users 53% of injection patients preferred the shorter needle. The average time between replacements of pump catheters was 4.1 days for the 17 mm catheter and 4.1 days for the 13 mm catheter, while it was 4.5 days for 17 mm Insuflons and 4.0 days for 13 mm Insuflons. There was a tendency towards lower insertion pain for the shorter catheter (2.0 cm VAS for 17 mm and 1.5 cm for 13 mm pump catheters, p = 0.06; 1.5 cm for 17 mm and 1.2 cm for 13 mm injection catheters, p = 0.22). Insuflon users scored the same pain when injecting through catheters of different lengths (0.6 cm for 17 mm catheter, 0.5 mm for 13 mm catheter).
Conclusion: Both needle lengths were appreciated by a considerable number of patients. Many Insuflon patients appreciated the new design which was slightly larger than the previous. Our findings illustrate that patients do have different preferences regarding technical devices used for insulin delivery, and that it an advantage if a large variety of designs can be available to fit individual needs.

PP 082

Does bacterial strains infect subcutaneous cannulas of the insulin pumps?

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Continuous subcutaneous insulin infusion CSII using personal insulin pumps becomes more and more popular and is one of the alternatives of intensive insulin therapy in diabetics. The aim of the study was to determine the microbiological pureness of the pump's subcutaneous cannulas.
Material & methods: We examined 35 cannulas received from 35 children with diabetes treated with CSII. The mean age of children was 10.13 ± 4.41, T1DM duration – 3.9 ± 2.5 yrs and mean HbA1c 7.26 ± 0.9%. Cannula culture was performed using semiquantitative technique (Maki). The swab from the skin was also taken after removing the cannula. A positive result was assumed when there was the growth of min. 10 colonies of bacteria in direct culture of the cannula.
Results: Microorganisms were found in 10 (28.6%) of the examined cannulas. Positive culture of coagulase-negative Staphylococci was present in 8 cases and these results mostly correspond to positive culture of skin flora. In 25 cases, the cannulas were clean, although a positive colonization of skin in 15 (40%) cases (coagulase-negative Staphylococcus (13); Staphylococcus aureus (2)) was detected. We did not observe any significant correlation between positive culture of cannulas and HbA1c, age, sex and weight, DM duration, skin's inserting region and local skin inflammation of diabetic children.
Conclusions: The subcutaneous cannulas of personal insulin pumps are infected by different microorganisms, especially strains from the epidermal flora. Accurate following of the aseptic rules when inserting cannulas and taking proper care of the injection site can protect from the infection.

PP 083

A case–control designed insulin-pump study in Danish T1DM adolescents

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Introduction: This study was designed to investigate the effect of insulin-pump treatment (CSII) compared to intensified multiple daily insulin injections (MDI) over 12 months in Danish adolescents.
Methodology: 30 T1DM adolescents at CSII and 26 matched MDI controls were included in an open randomised, intention-to-treat design after all participants had attended an educational brush-up regarding intensified diabetes treatment. Human insulin was used in both groups. Inclusion characteristics: mean age: 15.3/15.9 years, mean diabetes duration: 6.7/7.8 years and gender (M/F): 14/16 vs. 10/16 for CSII and MDI, respectively. HbA1c, hypoglycemia and DKA were recorded at each visit every 6–8 weeks. The HbA1c was modelled using mixed model with random effect of patient and patient by time.
Results: The model estimated the average HbA1c at trail onset to 9.24% (MDI) and 8.86% in CSII ($p = 0.33$). A fall in HbA1c were seen in both groups: 0.0163%/month (c.i.: –0.0486, 0.0159) for the MDI and 0.0004%/month (c.i.: –0.0289, 0.0280) in the CSII ($p = 0.647$). The between-patient ratio in the rate of change was 0.063%/month. The total number of severe hypoglycemia (unconsciousness or seizures) was 11 and 3 episodes and the number of DKA (bicarbonate 10–15 mmol/l) was 0 and 5 for MDI and CSII, respectively.
Conclusion: No difference between MDI and CSII regarding the level of HbA1c were seen, however a reduction in severe hypoglycemia were observed in CSII. CSII resulted in a larger number of moderate DKA episodes. Only a minority of the present participants seems to benefit from CSII, illustrated by the large between-patient ratio in the rate of change for HbA1c.

PP 084

Insulin Glargine treatment in adolescent T1DM decrease glucose variability and is associated with normalization of insulin-like growth factor-I

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Introduction: Fluctuation in B-glucose is associated with impaired glycemic control in T1DM particularly in adolescence. The IGF-I deficiency in adolescents with T1DM may contribute to increased glucose variability. We have assessed this possible association in adolescent T1DM patients started on Insulin Glargine (Glargine) since sustained insulin delivery at nighttime may improve GH receptor function and thereby increase IGF-I concentrations.
Methodology: We have studied twelve adolescent T1DM (8 females/4 males, Tanner stage 2–3) before and during 12 weeks of intensified treatment with Glargine. Prior to start and at 6 weeks, 24-hours blood sampling every 30 minutes was performed, B-glucose was tracked by CGMS and interstitial sc glucose was determined by microanalysis.
Results: B-glucose and CGMS determinations were well correlated throughout the 24-hour registrations. Interstitial sc glucose was generally lower and further analysis of the data is ongoing. The mean HbA1C levels decreased from $8.3 \pm 0.6\%$ to $7.1 \pm 0.4\%$ ($p < 0.001$). B-glucose variance decreased in all but 2 patients and the mean was significantly decreased on Glargine (23.3 ± 2.7 vs. 15.0 ± 1.7, $p < 0.005$). Gender, age and pubertal stage corrected IGF-I SDS were below –2 SD in half of the patients and the mean IGF-I concentration was increased up to 50% throughout the study ($p < 0.001$). Interestingly, the decrease in B-glucose variance was significantly associated with the increase in IGF-I ($r = 0.64$, $p < 0.05$).
Conclusion: In conclusion, HbA1C and glucose variance was improved after start of Glargine in T1DM adolescents. We suggest that normalization of the GH-IGF-axis may be involved in this improvement.

PP 085

Metabolic control and safety of insulin pump treatment in T1DM children under the age of 10 years

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The aim of the study was to assess the efficiency of continuous subcutaneous insulin infusion (CSII) using insulin pumps in prepubertal children with T1DM.
Methodology: Three groups of T1DM children using intensive insulin therapy were compared: Group I – 30 children with CSII-1; mean age 6.7 ± 2.2 years; Group II – 25 children treated with multiple injections (MI); mean age 7.0 ± 1.5 years; Group III – 35 children with CSII-2; mean age 13.9 ± 2.1 years. The age of children was similar in group I and II; DM duration (3 yrs) was the same for all groups. The following parameters were analysed (after 6, 12, 18 months): HbA1c, daily insulin requirement (DIR) U/kg, number of severe hypoglycaemia, DKA (cases/100 patients/year).
Results: In CSII-I, initial HbA1c in comparison to the final decreased from 7.1 to 6.9% and DIR was significantly reduced from 0.86 to 0.70 U/kg/24 h (after 6 months) and to 0.77 U/kg/24 h after 18 months ($p < 0.01$). HbA1c and DIR of MI group significantly increased respectively: from 7.0, 7.4, to 7.3% and from 0.68, 0.76, to 0.84 U/kg/24 h (after 6, 18 months). There was no noticeable difference of HbA1c and DIR in CSII-2 group after 18 months of observation. Significant difference of DIR was found in: CSII-1 vs. MI and CSII-2 ($p < 0.05$) in all examined months. The highest index of cases of severe hypoglycaemia, DKA was in MI group.
Conclusion: CSII provides good and safe metabolic control with reduced insulin requirement in T1DM children under 10 yrs of age.

PP 086

Three variants of functional intensive insulinotherapy (FIIT) in children and adolescents with T1DM

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The most desirable goal of metabolic control in diabetes is the safe achievement of normoglycaemia. The aim of the study was to assess the efficiency of FIIT based on: a long-acting analog (Glargin/Lantus), intermediate insulin NPH and continuous subcutaneous insulin infusion (CSII) using insulin pumps.
Methodology: FIIT was applied to 196 children with T1DM aged mean 10.9 yrs: CSII to 81 children, multiple injection (MI_{NPH}) with NPH in 70 and (MI_{LA}) with Glargin in 45 cases. The mean period of observation was 2.9 yrs for CSII and MI_{NPH} and 3 months for (MI_{LA}). Parameters: HbA1c, total daily insulin requirement, BMI, daily requirement of basal insulin and number of severe hypoglycemia were compared in all groups.
Results: We found significant decrease of HbA1c in CSII vs. MI_{NPH} (7.04 vs. 7.47%; $p < 0.05$) but not in MI_{LA} group (7.22%). Total daily insulin requirement was for: CSII – 0.75; MI_{NPH} – 0.80; MI_{LA} – 0.70 U/kg/24 h. BMI was similar in all groups – mean 17.72. The highest daily requirement of basal insulin was in MI_{NPH}. Number of DKA and episodes of severe hypoglycaemia were higher in MI_{NPH} vs. CSII (MI_{LA} – not calculated, because of short observation).

Conclusion: The possibilities of effective and safe functional intensive insulin treatment are extended with introducing to T1DM therapy: CSII and long acting insulin analog.

PP 087

Use of continuous subcutaneous insulin infusion (CSII) in patients with cystic fibrosis related diabetes (CFRD)

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Introduction: The intensive insulin treatment improved the clinical and nutritional status of this patients and prevented the long-term complications. The CSII is shown to be a safe and effective alternative in the insulin treatment of type 1 diabetes, in pediatric and adult patients. We have used the insulin pump therapy with rapid-acting insulin analogues with rapid-acting insulin analogues in three patients affected by CFRD.

Patient report 1: A 7.5 year-old boy with CF who CFRD was diagnosed at age 3,5 and insulin therapy with 4 injections for day was begun. At 5,5 year of age started the CSII treatment. During the two years of follow up with CSII the mean levels of HbA1c was reduced from 9,7% (in the year before the CSII) to 7,9% (in the first year of CSII) and 8,0% at second year of CSII; the mean levels of BMI was increased (15,2 in the year pre-CSII; 15,6 at first year and 15,8 at second year of CSII). The insulin requirement decreased from 0,69 U/kg/day before starting the CSII to 0,47 U/kg/day at 1 month, to 0,48 U/kg/day at 12 months and 0,49 U/kg/day at 24 months of CSII (60–62% as basal, 40–38% as bolus; 12–13% as nocturnal basal).

Patient report 2: A 24,7 year-old girl with CFRD diagnosed at 18,3 years of age who start the insulin treatment with 4 injections for day at 19,2 years of age. During the CSII treatment, starting at 21,2 years of age, the mean levels of HbA1c was reduced (7,8% in the year pre CSII; 6,2% at the first year of CSII and 6,4% at the second year) and the mean levels of BMI was increased (20,1 in the year before the CSII, 21,9 at the first year of CSII and 22,1 at the second year). The insulin requirement reduced from 0,82 U/kg/day before the CSII to 0,47 U/kg/day at 1 month (basal/bolus: 50%/50%; nocturnal basal: 13%), 0,35 U/kg/day at 12 month (basal/bolus: 40/60%, nocturnal basal 11%) and 0,34 U/kg/day at 24 months of CSII (basal/bolus 50/50%; nocturnal basal 8%).

Patient report 3: A 22 year-old boy with CFRD diagnosed at 15 year of age, started the CSII at 20 years of age (insulin treatment with 4 injections/day before starting the CSII). During the CSII the mean levels of HbA1c was reduced (7,1% at the first year of CSII and 7,1% at the second year vs. 9,3% at the year before the CSII) and the BMI levels was increased (21,2 in the year pre-CSII; 22,8 at the first year and 22,4 at the second year of CSII). The insulin requirement decreased from 1,41 U/kg/day before the CSII to 0,72 U/kg/day at 1 months (basal/bolus 52/48%; nocturnal basal 12,6%), 0,97 U/kg/day at 12 months (basal/bolus: 37/63%, nocturnal basal: 14%) and 0,87 U/kg/day (basal/bolus 50/50%, nocturnal basal 12%) at 24 months of CSII. No one of the three patients had DKA episode, sever hypoglycemia episodes, local lipohypertrophy and local skin infections during the CSII treatment

Conclusions: The use of CSII in patients with CFRD resulted to improve the metabolic control of diabetes and the nutritional status without concomitant problems related to this treatment. Further studies are required to determine the specificity of CSII about the distribution basal/bolus and nocturnal basal in this patients. Further studies are required to determine the specificity of CSII about the distribution basal/bolus and nocturnal basal in this patients.

PP 088

Insulin detemir provides better glycaemic control with reduced risk of hypoglycaemia and weight gain than NPH insulin in basal-bolus therapy

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This meta-analysis based on data from 6 multinational, open-label, randomized trials (treatment periods 16–24 weeks) compared insulin detemir (IDet) to NPH insulin (NPH) as basal insulin in basal-bolus therapy, assessing glycaemic control, risk of hypoglycaemia and body weight. Subjects with type 1 (IDet: n = 1336, NPH: n = 814) or 2 (IDet: n = 536, NPH: n = 363) diabetes received human soluble insulin or insulin apart before meals plus once- or twice-daily IDet or NPH. Demographic characteristics were well balanced by treatment. HbA_{1c}, fasting plasma glucose (FPG) and weight at endpoint were analyzed by ANOVA, adjusting for baseline. Within-subject variability in fasting blood glucose (FBG) was analyzed by likelihood ratio test. Relative risks (RR) for hypoglycaemia were evaluated by Cox-regression using a gamma frailty model, with treatment and HbA_{1c} as covariates. Hypoglycaemia was classed as major (BG < 2.8 mmol/l, assistance required) minor (BG < 2.8 mmol/l, assistance not required) or symptoms only (BG not measured, assistance not required).

	IDet Mean (SE)	NPH Mean (SE)	IDet-NPH Mean	95% CI
HbA1c	7.79 (0.03)	7.88 (0.03)	–0.09*	(–0.15; (–0.03)
#FPG(lab) (mmol/l)	9.70 (0.15)	10.80 (0.18)	–1.10*	((–1.46; (–0.73)
Weight (kg)	77.94 (0.09)	78.68 (0.10)	–0.74*	((–0.95; (–0.53)
	SD (CV)	SD (CV)		
FBG (mmol/l)	2.55 (33.3)	3.06 (37.5)	p < 0.0001	

	IDet % patients (events)	NPH % patients (events)	IDet/NPH RR	95% CI
Major nocturnal	1.7 (49)	2.5 (49)	0.58	0.30 1.15
Minor nocturnal	31.8 (1521)	37.6 (1371)	0.65*	0.57 0.76
Symptoms noct.	26.1 (1385)	28.4 (935)	0.79*	0.66 0.94
Major overall	4.5 (168)	5.0 (106)	0.97	0.61 1.53
Minor overall	62.0 (10527)	62.4 (7283)	0.86*	0.76 0.96
Symptoms overall	53.5 (9212)	52.3 (5144)	0.98	0.85 1.14

#Data from 4/6 trials. *p < 0.05. SE: standard error, CI: confidence intervals. CV: coefficient of variation.

Conclusion: Treatment with IDet provided improved control, with lower within-subject variability in FBG, and reduced the risk of non-major hypoglycaemia and weight gain.

PP 089

A randomized, prospective comparison between pump (CSII) and multiple daily insulin injections (MDI) substitution in children with type 1 diabetes

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Introduction: This study was performed to compare the efficacy of continuous subcutaneous insulin infusion (CSII) with Multiple Daily Injections (MDI) in children with type 1 diabetes.

Methods: Thirty nine (17 boys) type 1 children aged 4–15 years were included in a open randomized parallel comparison at study episodes of 3,5 months for each treatment modality, after a MDI run in of 3,5 months. At the end of the study, all children were followed up on CSII as a matter of preference. Parameters for metabolic control, quality of life and costs were checked at the end of each treatment (3,5 monthly) period, including the run in.

Results: Significant improvements were noted in the run-in phase in quality of life as well as in metabolic control. Thereafter no significant improvement of HbA1c or quality of life was found during CSII vs. MDI. All but one child chose to continue CSII. As expected insulin doses were 1/3 lower during CSII. Annual costs are about $3000 higher for CSII.

Conclusion: The results underline the need for properly designed comparisons, particularly in children.

PP 090

Management and education of patients with new onset type 1 diabetes mellitus treated with conventional therapy or multiple daily insulin injections; 12 month outcome comparison

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Introduction: In 2003, 133 patients were diagnosed with new onset type 1 diabetes. The decision on the insulin therapy [conventional management with 2 daily injections (57.0%) versus multiple daily injections (MDI) (43.0%)] was at the discretion of the attending physician. Two-injection regimen was NPH insulin in combination with either regular insulin or rapid-acting insulin (Humalog or Novolog). Multiple daily insulin regimens consisted of long acting glargin insulin (Lantus) and rapid-acting insulin (Humalog or Novolog).

Methodology: Review of the diabetes data of the patients with new onset type 1 diabetes diagnosed from January 2003 – December 2003 was performed. Patients received initial teaching during the hospitalization. Additional teaching sessions were schedule in two and six weeks after the discharge. Clinic follow up visits with the diabetes team (diabetes educator, nutritionist and attending pediatric endocrinologist) were every 4 months.

Results: Demographic and metabolic data are presented in the table. The differences in a HgbA1C values between different regimens are also presented. Patients treated with MDI reported less hypoglycemic events. Patients on MDI reported better satisfaction with the diabetes management due to the better flexibility of the MDI regimen and better accommodation to the lifestyle.

Conclusions: MDI regimen was consistent with the better HgbA1C values and with better patient satisfaction.

Insulin type	Number of patients	GENDER Male	GENDER Female	Hemoglobin A1C (%) First	Hemoglobin A1C (%) Last	AGE (years) Min	AGE (years) Max
L/H	43	24	19	12.1	7.3	1	17
N/R	32	19	13	10.9	7.9	1.7	14
N/A	41	24	17	11.6	7.7	1.9	15
L/A	14	9	5	11.2	7.4	4	14
N/H	3	0	3	13.0	9.0	1.4	11
Total:	**133**	**76**	**57**				

PP 091

The pedpumps study: ninety day memory read-out from 370 international pediatric patients demonstrate the safety and flexibility of continuous subcutaneous insulin infusion (CSII) in all age groups

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Introduction: The percentage of pediatric patients treated with CSII is increasing rapidly in many countries. Newer models such as the Medtronic Minimed 508 pump have a memory that stores all entries into the pump. This allows for the first time to assess pediatric intensive insulin therapy under real life conditions for up to 90 days.

Methodology: In a period of three months clinical data, local HbA1c and the memory readout of pediatric CSII patients (1 to 18 yrs) treated with the Medtronic 508 pump in 17 centers from 11 countries was recorded wit the Encapture™ software.

Results: A total of 375 patients (48% female, age: 12.9 ± 3.8 yrs, diabetes duration: 6.8 ± 3.7 yrs; preschool: n = 33; prepubertal (6 to 11 yrs): n = 96; adolescent (12–18 yrs): n = 248; average CSII duration: 1.6 ± 1.2 yrs; local HbA1c: 8.1 ± 1.2%) participated. The total insulin dose was lower than previously reported for injection therapy: 0.85 ± 0.20 U/kg. 24 hours distribution of basal insulin (mean ± SD: 48 ± 12% of total dose) varied significantly between centers and age groups. Covariance coefficient of daily total insulin was high adolescents (19 ± 9%), as well as in prepubertal (18 ± 8%) or preschool (17 ± 8%) children. The number of boluses per day (7 ± 3) was equally high in all age groups (average dose: 0.42 ± 1.6 U/kg). The rate of severe hypoglycaemia (coma/convulsions) was low (12.4 episodes per 100 patient years) as was the number of diabetes-related hospital days (124 per 100 patient years).

Conclusions: Pediatric CSII patients show a high variability in their insulin therapy. This relates both to age-dependent differences in the distribution of basal insulin as to the day-to-day variation in prandial insulin. Low rates of inpatient hospital days and rates of severe hypoglycaemia indicate the safety of this mode of therapy in different international pediatric diabetes centers.

Vascular complications

PP 092

Predictors of microalbuminuria and overt nephropathy in patients with type 1 diabetes: a population-based, a longitudinal survey

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Introduction: Microalbuminuria is an early marker of diabetic kidney disease, as renal structural lesions can be detected at this stage. Our aim was to identify risk factors for development of persistent microalbuminuria and overt nephropathy in a national based cohort of adults with childhood onset (<15 years) type 1 diabetes.

Methodology: 185 normoalbuminuric subjects with diabetes onset 1973–1982, were followed for 13.2 years (range 11.9–14.1), from 1989–1990 to 2002–2003. At follow up their mean age was 31.8 years (range 20.9–44.0) and mean diabetes duration 23.9 years (range 19.0–30.0). Overt nephropathy: AER ≥ 200 µg/min in at least to out of three consecutive overnight urine collections and persistent microalbuminuria: AER between 15 µg/min and 200 µg/min. Arterial blood pressure was measured twice in sitting position after 10 minutes rest with a standard mercury sphygmomanometer. Blood was collected using venepuncture in not fasting state. At follow up 17 of the subjects were on antihypertensive treatment, 7 of them were normoalbuminuric.

Results: After a mean of 24 years diabetes duration, 24 out of 185 (13%) subjects had diabetes nephropathy, including 7 (4%) subjects with overt nephropathy. Significant predictors for the development of all diabetic nephropathy were cholesterol (p = 0.005), HbA1c (p =

0.009) and ln AER (p = 0.021), whilst smoking, systolic blood pressure, gender, age and diabetes duration were not.
Conclusion: Several potentially modifiable risk factors predict the development of persistent microalbuminuria and overt nephropathy in a population with rather low prevalence of diabetic nephropathy. AER has an independent role as predictor for nephropathy in normoalbuminuric subjects.

PP 093
Acute respiratory viral infections aggravate arterial endothelial dysfunction in children with type 1 diabetes mellitus

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Introduction: Type 1 diabetes mellitus purports an increased cardiovascular risk partly due to accelerated atherosclerotic artery disease. Alteration in arterial endothelial function has been suggested as an etiological factor, yet its sole connection to the diabetic milieu appears unlikely. Diabetes increases the propensity for acute infections which, in turn, might increase as such the cardiovascular risk. In a cross-sectional study we investigated whether clinically manifest acute infections could exacerbate the arterial endothelial damage in diabetic children.
Methodology: Endothelium-dependent (flow-mediated) and glyceryl trinitrate (GNT) induced dilatory responses of the brachial artery were measured by ultrasonography in 26 children with diabetes type 1 (mean age and diabetes duration: 14 ± 3 and 6 ± 3 years respectively) without clinical manifestations of macroangiopathy. Of these 11 patients had clinical signs of upper respiratory tract infection (body temperature > 38°C and symptoms) within 6–8 weeks prior to the study day. Serum levels of oxidized LDL, LDL, HDL, total cholesterol, von Willebrand factor (vWF), C-Reactive protein, Orosomucoid, and HBA1c were also measured on the ultrasound day. Data are mean ± SD.
Results: The infection group had significantly lower flow-mediated dilatation (FMD) and higher levels of vWF than the remaining diabetic patients (FMD: 4.3 ± 2 versus 6.2 ± 2 % respectively; $p < 0.05$; and vWF: 1.3 ± 0.2 versus 1.9 ± 0.2 respectively; $p < 0.01$). In contrast no differences in the baseline brachial artery diameter for GTN induced dilatation, age, duration of diabetes, diabetic control and lipid profile were noted between these groups ($p > 0.1$). FMD of the whole diabetic group was impaired compared to controls (5.4 ± 2 versus 9.4 ± 2%, $p < 0.05$) and inversely correlated to vWF ($r = –0.4$, $p < 0.05$, CRP ($r = –0.6$, $p = 0.01$) and LDL cholesterol ($r = –0.6$, $p < 0.01$).
Conclusion: This is the first study to suggest that endothelial function may be further altered in diabetic children with antecedent clinically manifest acute infections. The findings warrant large scale prospective studies to verify the interplay between infections and diabetes in the pathogenesis of atherosclerosis.

PP 094
Rates of diabetes-related complications in a contemporary adolescent cohort

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Introduction: There is a paucity of data pertaining to rates of diabetes-related complications from paediatric clinics in the post-DCCT period. Many of the previously cited pre-DCCT rates of diabetes-related complications may now be less relevant. The purpose of this study was to assess the incidence of diabetes-related complications in a contemporary cohort of adolescents with type 1 diabetes.
Methodology: This was a retrospective cross-sectional survey of the Royal Children's Hospital diabetes clinic. Adolescents aged >10 years with type 1 diabetes for >5 years were studied. The main outcome measure included: Measures of metabolic control (HbA1C), rates of clinical correlates of microvascular complications (microalbuminuria, retinopathy) and rates of other diabetes-related complications (coeliac disease, hypothyroidism, hypertension, hypercholesterolaemia) and body mass index.
Results: 382 patients were studies (191 male). The mean age of the patients was 15 years 8 months and mean duration of diabetes was 9 years. The mean BMI Z score was +1.1. The mean systolic BP was 110.9 ± 14.1 mmHg and mean diastolic BP was 64.0 ± 8.7 mmHg. The mean HbA1c for males was 8.72% and for females was 8.80%. Five patients (1.5%) developed biochemical hypothyroidism with increased TSH. Seventy-five patients (22%) were found to have an elevated cholesterol level. Twenty-five patients (8%) had intermittent microalbuminuria and 6 (2%) had persistent microalbuminuria. Only 1 patient had macroalbuminuria (0.3%). Only 2 patients (0.7%) were diagnosed with mild non-proliferative diabetic retinopathy. Coeliac disease was diagnosed in 6% of patients. Neither the prevalence of nephropathy nor retinopathy showed a sustained increase with increasing duration of diabetes or increasing level of mean HbA1C.
Conclusions: In this representative and contemporary cohort of diabetic adolescents the incidence of microvascular diabetes-related complications, is quite low. The incidence of non-microvascular complications is similar to those incidences previously reported.

PP 095
Disposition index predicts endothelial function in healthy adolescents

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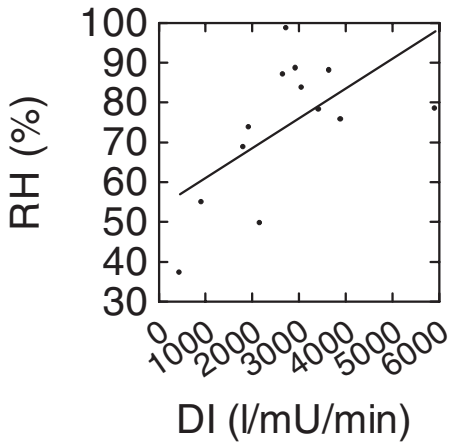
Introduction: The metabolic syndrome consists of a combination of cardiovascular and endocrine pathophysiology. In adults a link has been demonstrated between insulin action and endothelial function. The metabolic syndrome likely has its origins in adolescents, yet it is unknown whether insulin action and endothelial function are linked in this age group.
Methodology: The reactive hyperemic response (RH) was calculated as percent change in forearm vascular resistance, (venous occlusion plethysmography and arterial tonometry) between before and after 5 min of upper arm vascular occlusion, in 13 adolescents (6 male; age 14 ± 2 yrs, BMI 23 ± 4 kg/m^2, mean ± SD) to measure endothelial function. The frequently sampled intravenous glucose tolerance test was used to measure insulin sensitivity (S_I), glucose effectiveness (S_G), and the acute insulin response to glucose (AIR_G). The disposition index (DI) was calculated as the product of S_I and AIR_G. Plasma lipid levels were also measured.
Results: RH was not significantly related to BMI, S_I, S_G, or AIR_G but was negatively related to the DI ($r = –0.6$, $p < 0.05$, Figure). It also negatively correlated to plasma triglycerides ($r = –0.6$, $p < 0.05$). DI and triglycerides were also negatively related ($r = –0.6$, $p < 0.05$). Stepwise multiple linear regression showed that main relationship was between RH and DI.
Conclusion: The positive relationship between DI and RH demonstrates the link between cardiovascular and endocrine function begins in adolescents. It is particularly interesting that DI, and not S_I, was related to RH Since low DI is thought to be a better predictor of future type 2 diabetes and low endothelial function is a predictor of future cardiovascular.



PP 096

Enhanced soluble CD40 ligand is responsible for endothelial dysfunction and monocyte activation in patients with diabetes mellitus. Effect of improved metabolic control

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Introduction: Inflammation plays a pathogenic role in the development of accelerated atherosclerosis in diabetes. Soluble CD40L (sCD40L) is enhanced in diabetes but the molecular mechanisms linking sCD40L to accelerated atherosclerosis are still unclear. We tested the hypothesis that sCD40L may be involved in the process of vascular complications in diabetes and that exerts its effect by triggering complex inflammatory reactions on endothelial and mononuclear cells.

Methodology: Seventy diabetic patients (40 had type 2 diabetes and 30 type 1 diabetes) without cardiovascular disease were studied, and matched with 40 and 30 healthy subjects, respectively. Plasma and serum sCD40L, and plasma sICAM-1, sVCAM-1, E-selectin and MCP-1 were measured. Furthermore, the release of adhesion molecules and MCP-1, the ability to repair an injury in endothelial cells and the generation of O_2^- in monocytes were analyzed *in vitro* after stimulation with serum from patients or controls.

Results: Type 2 and type 1 diabetic patients had significantly higher plasma sCD40L than controls. Furthermore, sCD40L was directly associated *in vitro* with adhesion molecules and MCP-1 and impaired migration in endothelial cells, and with enhanced O_2^- generation in monocytes. Improved metabolic control was associated with a significant reduction of plasma sCD40L by 37.5 % in 12 type 1 diabetic patients. Furthermore, elevated sCD40L in diabetic patients significantly correlated with HbA_{1c}.

Conclusion: We conclude that up-regulation of sCD40L as a consequence of persistent hyperglycemia in diabetic patients results in endothelial cell activation and recruitment of monocytes and tissue macrophages to the arterial wall, possibly contributing to the accelerated atherosclerosis in diabetes.

PP 097

Benefits of free insulin supply in diabetes control and prevention of complications in type 1 diabetes patients

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Aim: To study the benefits of free insulin supply in Type I diabetes mellitus (T1DM) patients.

Materials: Over a 4 year period form Aug 2000 to till date; sixty-one patients with T1DM were studied. Their clinical presentation, biochemical and metabolic parameters in blood namely, plasma glucose (fasting-FPG and postprandial-PPPG) (mg/dl), glycosylated hemoglobin (GHb) urea (mg/dl), creatinine (mg/dl), cholesterol (mg/dl), triglycerides (mg/dl), HDL (mg/dl), 24 hr urine protein (mg/day), chest X-ray and ECG were evaluated at presentation and annually. Children less than 14 yrs and below poverty line was supplied free insulin covered by Novoaid. Other patients supported themselves for insulin therapy (self support group – SSG). Monthly and annual monitoring of biochemical parameters were evaluated (by Nicholas Piramal, India).

Results: The mean ± SD and M : F ratio of the whole group were 15 ± 6.2 yrs; 1 : 1. 30% of patients received Novoaid. About 85% of Novoaid patients followed up regularly with 92% visits, while 64% of the SSG followed-up with 26% visits. The baseline biochemical parameters at presentation are:

Group	FPG	PPPG	S.Urea	S.Cre	S.Chol	S.Tgl	S.HDL	U.Pro
Novoaid	155 ± 93	214 ± 105	26 ± 10	0.76 ± 0.25	138 ± 31	120 ± 87	39 ± 14	184 ± 215
SSG	175 ± 92	221 ± 120	29 ± 16	0.85 ± 0.35	137 ± 36	96 ± 60	38 ± 7	178 ± 190

One episode of ketosis and proteinuria was noticed 6 and 2; 12 and 6 in Novoaid and SSG group respectively. Hyperlipidemia and pulmonary tuberculosis was noticed in 4 each and one with liver abscess in SSG. There was a significant decline of GHb in Novoaid patients Vs. SSG (6.98 ± 1.1 *Vs.* 8.27 ± 3.5 [$p < 0.07$]) at end of four years.

Conclusions: Patients with Novoaid had better metabolic control, few complications compared to the SSG. The age limit of Novoaid should be raised until the patients can sustain themselves financially. Diabetes education to motivate the patients is important apart from these incentive measures.

PP 098

Evaluation of growth hormone and GHBP in children with IDDM (preliminary announcement)

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The abnormalities of functioning of growth hormone axis play a great role in IDDM patients in pathogenesis, diabetes complications, insulin-resistance, dawn phenomen, fat disorders. The aim of the study was the evaluation of growth hormone in urine and GHBP in prepubertal children with IDDM and estimate the influence of the kind of therapy.

Material and methods: 67 patients and 15 age matched, healthy children were included into the study. All children were prepubertal T < 2), suffering from IDDM for more then two years. All patients were divided into groups according to the kind of therapy: 22 were treated with conventional insulin therapy (CIT), 21 with multiple insulin injections (MII) and 24 with continuous subcutaneus insulin infusion (CSII). Blood and urine samples were taken between 7.30 and 8.30 a.m. in hospital in normoglycemia after the night without episodes of hyper or hypoglycemia. All analysis were made by RIA or ELISA commercial kits.

Results: growth hormone levels in urine were lower in diabetic children then in healthy ones and didn't depend on the kind of therapy. GHBP levels were lower in diabetic and were rising with the intensity of treatment.

Conclusions:
1. The abnormalities of growth hormone axis in IDDM children has no influence on growth hormone levels in urine but has on GHBP levels in blood.
2. The kind of therapy appear to have the influence on the levels of GHBP but not on GH.
3. There is necessary to estimate the influence of age, sex, body length and weight, BMI, time from beginning of the illness, quantity of insulin and correlations (in course).
Acknowledgement: Supported by: KBN 378/PO5/2002/23

PP 099

Evaluation of NPY, leptin and soluble leptin receptor in children with IDDM (preliminary announcement)

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The abnormalities of functioning of NPY-leptin axis in children with IDDM propably play a great role in IDDM patients (etiopathogenesis (?), diabetes complications, insulin-resistance, fat disorders and body composition). The aim of the study was the evaluation of NPY, leptin and soluble leptin rp. in prepubertal children with IDDM and estimate the influence of the kind of therapy.
Material and methods: 67 patients and 15 age matched, healthy children were included into the study. All children were prepubertal T < 2), suffering from IDDM for more then two years. All patients were divided into groups according to the kind of therapy: 22 were treated with conventional insulin therapy (CIT), 21 with multiple insulin injections (MII)and 24 with continuous subcutaneus insulin infusion (CSII). Blood samples were taken between 7.30 and 8.30 a.m. in hospital in normoglycemia after the night without episodes of hyper or hypoglycemia. All analysis were made by RIA or ELISA commercial kits.
Results: NPY levels were higher in diabetic in a statistically significant way and were rising with the intensity of treatment (the highest in CSII patients). Leptin levels were higher in IDDM patients (the highest in MII). S-rp. leptin levels were higher in IDDM in statistically significant way (the highest in CSII patients).
Conclusions:
1. The levels of all measured parameters were different in diabetic patients, but only NPY and s-rp. leptin in a statistically significant way.
2. The kind of therapy appears to have the influence on the levels of measured parameters.
3. There is necessary to estimate the influence of age, sex, body length and weight, BMI, time from beginning of the illness, quantity of insulin and correlations (in course).
Acknowledgement: Supported by: KBN 378/PO5/2002/23

PP 100

The multicenter adolescent diabetes study (MAD) in Germany: How successful and satisfied are adolescents with the new therapeutic strategies?

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Introduction: Previous large surveys have reported average HbA1c values well above 8% in the adolescent age group. After the recent introduction of several new therapeutic strategies the MAD study analyzed the prevalence of the different regimens of insulin therapy, glycemic control and treatment satisfaction.
Methodology: The MAD study group consists of seven large pediatric diabetes centers. In a period of three months clinical data, instant HbA1c with the same method (Metrika, Sunnyvale, CA) and the Diabetes Treatment Satisfaction Questionnaire (DTSQ, C. Bradley) were recorded in consecutive adolescent patients (11 to 18 years).
Results: A total of 840 patients (49,8% female, age: 14.6 ± 2.0 years, diabetes duration: 5.9 ± 3.8 years) were studied. The average HbA1c was 7.8 ± 1.5% with significant center differences, increases for longer diabetes duration but no effects of gender. The rate of severe hypoglycaemia was low (14.1 episodes per 100 patient years). Glargine was the most frequent basal insulin regimen (n = 274) followed by NPH (n = 229), NPH + Semilente (n = 215) and CSII (n = 122). 41 ± 13% of the daily dose was basal insulin. 38% had rapid acting insulin analogues as part of their regimen. 45.5% of the adolescents with injection therapy took more than 4 daily injections. Treatment satisfaction was high (score range 8 to 48, median score 36). Even after adjusting for center effects significant differences ($p < 0.001$) were present for the modes of therapy: CSII (38.4 ± 5.1), Glargine (34.6 ± 6.4) NPH (34.4 ± 6.2), Semilente (33.6 ± 6.4).
Conclusions: The new therapeutic strategies with short and long-acting insulin analogues are used frequently in this age group. Although the cross-sectional nature of the study precludes any implications of a causal relationship, average treatment satisfaction, rate of hypoglycemia and glycemic control are now closer to the target range also in the difficult time of adolescence.

PP 101

Beta-fibrinogen gene G/A-455 polymorphism in relation to subclinical diabetes complications in children and adolescents with type 1 diabetes

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Introduction: The aims of study were to assess the distribution of the beta-fibrinogen gene polymorphism in type 1 diabetic children and adolescents and to evaluate possible association between fibrinogen genotype and subclinical complications of diabetes.
Methodology: Beta-fibrinogen gene G/A-455 polymorphism was investigated in 134 children and adolescents with type 1 diabetes (age: 15.0 ± 3.1 years, diabetes duration: 5.3 ± 1.9 years) and in 100 non-diabetic controls (age: 15.2 ± 2.9 years) using polymerase chain reaction. Assessments for subclinical nephropathy (timed overnight urinary albumin excretion), retinopathy (fluorescein angiography), autonomic (cardiovascular tests) and peripheral neuropathy [current perception threshold (CPT) testing at 2000, 250 and 5 Hz on median and peroneal nerves] and clinic blood pressure were carried out in every patient.
Results: The fibrinogen genotypes were distributed in patients as follows: 75 (56%) GG, 51 (38%) GA, 8 (6%) AA. A similar distribution occurred in the control group: 57 (57%) GG, 37 (37%) GA, 6 (6%) AA. No difference was found regarding clinical parameters, subclinical nephropathy, retinopathy, autonomic neuropathy and mean systolic and diastolic blood pressure in the three groups. However, patients with GG genotype had higher CPT values on the peroneal nerve than patients with GA or AA genotypes [median (IQ range) 3.9 (2.9–5.3) vs. 3.3 (2.3–4.4) and 2.8 (2.1–3.9); $p = 0.016$]. Eleven patients in the GG group had abnormal CPT result compared with one patient in the GA and no patient in the AA group ($p = 0.0121$). GG genotype represented an independent risk of having peripheral nerve dysfunction as compared with the combined cohorts of GA and AA genotypes (adjusted RR [95% CI]: 6.5 [1.9–10.9], $p = 0.011$).
Conclusion: Patients with type 1 diabetes do not differ from the non-diabetic population regarding the polymorphism of the beta-fibrinogen gene. This polymorphism is independently associated with peripheral nerve abnormality. GG genotype carriers could have an increased risk of sensory peripheral neuropathy.

PP 102

Patients with type 1 diabetes diagnosed in childhood or adolescence have more advanced preclinical coronary atherosclerosis than non-diabetic controls

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Introduction: Little is known about preclinical stages of atherosclerosis in the coronary arteries of type 1 diabetes (T1DM) patients. In the present study we have evaluated the atherosclerotic burden in a group of T1DM patients without symptoms of coronary artery disease compared to controls.
Methodology: Using intravascular ultrasound (IVUS) we performed quantitative analysis of coronary segments in 29 TIDM and 29 non-diabetic age and sex matched controls. Mean age of patients was 43.4 years, mean age at diagnosis of diabetes was 12 years. Mean HbA1c during 18 years prior to the IVUS examination was 8.3%. BMI was 24.7 kg/m^2, mean blood pressure was 129/79 mmHg and they had near to normal lipid profiles.
Results: Mean % plaque area (PA) was greater than 30% in 71% of the patients and in 33% of the controls ($p < 0.0001$). Mean plaque thickness (PT) was 0.59 mm ± 0.38 in patients and 0.44 mm ± 0.30 in controls ($p < 0.0001$). Maximal PT was greater than 0.5 mm in 47% of the diabetic segments vs. 30% of the control segments ($p < 0.0001$). Mean % PA was 34.0 ± 13.3 in patients and 24.5 ± 10.5 in controls ($p < 0.0001$). Mean lumen area was 8.6 mm^2 ± 3.8 in patients and 12.1 mm^2 ± 4.3 in controls ($p < 0.0001$) and mean vessel area was 13.2 mm^2 ± 5.3 vs. 16.2 mm^2 ± 5.5 ($p < 0.0001$).
Conclusion: The present data show that T1DM patients diagnosed before adulthood have an accelerated atherosclerotic process already in the asymptomatic phase of the disease suggesting a need for earlier preventive measures.

DKA – Hypoglycaemia

PP 103

Morbidity, mortality and cost associated with diabetic ketoacidosis (DKA)

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In the U.S. population, DKA affects 29% of children at diagnosis of diabetes and subsequently 8 out of 100 patients every year. Current spectrum of co-morbidity, mortality and cost of DKA is largely unknown. We analyzed 420 admissions for DKA in children aged 0–18, at The Children's Hospital in 1/1/99–6/1/03. Most (68%) of the patients were hospitalized; the remaining 32% were seen only in the Emergency Department (17% for a short visit and 15% for observation/treatment shorter than 24 h). Children were of non-Hispanic white (65%), Hispanic (20%), African American (10%) or other ethnicity (5%). Under-insurance was present in 29% (23% had indigent coverage, 6% had no insurance). Half of the DKA events occurred at diagnosis (n = 211) while 209 events occurred later, in 133 established patients. Characteristics of these two types of DKA admissions are compared:

	DKA at diagnosis of diabetes (N = 211)	DKA in established diabetes (N = 209)	p-value
Median age, yr	8.0	14.7	<0.0001
Gender, % females	45%	62%	0.0007
Under-insurance, %	28%	37%	0.004
Race, % minorities	26%	39%	0.003
Median cost, $ (range)	$9106 ($325–582 184)	$ 6282 ($581–112 788)	<0.0001
Length of stay, days (range)	2 (0–61)	1 (0–15)	<0.0001
Co-morbidities, N (%)	74 (35%)	121 (58%)	<0.0001
Cerebral edema, N (%)	4 (1.9%)	4 (1.9%)	NS
Mortality, N (%)	2 (0.9%)	0	NS

DKA events in established patients affected more often older children, females, under-insured, and minorities than DKA at diagnosis. Despite lower prevalence of significant co-morbidities and our policy of early discharge and outpatient onset education, DKA admissions at diagnosis were more costly and longer then those in established patients. Cerebral edema and mortality were infrequent in both groups. DKA remains a significant problem in children with newly diagnosed and established diabetes.

PP 104

Risk factors for diabetic ketoacidosis at onset and during the course of type-1-diabetes: multicenter analysis based on 20201 pediatric patients from 154 German/Austrian centers participating in the DPV initiative

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Background: DKA at onset reflects the awareness of diabetes among pediatricians/communities, while the subsequent rate of DKA is an indicator for the quality of care and patient compliance/empowerment.
Methods: 152 German and 2 Austrian centers, providing acute diabetes care, participate in the DPV-Science initiative. Up to 5/2004, the total number of T1DM patients documented was 20201.
Results: At onset of diabetes, any degree of DKA (pH < 7.3) was present in 20% of subjects, while severe DKA (pH < 7.1) was present in 5%. DKA was more prevalent in young patients (<5 years, $p < 0.0001$). During the time-span 1995–2003, the percentage of patients presenting with DKA was stable. A strong relationship between the degree of DKA and the length of initial hospitalisation was present (no DKA: 14.2 days, DKA with pH < 7.1: 17.5 days, $p < 0.0001$). Initial insulin requirement was higher and duration of remission shorter in patients presenting with DKA. During the subsequent course of diabetes, the frequency of acute hospital admission due to hyperglycemia and/or DKA was 4.2 events/100 patient-years. When events with documented DKA (pH < 7.3) were evaluated separately, the rate was 2.7/100 pat.-years (severe DKA with pH < 7.1: 1.1 events/100 pat.-years). Pubertal age ($p < 0.0001$), female gender ($p < 0.001$) and foreign nationality ($p < 0.02$) were significant risk-factors for acute admission due to hyperglycemia/DKA during the course of diabetes. On average, hospitalisation lasted for 6.7 days. Two deaths due to DKA/cerebral edema are recorded in the database (age/duration: 18.2/12.9 years and 18.6/5.6 years), however underestimation in the registry is possible.

Conclusion: In Germany/Austria, DKA at onset is present in 20% of pediatric patients and related to younger age at onset. In contrast, in our survey, DKA during the course of diabetes was considerably less frequent compared to reports in the literature from other parts of the world. Most cases of DKA during therapy occurred in adolescence.

PP 105

The accuracy of clinical assessment of dehydration, during diabetic ketoacidosis in childhood

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Introduction: Our objective was to examine the accuracy of the assessment of clinical dehydration in children with type 1 diabetes and diabetic ketoacidosis (DKA).

Methodology: A total of 37 children with type 1 diabetes and DKA were assessed in our emergency department regarding their hydration status. Clinical hydration assessment was carried out by two independent medical staff at the time of presentation. An absolute measure of hydration was calculated retrospectively by subtracting the admission weight from the discharge (rehydrated) weight. The accuracy of clinical assessments was then evaluated.

Results: The mean value for measured dehydration was 8.7%. There was good agreement in the clinical assessment of dehydration between the two assessing doctors (kappa value = 0.5), but no agreement between clinical assessment and measured dehydration (kappa value = 0.05). In patients who were <6% dehydrated (measured) the trend was to overestimate dehydration, whereas in patients >6% dehydrated (measured) the trend was to underestimate dehydration. Seventy percent (26/37) of the patients had their hydration status incorrectly assessed by the primary assessing doctors, 24% (9/37) overestimated and 46% (17/37) underestimated.

Conclusion: Clinical assessment of dehydration in DKA in children shows good inter-observer consistency, however such assessment often bears little relationship to the actual hydration of the patient. Our data suggest that in general the degree of dehydration in DKA is poorly estimated by clinical assessment. For patients presenting with DKA an estimate of 7–9% dehydration should be used to estimate fluid requirements.

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Reduction of hypoglycemic episodes and improvement of fasting glycaemia in type 1 diabetic children treated with insulin glargine

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Introduction: In paediatric age it is very difficult to solve the problem of fasting hyperglycaemia and nocturnal hypoglycaemia. Insulin glargine is absorbed slowly and has a prolonged action period of 24 hours (without peak). According to recent studies, it can provide good glycemic control with a reduced risk of hypoglycaemia.

Aim of the study: To evaluate the effectiveness of insulin glargine in children and adolescents with type 1 diabetes.

Patients and Methods: 65 patients (31 M, 34 F), aged 2.5–18.2 years (10.1 ± 4.2 yrs), with normal body weight (BMI SDS: 0.5 ± 1.2) and diabetes duration >1 year (5.3 ± 2.7 years), on intensive insulin therapy (rapid insulin before meals and NPH insulin at 10.30 p.m.). NPH insulin was replaced with insulin glargine at bedtime (once-daily) in all patients. Follow-up: 0.3–3 years (0.9 ± 0.5 years). Insulin requirement, BMI, HbA1c, mean fasting glucose and hypoglycaemic episodes (<60 mg/dl) per month, were evaluated before and during glargine treatment.

Results: A significant reduction in the number of hypoglycaemic episodes/month ($p < 0.0001$), fasting glycaemia ($p < 0.0001$) and insulin requirement ($p < 0.05$) was found. We did not find either any significant improvement in HbA1c levels, or a change in body weight.

	with NPH	with Glargine	*t*-test
Insulin requirement (IU/kg/day)	1.0 ± 0.2	0.92 ± 0.2	$p < 0.05$
HbA1c (%)	8.3 ± 1.1	8.2 ± 1.0	n.s.
BMI (SDS)	0.5 ± 1.2	0.5 ± 1.3	n.s.
Hypoglicaemic episodes/month (<60 mg/dl)	9.04 ± 6.1	6.0 ± 5.6	$p < 0.0001$
Fasting glycaemia (mg/dl)	237.4 ± 65	146.5 ± 31	$p < 0.0001$

These data were also confirmed when testing patients based on two parameters: age at the beginning of glargine treatment (<6 years, 6–12 years, >12 years) and duration of glargine treatment (<6 months, 6–12 months, >12 months).

Conclusions: Although HbA1c levels did not improve, glargine therapy caused a better glycemic stability for the whole day and in particular it reduced non-severe hypoglycaemic episodes and fasting glycaemia. Further studies can indicate which subjects will benefit by this therapy and if it is possible to improve the metabolic control for a long time.

PP 107

It is possible to prevent nocturnal hypoglycaemia (NH) with CGMS in paediatric age?

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Aim: To evaluate if the periodic use of CGMS allows to prevent nocturnal hypoglycaemia (NH) without impairing metabolic control.

Methodology: Multicentre study in 95 children and adolescents with diabetes was made (sex: F58/M37, age: 11.60 ± 3.42; evolution time: 5.56 ± 3.2 years; BMI 19.38 ± 3 kg/m2; insulin dose: 0.90 ± 0.27 UI/Kg/day, doses/day 3.35 ± 0.78, HbA1c-*SDS:* 6.16 ± 3). The children carried the CGMS during out-patient conditions in two different moments (V1 and V2) separated by 2.5–3 months. Metabolic control was evaluated by the haemoglobin A1c. We defined that CGMS was useful to prevent NH if in the V2 there was either lower number of children with NH or the NH events, or if their duration was shorter.

Results: In 106/295 nights NH was found in V1 and 63 children were affected (66.3%). The number of NH events was 162. Average duration of NH was 103.1 ± 83.7 min. In V2, 23/63 children (36.5%) did not have NH again (**G2**) ($p < 0.000$). Of the 40 patients who had NH again in V2 (G1), the number of nights with NH per child (1.8 ± 0.91 vs. 1.76 ± 0.90) (V1 vs. V2), the number of NH events (2.76 ± 1.78 vs. 2.66 ± 2.22) and its total duration were similar. There were no differences neither in demographic characteristics nor in the insulin treatment between children with or without NH in V2. There was a lineal correlation between NH and better metabolic control.

Table 5. Metabolic Control per Groups and Visits

GROUP (number)	Hb A1c (%) V1 vs. V2	Hb A1c-SDS V1 vs. V2*
G1 (40)	7.54 ± 1.37 7.46 ± 1.31	5.53 ± 3.07 5.37 ± 2.76
G2 (23)	7.62 ± 1.32 7.80 ± 1.22	5.95 ± 3.48 6.14 ± 2.99

*P < 0.05

Conclusions: The study demonstrates that better metabolic control is associated with the increased in NH. The periodic use of the CGMS is not able to prevent nocturnal hypoglycaemic in every children with type 1DM.

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Blood β hydroxibutirate measurement in children with T1D on CSII

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Introduction: Diabetic ketoacidosis (DKA) is a potentially serious complication in children with T1D using CSII. Elevation of β hydroxibutirate (β OHB) in capillary blood is an early sign of DKA. We tested the impact of β OHB measurements on decision-making in patients using CSII.
Methodology: 62 children and adolescents (7–16 years old) using CSII were investigated. Urine ketones (Ketodiabur, Roche) and β OHB in the capillary blood (OPTIUM, Medisense) were determined whenever the blood glucose was above 15 mmol/L. 288 such measurements were independently evaluated by 4 diabetologists initially blinded for β OHB, and subsequently knowing β OHB and urine ketones. Chi square test was used for the analysis.
Results: 1155 decisions were analysed. No statistically significant differences were found between decisions made with our without the information on β OHB when all measurements were pooled. When 200 decisions with initial β OHB >0.4 mmol/L were analysed separately, statistically significant differences were found in the decisions regarding insulin application form ($p < 0.0001$) and insulin set replacement ($p = 0.015$).
Conclusion: Determinations of β OHB in blood influenced the decision making in routine treatment of patients using CSII, increasing the safety and reducing the treatment intensity and costs.

Table 1. Decisions with initial β OHB >0.4 mmol/l.

	Insulin application		Insulin bolus		Freq. of BS test		Fluid replacement		Insulin set change	
	Pen	Pump	Standard	0.1 U/kg	1 hour	2 hour	Ent.	i.v.	Yes	No
Urine ketones only	112	88	101	99	189	11	147	53	90	110
β OHB and Urine ketones	66	134	97	103	182	18	155	45	65	135
P value	<0.0001		NS		NS		NS		=0.015	

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Continuous influence of ethnicity on metabolic control and acute complications in children and adolescents with diabetes mellitus type 1 (T1DM). In Germany and Austria. Results of a multicenter study

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Introduction: The influence of ethnicity on metabolic control in T1DM is well known. Despite educational and psychological interventions there is only small progress in this problem. So, we wanted to study, if metabolic control improved and acute complications are less frequent now.
Methodology: Data from 91 German and 2 Austrian pediatric diabetes centers were available for further investigations. Patients with an age <18 years and a diabetes onset <15 years and a duration of >1 year were included in the study. At the end of March 2004 anonymised data of n = 10327 patients were collected locally and sent for central statistical analysis to Ulm. HbA1c-values were mathematically transformed and corrected to the DCCT-standard (normal 4–6%).
Results: 509 patients (4.4%) had two parents born abroad. 179 children and adolescents had one German/Austrian and one parent of foreign descent compared to 9640 German/Austrian patients. The 3 groups were not different for sex and age of manifestation. German/Austrian patients injected insulin more often per day compared to the patients of foreign origin: 3.86 vs. 3,81 injections/day, $p < 0.04$. The insulin-dose per kg body weight in the latter group was lower with a median of 0.84 in contrast to the Germans/Austrians with 0.88 E/kg, $p < 0.02$. HbA1c was higher in patients of foreign origin compared to their peers: 8.1 vs. 7.96%; multivariant model: $p < 0.02$. On the other hand despite poorer control the rate of severe hypoglycemia (unconciousness/seizure) was higher for patients of Non-German descent: 5.8 vs. 4.3 events per 100 pat.-years ($p < 0.01$). Patients of foreign descent were readmitted to the ward more often than Germans/Austrians: 0.43 vs. 0.38 /year, $p = 0.06$.
Conclusion: Ethnicity still has a major impact on metabolic control in children and adolescents with diabetes mellitus type 1 in Germany/Austria. Contributing factors have to be examined in prospective studies.

PP 110

Incidence and pattern of hypoglycemic events in children and adolescents with type 1 diabetes during diabetes camps

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Introduction: Aim of this study is to investigate pattern of hypoglycemic events (HE) in children and adolescents with type 1 diabetes during educational diabetes camps (EDC) in Belarus.
Methodology: We analyzed the records of 108 children and adolescents with type 1 diabetes participating in EDC in 2001–2003 yrs (M/F 48/60, mean age 11,9 ± 0,18 yrs: M/F 11,7 ± 0,17/12,1 ± 0,2 yrs, mean diabetes duration 3,8 ± 0,31 yrs: M/F 4,3 ± 0,35/ 3,4 ± 0,29 yrs). The records indicated 6–7 blood glucose values per day for about 10 days of every EDC, changes in doses of insulin, carbohydrates intakes. All episodes of hypoglycemia (HG) were confirmed by medical staff and leaders with glucose meters set for whole capillary blood. We evaluated the number of HE during the first and second parts of camps and changes in insulin doses. The prevalence of different types of HG was estimated.
Results: Mean incidence of HG at camps was 0.61 ± 0.04 hypoglycemic events per child per one day (HE/child/day) without statistical difference between males and females. HG did not occur often at the beginning of camps. But incidence of HG during the second part of camps was significantly higher compared with first part (0.68 ± 0.05 vs. 0.52 ± 0.05 HE/child/day, $p < 0.05$) with higher frequency in males then in females (0.78 ± 0.06 vs. 0.61 ± 0.05 HE/child/day, $p < 0.05$). Insulin doses in campers were increased at the beginning of camps in comparison with doses at home to attain good metabolic control and had slight increase during the second part of camps achieved statistical difference (at home 0.89 ± 0.2 U/kg/day, first part 0.93 ± 0.02, second part 0.95 ± 0.02, $p < 0.05$). Changes in doses were similar in males and females. HG with blood glucose less 3 mmol/l was noticed in 33.7% of all HE and HG with pronounced rebound phenomenon was

detected in 5,6% of HE with same frequency in males and females. Night time HG occurred in 13.5% of HE more often in females (18.7% vs. 7.6% in males, $p < 0.05$). There was one case of severe HG in a boy (0.12% HE). Marked damn phenomenon was evident in 18 children (16,6% of campers) M/F 3/15, age M/F 12.1 ± 0.21/12.6 ± 0.18 yrs.

Conclusion: Results of this study showed the pattern of increasing incidence of HE towards the second part of camps reflecting improvement in insulin sensitivity. Intensive education is necessary to minimize HE while improving diabetes control.

PP 111

Increased incidence and severity of diabetic ketoacidosis among uninsured children with newly diagnosed type 1 diabetes

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This study analyzed pediatric subjects at the time of initial diagnosis of type 1 diabetes (T1DM) with two objectives: 1) to determine the incidence and severity of diabetic ketoacidosis (DKA), and 2) to stratify these subjects according to insurance status. The subject population included all children less than 18 years who presented with new onset T1DM from June to December 2003 and were subsequently followed at the Barbara Davis Center. The insurance status was collected on all subjects, and the initial pH was collected on subjects who presented to an emergency department and/or were admitted to the hospital. Overall, 359 patients presented with new onset T1DM. Forty-three (12.0%) of these children had no insurance. One hundred two (28.4%) subjects presented with DKA. When stratified by insurance status, 26 (60.5%) of the 43 uninsured subjects presented with DKA compared to only 76 (24.1%) of the 316 insured subjects, $p < 0.001$, OR = 1.5. Further stratification based on pH severity revealed that uninsured subjects tended to present with more severe DKA than subjects with insurance (table). The proportions among the most life-threatening DKA (most severe pH ≤ 6.90) included 7 (26.9%) of 26 uninsured subjects compared to 7 (9.2%) of 76 insured subjects, $p = 0.04$.

Subjects with DKA, according to severity and insurance status

Insurance Status	Venous pH: <7.10	Venous pH: 7.10–7.19	Venous pH: 7.20–7.29	No DKA
Insured (incl. medicaid) N = 316	25	26	25	240
Uninsured N = 43	13	8	5	17

Chi-square test for trend, $p = 0.09$

In conclusion, subjects without insurance were more likely to present at the time of initial diagnosis with DKA than subjects with insurance. Furthermore, when the subjects without insurance presented with DKA, the condition tended to be more severe and life-threatening, as indicated by a lower initial pH. A potential explanation is that subjects without insurance may delay seeking timely medical care and therefore present more critically ill, whereas subjects with insurance may have their T1DM diagnosed earlier. This has public health implications as the United States debates universal health coverage, as modeled in the international community.

PP 112

The impact of a decade of changing treatment on rates of severe hypoglycemia in a population-based cohort of children with type I diabetes

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Introduction: The last decade has seen improved understanding of the pathophysiological mechanisms leading to hypoglycemia in T1DM. Along with this, treatment approaches have also changed dramatically. We report the impact of changes to treatment on the incidence of severe hypoglycemia and its risk factors in a large population based cohort of children with type 1 diabetes.

Methods: The cohort consisted of 1335 children (age 9.5 ± 4.3 years, mean ± SD) yielding 6928 patient years of data. Prospective assessment of severe hypoglycemia (an event leading to loss of consciousness or seizure) and associated clinical factors and outcomes was made between 1992–2002. Patients were reviewed every three months. Data were analysed using the negative binomial regression model.

Results: A total 944 severe events were recorded. The incidence of severe hypoglycemia increased significantly by 29% per year for the first 5 years but appeared to plateau over the last 5 years. The overall average HbA1c significantly reduced (by 0.2% per year) over the whole follow-up period. An increased risk of severe hypoglycemia was associated with lower HbA1c, younger age, male sex and lower parental socio-economic status. Of insulin therapies only pump treatment was associated with reduced rates of severe hypoglycemia.

Conclusions: Severe hypoglycemia remains a major problem for children and adolescents with Type 1 diabetes. These data suggest however that recent approaches to therapy may be allowing a degree of improved control without the expected increased risk of severe hypoglycemia.

PP 113

Can cerebral oedema be identified before the reduction in conscious level?

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Introduction: To determine whether, in cases of cerebral oedema during treatment for DKA, there is any evidence of raised intracranial pressure before the clinically recognised onset of acute brain swelling.

Methodology: 44 children (ages 1–16, mean 8.9 years) were identified as having an episode of cerebral oedema (CO) as part of a large prospective case–control study. Heart rate (HR), systolic and diastolic blood pressure (SBP and DBP) were recorded from the start of fluid treatment until the cerebral oedema event (reduced conscious level plus other evidence of raised intracranial pressure); sufficient data were available before the event in 26/44 cases. HR and BP records were available from 60 of 212 control children from the same study (with DKA but no CO), and clinical course was examined in a random selection of 30 controls.

Results: Headache was a feature during treatment in 10/44 cases and 0/30 controls ($p = 0.004$). In 5 of the cases headache occurred 2–12 hours before the event, and before respiratory arrest and death in 2 of these. A fall in HR from maximum (max) at admission to less than 70% max occurred in 11/26 cases and 2/60 controls at some time during the 6 hours before the event or equivalent time ($p < 0.0001$). The lowest HR in the cases during the 6 hours before the event was 73 ± 18% of maximum; in controls, it was 84 ± 8% ($p = 0.002$). There was no change in SBP or DBP before the event in the cases; a gradual fall during treatment was seen in cases and controls.

Conclusion: During treatment of DKA, a fall in HR and the presence of headache are associated with later development of CO. If either of these should occur, treatment with mannitol or hypertonic saline may prevent CO and subsequent death or disability.

Obesity – Type 2 diabetes

PP 114

Reproducibility of OGTT in obese children

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Introduction: The number of obese children with insulin resistance and type 2 diabetes is increasing rapidly. Therefore, more oral glucose tolerance tests (OGTTs), with glucose and insulin are being conducted for children, as gold standard clamp testing or IVGTT are invasive and unsuitable for clinical settings. This study aims to assess the reproducibility of OGTT results in obese children with insulin resistance.
Methodology: 17 obese children (9 to 16 years) attending the Obesity Clinic at Princess Margaret Hospital for Children in Western Australia each had 2 OGTTs, eight weeks apart. All children were instructed to maintain their current lifestyle patterns (diet and exercise) during this time. OGTTs were performed under standard conditions with 1.75 g/kg of glucose (max 75 g) after a 12 hour fast.
Results: At all time points (0, 60 and 120 mins), insulin and glucose were higher and had a greater standard deviation at the second OGTT, except for fasting glucose. There was a significant difference at all time points for insulin and glucose between the two OGTTs ($p < 0.05$). HOMA-IR modelling for insulin resistance and HOMA-B modelling for β-cell function also showed a significant difference between the 2 testing periods. QUICKI was not significantly different.
Conclusion: During an 8 week control period, results from OGTTs revealed significantly poor reproducibility. The use of these tests to assess children's insulin resistance and changes over time with or without intervention must be seriously questioned. The use of HOMA and QUICKI rely heavily on fasting insulin and glucose results respectively, so their usefulness in individuals or for monitoring changes is limited. With the increase in overweight and obesity in our paediatric population, better simple measures of insulin resistance need to be developed.

PP 115

Hyperinsulinaemia and response to metformin in non-diabetic obese children and adolescents

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Introduction: Despite the rising prevalence of obesity in childhood, there is little consensus on whether pharmacological interventions are justified in children. On the basis of brief randomised trials, Metformin is being increasingly used in those with abnormal glucose/insulin homeostasis. However, there is little data on the long-term outcomes of, or predictors of response to, metformin, in clinical situations.
Methodology: We prospectively identified 157 obese (BMI ≥95th centile) children and adolescents undergoing an oral glucose tolerance test (OGTT; 1.75 mg of glucose/kg) since 2001, of whom 74 (47%) continued to have clinical follow-up. All subjects subsequently received standard dietetic education. Metformin (low dose <1 g/day or high dose 2 g/day) was used in those with fasting hyperinsulinaemia and/or hyperinsulinaemia during the OGTT. Hyperinsulinism was defined by pubertal stage: prepubertal ≥15 mU/L; mid-puberty ≥30 mU/L; post-puberty ≥20 mU/L. Responders to metformin were defined a priori as those with reduction in BMI ≥0.1 SD.
Results: 26 (35%; 21 females) subjects had been treated with metformin (mean age 13.2 yr, range 4.6–18 yr). Controls: n = 48; 37 females; mean age 11.0 yr. Mean BMI z-score at baseline was not significantly different between groups. Those in the metformin group had significantly lower BMI at 12 months, falling 0.4 SD (SE 0.2) compared with a fall of 0.2 SD (SE 0.05) in controls ($F = 7.3$, $p = 0.01$). Response to metformin was greatest in those with fasting hyperinsulinism, with mean BMI reduction of 0.4 SD compared with 0.07 SD in those in the metformin group with normal fasting insulin. Sex, age, pubertal stage, ethnicity, presence of acanthosis, BMI before treatment and metformin dose were not associated with response.
Conclusions: Benefits of metformin in reduction of BMI in obese non-diabetic children and adolescents are maintained at 12 months. Those with fasting hyperinsulinaemia appear more likely to benefit than those with post-prandial hyperinsulinaemia.

PP 116

Survey of current medical treatments for childhood-onset type 2 diabetes mellitus in Japan

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Introduction: The prevalence of childhood-onset type 2 diabetes mellitus has increased dramatically over the past two or three decades in Japan. Medication for children with type 2 diabetes has not been approved by the Ministry of Health, Welfare and Labor, and the information on antihyperglycemic agents is insufficient. This survey was conducted to elucidate the current use of antidiabetic medication in children with type 2 diabetes and the efficacy, safety, and problems associated with the use of these agents in Japan.
Methodology: Clinical data sheets were sent to the councilors of the Japanese Society for Pediatric Endocrinology and the members of the Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes in June 2003. Clinical data on 259 children (younger than 18 years of age; 121 males and 138 females) with type 2 diabetes treated at 42 medical centers throughout Japan were received between June 2003 and September 2003 and analyzed. 170 subjects (66%) were diagnosed through school-age screening for glycosuria.
Results: 94 males (78%) and 86 females (63%) were obese at the time of diagnosis. 172 subjects (66%) were treated using antihyperglycemic agents. α-GI was the most popular antihyperglycemic agent, followed by insulin, metformin, SU, and nateglinide. Metformin was mainly prescribed for children with a higher HbA1c and higher relative overweight. The HbA1c level of the 14 subjects who received only metformin decreased from 9.1 ± 1.9% to 6.7 ± 1.3% without a significant improvement in obesity. Three cases of adverse events were reported, but causal relations with metformin were not clear.
Conclusion: α-GI, insulin and metformin were mainly prescribed to childhood-onset type 2 diabetes patients in Japan. This survey suggests that metformin is safe and effective for the treatment of type 2 diabetes in children. Further study is needed for a higher dosage (1500 mg) of metformin in children.

PP 117

Diagnosis of diabetes mellitus in Japanese children and adolescents using new diagnostic criteria of OGTT for diabetes mellitus

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Introduction: To attempt to clarify the adequacy of the new diabetes criteria (ADA and WHO) to diagnose diabetes mellitus in children with less severe symptoms of diabetes.
Subjects and Methods: This was a nation-wide project of the Study Group of Research on Children and Families led by the Ministry of Health, Labour and Welfare in Japan. OGTT data were collected from 418 subjects with positive urine glucose detected by urine glucose screening at school. OGTT was performed using 1.75 g/kg (max. 75 g) glucose. HbA1c values were also assessed for diagnosing diabetes mellitus.
Results: Fasting plasma glucose (FPG) and 2-hour post-load glucose (2hPG) showed a significant positive correlation ($r = 0.880$, $p < 0.01$). 304 subjects (72.7%) were normal and their average HbA1c value was 4.8 ± 0.5%. 78 subjects (18.7%) were consistent with a diagnosis of diabetes based on both FPG or 2hPG criteria. Their HbA1c value was 8.5 ± 2.4%. However, 23 of 78 patients (37.1%) with diabetes mellitus diagnosed with the criteria of 2hPG did not coincide with the criteria of FPG. 36 subjects (8.6%) were IGT and their average HbA1c value was 5.4 ± 1.0%. 71 patients with diabetes were type 2 diabetes, and basal insulin level was determined in 56 patients out of 71 patients. Obese males and females showed significant increased insulin resistance assessed by basal insulin levels and HOMA index.
Conclusion: This study shows that the specificity of FPG is significantly high. However 2hPG is much more sensitive to diagnose diabetes mellitus in Japanese children and adolescents. OGTT should be performed in patients with positive urine glucose who show normal fasting blood glucose. Two thirds of type 2 diabetes patients show Increased insulin resistance.

PP 118
Childhood obesity and insulin resistance

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Introduction: The increasing incidence of childhood obesity over the last decade, led to the appearance of type 2 Diabetes Mellitus(DM2) in children as well. It appears that obesity constitutes the most serious risk factor for the initial metabolic disturbance in the course of DM2, that is insulin resistance.
Aim: To evaluate the frequency of appearance of insulin-resistance in the obese children as well as factors influencing its onset, in order to estimate their risk to develop DM2.
Methodology: Seventy four euthyroid children (47 girls), overweight or obese,of mean age 10.15 years, were assessed. Calculated insulin-resistance indexes included fasting Glu/ins <6 and HOMA-IR >2.5. Comparison was accomplished between the group with insulin-resistance and the one without, as for age, duration of obesity, body mass index(BMI), family history of DM2 and lipid levels.Eventual correlation of Glu/ins ratio with BMI and duration of obesity was estimated through Pearson's correlation test.
Results: The duration of obesity in children was 6.78 ± 2.3 years.Their mean BMI was 28.47 ± 5.5, mean Glu/ins 6.65 ± 5.7 and HOMA-IR 6.92 ± 4.72. Half of them were insulin-resistant,according to both indexes. 41.62% had either a 1st or 2nd degree relative with DM2. Glu/ins ratio correlated significantly with BMI ($r = -0.74$, $p < 0.001$) as well as with duration of obesity ($r = -0.42$, $p = 0.032$). Children with insulin-resistance compared to those without, showed significant difference as for duration of obesity ($p < 0.01$), BMI ($p < 0.003$), age ($p = 0.024$), total cholesterol ($p = 0.004$) and triglyceride ($p = 0.01$) levels. Contrary, they didn't differ significantly as for percentage of positive family history or HDL and LDL levels.
Conclusions: A high percentage of obese children shows insulin resistance, which though leading to DM2, yet is reversible at onset.Thus,it should be searched for with simple methods in obese children for promoting early intervention. Besides, insulin-resistence, usually detected at peripubertal age, correlates strongly with BMI and duration of obesity, revealing that prevention regarding dietary habits and physical exersice should be inforced early in life.

PP 119
Changing clinical profile of diabetes mellitus in children from North India

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Introduction: An increase in the prevalence of type 2 DM is clearly evident among children and adolescents. There is evidence that recognized major risk factors for type 2 DM like obesity is currently prevalent in youth and have recently increased. Aim of our study is to evaluate clinical profile of diabetes in children.
Methodology: We have studied the clinical profile of 16 consecutive patients of diabetes in young presented to our center over a period of 30 months.
Results: Eight (50%) patients were diagnosed as type 1 DM, 6 (37.5%) patients had type 2 DM, 1 patient was a case of Fibrocalcific pancreatic diabetes and 1 had secondary diabetes due to Cushing Disease. In type 1 DM mean age was 13 ± 3 years, mean BMI was 20 ± 3.8 kg/m^2 and insulin level was low in all patients. One patient presented in ketoacidosis. In type 2 DM mean age was 16 ± 3 years, mean BMI was 26 ± 2.8 kg/m^2, and insulin levels was high normal in all. Five patients had family history of diabetes. One patient was a case of Down syndrome and one had transient diabetes during fever. Four patients are doing well on oral hypoglycemic and 2 are on life style modification only. On average follow of 12 months no patient had complications. One patient with FCPD presented with severe osteomalacia and mild ketosis.
Conclusion: Type 2 DM is an emerging problem in India and can be managed with oral hypoglycemic agents. It is prudent to suspect type 2 DM in children.

PP 120
Association between uncoupling protein 2 gene polymorphism and obesity in children and adolescence

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Introduction: The etiology of obesity in children and adolescents has not been completely understood. Some investigations reported, the exon 8-ins/del polymorphism of uncoupling protein 2 (UCP2) gene seems to play a role in the occurrence of obesity, and to investigate the relationship between a 45 bp insertion/deletion (ins/del) polymorphism in the 3′-untranslated region of exon 8 of uncoupling protein 2 (UCP2) gene and obesity in Chinese children and adolescence.
Methodology: UCP2 gene ins/del polymorphism is assayed by PCR in 203 obesity (age 12.64 ± 2.92 years) and 230 normal-weight (age: 12.95 ± 1.01 years) subject.
Results: The UCP2 exon 8 variant is confirmed in two groups by PCR and nucleotide sequencing. The insertion homozygote is found to be a 45 bp insertion in the 3′-untranslated region, which is a duplication following the same 45 bp. In the deletion homozygote the duplication is not present. 256 subjects have del/del, 72 subjects have ins/del, 5 subjects have ins/ins. The 'D' allele frequencies are 90.4% and 90.6% for

normal-weight subject and obesity subject, respectively, and 9.6% versus 9.4% for the 'I' allele. The frequency of the 45 bp ins/del genotype and allele of UCP2 gene does not show any significant difference between obesity and normal-weight subject (genotype: $\chi^2 = 1.74$, P = 0.44, allele: $\chi^2 = 0.01$, P = 0.92). Weight and BMI does not show any significant difference between 'D' allele and 'I' allele also.
Conclusion: The insertion/deletion polymorphism in the 3′-untranslated region of exon 8 of uncoupling protein 2 (UCP2) gene is not related to obesity in Chinese children and adolescence.

PP 121

Indices of insulin sensitivity and secretion based on fasting data in comparison with parameters from the minimal model analysis; the impact of various metabolic involvements on indices

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Introduction: To evaluate the usefulness of several fasting indices of insulin sensitivity and secretion in children and adolescents with various metabolic involvements in comparison with parameters by the minimal model (MM) analysis as one of gold standards.
Methodology: Forty-seven obese and 82 type 2 diabetes (T2DM) children and adolescents underwent the MM analysis. In T2DM normoglycemic sub-group was defined by FPG <100 mg/dl and HbA1c <5.8%. Regarding insulin resistance, SI (insulin sensitivity) by MM was compared with HOMA model of insulin resistance (HOMA-R), quantitative insulin sensitivity check index (QUICKI), fasting glucose to insulin ratio (FGIR), and fasting insulin (Ib). Regarding insulin secretory function, AIR (acute insulin response) by MM was also compared with HOMA of beta-cell function (HOMA-B), FGIR, and Ib. The degree of P value in linear regression was represented by A (<0.001), B (<0.005), C (<0.01) and D (<0.05).
Results: No difference was shown in SI, HOMA-R, QUICKI and Ib between obesity and T2DM groups. In obese children, SI showed significant correlations with FGIR (A), QUICKI (A), Ib (A) and HOMA-R (A): AIR correlated with HOMA-B (A) and Ib (A) and FGIR (B). In T2DM, SI showed weaker correlations with QUICKI (C), HOMA-R (D) and Ib (D): AIR showed high correlations with HOMA-B (A), Ib (A) and FGIR (B), while in the hyper-glycemic sub-group AIR showed only weak correlation with Ib (D) and not with FGIR. In all patients together, SI showed a significant correlation with QUICKI (A), Ib (B), HOMA-R (B) and FGIR (D); AIR showed a significant correlation with HOMA-B (A) and FGIR (A) and Ib (B), where FPG or HbA1c was inversely correlated with AIR.
Conclusion: The usefulness of the several fasting indices of insulin sensitivity and secretion has been noted in children and adolescents with various metabolic involvements. However we need caution in the fasting indices, when applied to T2DM patients, especially hyperglycemic state.

PP 122

Lean teenagers but high prevalence of obesity and diabetes in adults of three remote Aboriginal Communities of Western Australia

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Background and aims: Transition from the hunter-gatherer lifestyle has led to a high incidence of obesity and type 2 diabetes in Australian Aboriginals, with overall prevalence estimated at 10–30%. Diabetes and its sequels are a main cause of premature mortality in Australian Aboriginals.
Materials and methods: As part of a community based intervention project, 479 residents (11–76 yr) of three remote Australian Aboriginal Communities were screened for diabetes and obesity. Basic assessment included medical history, physical examination, and laboratory investigations. Diabetes prevalence was determined using WHO and ADA criteria.
Results: Diabetes prevalence in the three communities was 33%, 32%, and 32%, respectively. The overall prevalence was 32.2%. There were no gender differences in prevalence. Median age of the diabetes individuals was 45.7 yrs (range 24.8–76.3 yrs). 60% of the adults were overweight or obese, whereas 13.8% of the children were overweight. The average individual became overweight (Western BMI standards of >25 kg/m^2) by the age of 25 years (females) or 28 years (males).
Conclusion: Diabetes prevalence is still extremely high in Aboriginal Communities of Western Australia. Addressing the underlying causes of the transition from what appears to be a relatively lean group of children to the high rates of overweight and obesity in the adult population should be a focus in prevention programs.

PP 123

Prevalence of overweight and obesity in Princess Margaret Hospital Diabetic Clinics

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Introduction: Type 1 diabetic patients may be at risk of weight gain for a number of reasons. Since obesity is an additional risk factor for certain diabetic complications, prevention of overweight and obesity should be a therapeutic goal.
Methodology: We examined the prevalence of overweight and obesity in a population based sample of 688 children and adolescents with Type 1 diabetes. Subjects had a duration of diabetes of at least 1 year. BMI z-scores were calculated using Centre for Disease Control data (2000). BMI cut-off points defining overweight and obesity (>97th centile) (1), were applied to the most recent individual BMI values. Age, gender, HbA_{1c}, region of residence, duration of diabetes and insulin regimen were examined to determine if there was any relationship with BMI and BMI z-score.
Results: Of the total sample 34.5 % were overweight and 9.0% obese. The mean BMI z-score was 0.82. There was no significant difference between males and females. Nor was a relationship found between gender, HbA1c, region of residence, duration of diabetes and BMI. A significant relationship was found between age and insulin regimen and BMI. 103 age matched children on pump therapy had significantly lower BMI than the population on injections.
Conclusion: This study has found the prevalence of obesity in this diabetic population to be significantly greater than expected and two fold greater than that reported in non-diabetic Australian children. It appears that children with Type 1 diabetes are at greater risk of overweight and obesity. The high prevalence is a concern and indicates the need for identification of the underlying reasons for weight gain and a more intensive approach to weight management of all young type 1 diabetic patients.
(1) Cole TJ et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000; 24:679–684.

PP 124

Thai obese adolescent girls with polycystic ovary syndrome (PCOS) have higher insulin resistance than in those without PCOS

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Introduction: The incidence of obesity in children and adolescents has been increasing worldwide including Thailand. The incidence of Type 2 DM (T2DM) in Thai children also increased from 5% (1986–1995) to 17.9% (1996–1999) of children with new-onset diabetes. Obesity is strongly associated with insulin resistance which leads to Type 2 DM. PCOS is commonly found in obese women at reproductive age. It is characterized by menstrual abnormalities and hyperandrogenism. One of the proposed pathogenesis of PCOS is insulin resistance-induced ovarian hyperandrogenism.
We hypothesize that the degree of insulin resistance in Thai obese adolescent girls with PCOS is higher than in those without PCOS.
Methodology: We retrospectively reviewed demographic and hormonal data of six Thai obese adolescent girls with PCOS who attended our Pediatric Endocrinology Clinic from 1999 to 2004. Their data were compared with the data of weight and BMI-matched Thai obese adolescent girls who menstruated regularly.
Results

	Girls with PCOS (N = 6)	Girls with regular menses (N = 6)	P value
Age (yrs)	14.2 ± 0.9	14.8 ± 1.5	0.6
Weight (kgs)	93 ± 8.7	89.2 ± 7.8	0.8
BMI (kg/m^2)	36.3 ± 5.8	36.4 ± 8.5	0.6
SBP(mmHg)	128 ± 8.6	124 ± 5.2	0.3
DBP (mmHg)	68 ± 5.6	74 ± 3.5	0.1
Acanthosis negricans	6/6 (100%)	6/6 (100%)	1.0
Family Hx of T2DM	5/6 (83%)	6/6 (100%)	0.3
Presence of T2DM	3/6 (50%)	0/6 (0%)	0.1
Fasting insulin level (uU/ml)	**51 ± 10.6**	**22.3 ± 3.0**	***0.04**
Fasting serum glucose (mg/dl)	104.7 ± 10.5	85.8 ± 3.6	0.1
Fasting Insulin: glucose ratio	0.5 ± 0.1	0.3 ± 0.0	0.1
2 hour insulin level (uU/ml)	225.4 ± 65.7	145.2 ± 24.4	0.3
2hr serum glucose (mg/dl)	201.5 ± 36.1	138 ± 9.5	0.1
HOMA-SCORE	**13.5 ± 3.0**	**4.7 ± 0.6**	***0.03**
Cholesterol (mg/dL)	194.8 ± 8.7	190 ± 20	0.3
TG (mg/dL)	149.4 ± 40	89.17 ± 12.3	0.2
HDL (mg/dL)	47.2 ± 4.3	50.67 ± 8.3	0.7
LDL (mg/dL)	143.8 ± 17.9	116.8 ± 26.1	0.4

***Significance (P < 0.05)**

Conclusion: Thai obese adolescent girls with PCOS have higher degree of insulin resistance measured by fasting insulin levels and HOMA-SCORE compared to those without PCOS. No difference in serum glucose and lipid profiles is observed. Since insulin resistance is highly associated with increased cardiovascular risks, our finding suggests that obese adolescent girls with PCOS might be at higher risk of developing cardiovascular disease in adulthood compared to those without PCOS.

PP 125

The association the Trp64Arg polymorphism of the β3 adrenergic receptor with insulin resistance syndrome in children with the obesity

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Introduction: The sympathetic nervous system is important regulator of energy expenditure and lypolysis. Recently has been described a β3 adrenergic receptor (β3AR) variant replacing the Tryptophan in codon 64 of the gene with Arginine (Trp64Arg), associated in adults with insulin resistance (IR) and earlier onset of the DM2, however not all studies confirm these findings.

The aim of the study: was to establish the influence of variant Trp64Arg β3AR on the BMI, insulin and glucose concentration during OGTT and IR in obesity children.
Patients and methods: The analysis comprise 60 obesity children. According to data derived from OGTT we assessed the whole-body IR acc to Belfiore ($IRI_{Belfiore}$). Genomic DNA was extracted from peripheral blood leukocytes. Exon I of β3AR gene was amplified using PCR method. The presence of mutation in codon 64 (Trp64Arg) of β3AR gene and frequency of allelic variant Trp64Arg was checked by RFLP method after PCR product digestion with BstNI enzyme.
Results: In obesity children with Trp64Arg variant the values of BMI SDS was: 2.71 ± 0.66, while in obesity children and normal Trp64Trp variant: 2.39 ± 0.33 (NS). The glucose and insulin concentrations during OGTT in children with Trp64Arg were not different from that in with Trp64Trp. Insulin resistance confirm in 42.8% children with Trp64Arg and in 45.6% children with Trp64Trp (NS).
Conclusions: In children with obesity we did not find the influence variant Trp64Arg of β3 adrenergic receptor on BMI values.
1. In children with obesity we did not find the influence variant Trp64Arg β3 adrenergic receptor on the glucose and insulin concentrations during the oral glucose tolerance test.
2. In analysed group of children with obesity we did not find relationship between the presence variant Trp64Arg of β3 adrenergic receptor and insulin resistance.

PP 126

The concentrations of long-chain polyunsaturated fatty acids in microsomal membranes depending on the presence of insulin resistance in obesity children

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Introduction: The pathomechanism, which leads to insulin resistance (IR), has not yet been fully understood. Insulin controls the activity of desaturases delta 6 and delta 5, catalysing the production of long-chain polyunsaturated fatty acids (LC PUFA) in humans. Cell membrane fluidity depends on the ratio of saturated to unsaturated fatty acids (FA) in phospholipids. An increased content of LC PUFA in microsomal membranes modifies the hormone-receptor binding, affecting signal transmission and determining the metabolism of carbohydrates and lipids.
The goal of the study: was an evaluation of IR effects on the contents of FA (especially of LC PUFA), included in the structure of erythrocyte membranes in children with obesity.
Material and methods: Forty seven children were included into the study: 23 – with obesity and IR, 13 – with obesity but without IR, and 11 healthy children with normal body mass (controls). On the basis of results of the fasting glucose and insulin, we calculated a hepatic IR – IRI_{HOMA}. According to data derived from OGTT, we assessed the whole-body IR – $IRI_{Belfiore}$. Concentrations of FA in erythrocyte membrane phospholipids and in peripheral blood serum were determined by means of gas chromatography technique.
Results: A positive correlation between IRI and saturated FA concentrations was found, while the correlation between IRI and LC PUFA concentrations in erythrocytes was negative. The metabolic index for LC PUFA in the n-3 family in the group of obese children with IR was 16.06 ± 11.61 and 33.95 ± 10.50 in the healthy controls. No similar correlations were observed in the analysis of serum FA contents in the examined children.
Conclusions: LC PUFA concentration in erythrocyte membrane is negatively correlated with IRI. This effect may lead to further resis-

tance to insulin and to hyperinsulinaemia, what is an etiologically significant risk factor of the metabolic syndrome.

PP 127

To study the prevalence of type 2 diabetes in obese children and adolescents

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Introduction: An increase in the prevalence of Type 2 Diabetes Mellitus (T2DM) in children and adolescents is being reported worldwide. Obesity is a common finding in these children. These adolescents may remain asymptomatic and present with complications at the time of diagnosis. Hence screening obese children and adolescents for T2DM is very important for establishing an early diagnosis and preventing diabetes related complications.

Since the prevalence of T2DM in the Indian population is very high, our aim was to determine the prevalence of T2DM in obese Indian children and adolescents, referred to our obesity clinic.

Methodology: 226 obese children and adolescents from the age of 10–19 years, were screened for T2DM. Obesity was defined as a BMI >95th percentile for age and sex.

Screening was done by checking fasting plasma glucose(FPG) levels. Oral glucose tolerance tests (OGTT) was done in selected individuals. A subject was considered to have DM, if FPG was above 126 mg/dl or a blood glucose value during OGTT was >200 mg/dl. Positive family history, absence of ketonuria, normal fasting C-peptide level, signs of insulin resistance, elevated HbA1C and good response to oral therapy, supported the diagnosis of T2DM.

Results: 226 obese children (107 females and 119 males) from 10–19 years age were screened for T2DM. 7/226(3%) (4 females and 3 males) subjects had diabetes as per the diagnostic criteria. Mean BMI of these subjects was 31(26–33.7). Family history of diabetes was present in 6/7. All subjects were asymptomatic with significant Acanthosis Nigricans at the time of diagnosis. HbA1C, Insulin and C-peptide levels were done in all the subjects to support a diagnosis of T2DM. Response to diet, exercise and oral therapy was good.

Conclusion: The prevalence of T2DM in our obese adolescents was 3%. Hence we must screen all these subjects for T2DM, since they may be totally asymptomatic.

PP 128

Comparison of the rates of obesity/overweight between South Asian and White Caucasian children with type 1 diabetes

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Background: The increased prevalence of obesity in adolescents with type 1 diabetes (TIDM) and among South Asian (SA) children with type 2 diabetes is well recognised. However, little information exists on the differences in obesity between white Caucasian (WC) and SA children with TIDM.

Aim: To compare obesity/overweight rates between SA and WC children with TIDM in Leicestershire, UK and to correlate these with age, duration of diagnosis, daily insulin requirements and metabolic control.

Method: Retrospective analysis of case notes of children with TIDM, between the ages of 2–18 years and diagnosed for more than one year. The following parameters were examined: age, sex, duration of diagnosis, weight, height, body mass index (BMI), insulin dosage and HbA1c. BMI was calculated and plotted on Cole charts (overweight above 91st centile and obesity above 98th centile).

Results: Data were collected on 150 children. 25% (38/150) of our study population were SA with the remainder being WC. The mean BMI of the whole population was 20 kg/m^2 (17 to 24) and mean HbA1c 8.6% (8.0% to 9.9%). Overall, 35% (n = 53) of children were either overweight or obese with 18% (n = 27) of the total being obese. There were no statistically significant differences in the rates of obese/overweight between WC and SA. In the obese/overweight subgroup (n = 53), mean BMI was 24 kg/m^2 (20–27) in SA (13/53) compared to 26 kg/m^2 (24–30) in the WC (40/53). Furthermore, there was no significant difference in the 2 subgroups in relation to age, duration of diagnosis, daily insulin requirement and metabolic control (mean HbA1c 8.4% vs. 8.8% respectively)

Conclusion: 35% of TIDM children were obese/overweight with no difference in the rates between SA and WC. The management of childhood diabetes needs to focus not only on glycaemic control but also on efforts to prevent excessive weight gain and to reduce other cardiovascular risk factors.

PP 129

Survey of physicians' diagnostic and treatment practices for obese children and adolescents: implications for suggesting the management guidelines

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Introduction: Incidence of childhood obesity and Type 2 diabetes (T2DM) is increasing worldwide. Metabolic syndrome (MS) is associated with obesity, T2DM and cardiovascular diseases. We investigated physicians' practices for the diagnosis and treatment of childhood obesity and MS.

Methodology: An e-mail survey was sent to 768 members of the International Society of Pediatric and Adolescent Diabetes with the e-mail address.

Results: The response rate was 10%. The majority of respondents (82%) were pediatric endocrinologists practicing in university settings and children's hospitals in Europe and North America. The major criteria used to establish the risk and diagnosis of obesity and/or MS are acanthosis nigricans (89%), family history of obesity and T2DM (81%), and body-mass index (77%). 89% of participants obtain detailed dietary histories. All respondents ask about physical exercise and sedentary life style. All participants include heights and weights as part of the diagnostic work up. About 80% measure blood pressure, fasting glucose, fasting insulin, fasting lipids and thyroid function tests. After initial assessment, 61% of respondents follow up patients up to three months, while 25% of respondents followed up patients every four months or longer. 72% of participants will treat obese adolescents for impaired glucose tolerance (IGT) and/or insulin resistance (IR), while 80% of respondents will treat obese adolescent females with IGT/IR and polycystic ovarian syndrome. In addition, 82% of physicians recommend metformin with dietary and life style modifications. Adolescents and prepubertal children with hypercholesterolemia/hyperlipidemia and family history of obesity, hyperlipidemia and/or early cardiovascular events, are treated by 67% and 51% of respondents, respectively. Although 88% of respondents are concerned about hypertension they use different approaches to manage it.

Conclusion: Our survey revealed variability in physicians' management of childhood obesity. We propose that universal guidelines are established for the prevention, diagnosis and treatment of childhood obesity and MS.

PP 130

Slipped upper femoral epiphyses at presentation: a marker of obesity and severe insulin resistance

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Objectives: There is presently no consensus regarding the need for screening for endocrinopathy in adolescents presenting with slipped upper femoral epiphyses (SUFE). This study investigates the magnitude of obesity and prevalence of endocrine disease in 16 consecutive adolescents presenting with SUFE over a 7-year period (1998–2004).
Methods: Height, weight and blood pressure were measured; body mass index (BMI) derived and the presence of impaired glucose tolerance/diabetes mellitus, dyslipidaemia and abnormal thyroid function determined by oral glucose tolerance testing and fasting serum lipid and thyroid function profiling.
Results: The mean age was 11.8 years (range 9–14), with mean weight standard deviation score (SDS) of 3.54 and a mean BMI SDS of 2.23. The mean height SDS was 0.2, with growth hormone deficiency suspected in one adolescent having a height SDS of –3.7. The mean Homeostasis Model Assessment (HOMA) insulin resistance index (IRI) was 4.88, with three (18.8%) adolescents having Impaired Glucose Tolerance (IGT), although the $HbA1_C$ was normal in all subjects. Six adolescents (37.5%) had systolic hypertension, of which two (12.5%) had diastolic hypertension. Eight (50%) adolescents were dyslipidaemic, with five (31.3%) having raised total cholesterol, six (37.5%) having raised triglycerides and four (25%) having raised low-density lipoprotein cholesterol. None of the adolescents were hypothyroid although one had a raised thyroid stimulating hormone level.
Conclusion: Obesity and insulin resistance are prominent endocrine co-morbidities in adolescents presenting with SUFE. It is prudent to formulate a screening protocol for endocrinopathy in such children.