OP1

Increased concentrations of soluble CD40 ligand may help to identify type 1 diabetic adolescents and young adults at risk for developing persistent microalbuminuria

F. Chiarelli[1], A. Mohn[1], C. Giannini[1] & F. Cipollone[2]
[1]Department of Paediatrics, University of Chieti, Chieti, Italy,
[2]Department of Medicine, University of Chieti, Chieti, Italy

Soluble CD40 ligand (sCD40L) is enhanced in diabetes. We previously demonstrated that upregulation of sCD40L as a consequence of persistent hyperglycaemia results in endothelial cell activation and monocyte recruitment to the arterial wall, possibly contributing to accelerated atherosclerosis development in young type 1 diabetic patients. To the best of our knowledge no study evaluated the relationship between sCD40L and microalbuminuria. In January 1989, sCD40L was measured in 268 normoalbuminuric diabetic adolescents and young adults (age 11–24 years; onset of diabetes before age 18 years; duration of diabetes longer than 7 years). Participants were clinically examined at baseline and biennially thereafter. sCD40L was measured every 2 years during the 16-year follow-up period. sCD40L was also measured in parents and offsprings. Over 16 years, 25 (14 M/11 F) out of 268 patients (9.3%) developed persistent microalbuminuria; no patient developed overt nephropathy. The risk of developing microalbuminuria was higher in children with increased sCD40L (using 7 ng/ml as the arbitrary cut-off point) (group A) compared with those with normal sCD40L at the beginning of the study (group B). sCD40L was not significantly correlated with HbA1c or duration of diabetes. The percentage of offsprings with both parents having sCD40L above the median values was significantly higher in group A than in group B. The OR for the occurrence of microalbuminuria after adjustment for confounding variables (AER, sex, HbA1c, mean blood pressure, cholesterol, triglycerides) in diabetic adolescents with elevated baseline sCD40L was 4.8 (95% CI of 1.9–12.1). These results demonstrate that enhanced sCD40L in the first years of diabetes may be one of the predictors and risk factors for incipient diabetic nephropathy in adolescents and young adults with onset of diabetes during childhood. Persistently increased sCD40L concentrations may help to identify normotensive, normoalbuminuric patients with type 1 diabetes who are predisposed to develop microalbuminuria and incipient diabetic nephropathy.

OP4

Nation-wide improvement in HbA1c and complication screening in a benchmarking project in childhood diabetes

H. D. Margeirsdottir, J. R. Larsen, C. Brunborg & K. Dahl-Jørgensen
Ullevaal University Hospital, Oslo, Norway

Introduction: Intensive diabetes management may delay the onset and slow the progression of late complications. However, treatment goals may be difficult to achieve in children and adolescents.
Aim: To investigate weather anonymous comparison, between treatment centres, of quality indicators for childhood diabetes leads to improvement in diabetes care.
Methods: The results are based on data from a national prospective quality study of childhood diabetes in Norway. All diabetic children in Norway are treated at the pediatric clinics of the government hospitals. Data concerning treatment and acute and chronic complications are collected prospectively yearly with standardized methods, based on WHO Basic Information Sheet, and benchmarked. HbA1c is measured at a central DCCT approved laboratory.
Results: The participation in the study has increased gradually, with 398 type-1 diabetes patients from eight hospitals included in 2001 and 1417 patients from 23 hospitals included in 2004. There was no difference in mean age of the patients, diabetes duration or BMI between the years. The mean HbA1c of all hospitals has improved: 8.6 (2001), 8.3% (2002), 8.4% (2003) and 8.1% (2004) and the HbA1c was significantly lower in 2004 than 2001-2003 ($p < 0.01$). The use of insulin pumps has increased significantly ($p < 0.01$): 1% (2001), 15% (2002), 21% (2003), and 28% (2004) while the incidence of DKA has not increased during the same period. The incidence of severe hypoglycaemia tends to improve. Screening according to international guidelines has improved in every way. The proportion of patients not screened for microalbuminuria according to ISPAD guidelines has decreased from 26% in 2001 to 0.2% in 2004 ($p < 0.01$). The proportion of patients not screened for retinopathy according to ISPAD guidelines has decreased from 42% in 2001 to 14% in 2004.
Conclusion: A prospective nation wide benchmarking study of diabetes treatment in Norway shows a significant improvement in HbA1c and complication screening.

OP2

Relationships between resting energy expenditure, adiponectin and changes in the body composition of young children – a longitudinal study

J. Hosking, B. S. Metcalf, A. N. Jeffery, D. S-L. Gardner, L. D. Voss & T. J. Wilkin
Peninsula Medical School, Plymouth Campus, Plymouth, Devon, UK

Introduction: Adiponectin is inversely related to adiposity and thought to protect against diabetes by reducing insulin resistance. It may also protect against weight gain and is inversely associated with resting energy expenditure (REE) in adults. Little is known of these associations in children.
Aim: To investigate relationships between REE, adiponectin and change in weight and body composition in pre-pubertal children.
Methodology: Adiponectin by ELISA, REE by indirect calorimetry and fat-free mass (FFM)/fat mass (FM) by DEXA measured in 151 children at age 6.9 ± 0.3 years, and repeated 1 year later.
Results: (1) There were no correlations between adiponectin and REE independent of body composition at either time-point (all r between –0.02 and ±0.11, $p > 0.35$). (2) Neither REE, nor adiponectin at 6.9 years were significantly associated with weight change (all r between –0.01 and ±0.20, $p > 0.09$). (3) There were no significant correlations between REE at 6.9 years and FFM gain (boys: $r = 0.06$, $p = 0.60$, girls: $r = 0.08$, $p = 0.53$) or FM gain (boys: $r = 0.19$, $p = 0.09$, girls: $r = –0.06$, $p = 0.62$) independent of initial body composition or adiponectin. (4) In boys only, there was an inverse correlation between adiponectin at 6.9 years and FFM gain ($r = –0.28$, $p = 0.02$).
Conclusions: (1) Adiponectin does not appear to play an important role in energy balance of young children. The inverse association between adiponectin and REE observed in adults has yet to emerge. (2) We found no evidence that low REE is associated with weight gain or adverse change in body composition nor, that adiponectin confounded any such relation. (3) Moreover, adiponectin was (unexpectedly) weakly inversely associated with change in FFM in boys, despite the lack of association with change in total weight, suggesting that adiponectin could influence apportioning of body mass as fat, and highlighting the importance of measuring body composition.

OP3

Weight at birth and at diabetes onset are increased in children with early onset of type 1 diabetes

O. Kordonouri[1], R. Hartmann[1], J. Langenheim[2], I. Stoelzel[2] & T. Danne[1]
[1]Children's Hospital at the Bult, Hannover, Germany, [2]Clinik of General Paediatrics, Charité Medical Centre, Berlin, Germany

Background: A recent theory discusses that factors of insulin resistance, such as increased body weight, may lead to an accelerated course even in type 1 diabetes (T1D). To verify this 'accelerator hypothesis' in a large group of children and adolescents with T1D, we investigated the relationship between the time of T1D onset and the child's body weight either at birth, in early infancy, or at presentation of the disease.
Patients and methods: In 207 children and adolescents (56.0% male, 2.9% non-European) with a median age of 7.1 years at T1D onset (range 0.7–17.4 years), the weight and height measurements at birth (37–42 weeks of pregnancy) as well as during routine preventive medical checkups at 6, 12 and 24 months of age were retrospectively evaluated. For the calculation of standard-deviation scores (SDS) of the body-mass index (BMI), the data were age and gender adjusted based on reference data collected of 34 422 healthy children living in Germany.
Results: Compared with data of the reference group, children with T1D were significantly heavier both ($p < 0.001$), at birth (BMI-SDS 0.32 ± 0.94) as well as at time of T1D onset (BMI-SDS 0.25 ± 0.93). Birth weight and weight gain within the first 2 years of infancy were not correlated with the time of presentation. However, there was a negative correlation between weight and age at onset of T1D ($r = -0.18$, $p = 0.012$). At the time of presentation, children below 5 years of age had a higher BMI-SDS (0.41 ± 0.88) than those children presenting between 6–9 years (0.25 ± 0.96) or between 10–17 years of age (0.00 ± 0.94).
Conclusions: Children with T1D are heavier at birth as well as at time of presentation of disease compared to healthy children of the reference group. Furthermore, an increased weight at the time of presentation is associated with an earlier onset of T1D. However, T1D acceleration is not influenced by birth weight or weight gain during the first years of life.

OP5

Carotid intima-media thickness in type 1 diabetes children and adolescents is not affected by the metabolic control and disease duration

A. Salvatoni[1], S. Chiaravalli[1], R. Cardani[1], E. Rezzonico[2], A. Stifani[2], I. Ghezzi[2], S. Piantanida[2] & L. Nespoli[1]
[1]Pediatric Clinic, University of Insubria, Varese, Italy, [2]Cardiology, Department Obstetric-Neonatology and Pediatric Department, A.O. Ospedale di Circolo, Varese, Italy

Introduction: It is still unclear whether type 1 diabetes mellitus triggers precocious atherosclerosis disease or is a worsening factor of preexisting lesions. Previous studies showed increased carotid artery intima-media-thickness (IMT) in adolescents with type 1 diabetes. IMT was correlated to LDL cholesterol and lipoprotein B, and patients with complications had significantly thicker carotid IMT than those without complications. Surprisingly IMT was not correlated to metabolic control and duration of the disease.
Aim: The aim of this study is to evaluate IMT in a group of children and adolescents with type 1 diabetes mellitus to further confirm the results of the previous studies.
Methodology: We studied 50 patients with T1DM, 26 boys (mean age 13.5; age range 1.8–21.8 years), with a mean disease duration of 64 months (range 12–196). The patients were all in intensive treatment with four or more daily subcutaneous insulin injections. Carotid IMT was measured at both sides and the values were adjusted for the age. The following parameters were also taken into account: relative BMI, HbA1c, insulin requirement, systolic and diastolic blood pressure. *Z*-score of systolic and diastolic blood pressure was calculated according to the normal values for age, gender and height (Pediatrics 2004; 114:555–76). All patients were free of diabetes complications.
Results: The mean of IMT measured on both sides adjusted for age resulted directly correlated to standardized diastolic blood pressure ($p < 0.05$; $r^2 = 0.075$) and inversely correlated to the duration of the disease ($p < 0.05$; $r^2 = 0.081$). We didn't find any correlation with HbA1c and insulin requirement and RBMI. Moreover diastolic and systolic blood pressure was not correlated to the duration of the disease and HbA1c.
Conclusion: Our results confirm that IMT is not correlated to metabolic control and duration of the disease in the T1DM patients without complications.

OP6

Services provided by the diabetes team: do they affect glycemic outcome?

P. G. F. Swift, C. E. de Beaufort, T. C. Skinner, on behalf of Hvidøre study group
[1]Children's Hospital Leicester, Leicester, UK, [2]DECCP, Luxembourg, Luxembourg, [3]Department of Psychology, Southampton, UK

Objective: To evaluate whether services offered by different diabetes centers have an influence on the metabolic control in a large international cohort of adolescents with type 1 diabetes.
Methodology: Cross-sectional clinical data was collected and questionnaires completed by adolescents and parents/carers attending clinics in 21 international centers. HbA1c (DCCT adjusted) was measured centrally.
Results: Questionnaires were completed by 2062 adolescents (age 14.4 ± 2.3 years; 50.6% male; diabetes duration 6.1 ± 3.5 years). Mean HbA1c: 8.2% ± 1.4 with a significant difference between centers ($F = 12.3$; $p < 0.001$). In six centers more than 80% of adolescents reported access to a 24-h hotline. These centers had a significantly lower HbA1c than other centers (>80% report a hotline HbA1c = 7.8; <80% report a hotline line HbA1c = 8.4; $p < 0.001$). However, there were no differences between individuals who reported access to a hotline and those who did not. In 15 centers, more than 70% of parents reported access to a 24-h hotline, and these centres had significantly lower HbA1c (>70% report a hotline HbA1c = 8.4; <70% report a hotline HbA1c = 8.8; $p < 0.001$). The more visits to the doctor as reported by adolescents were associated with a lower HbA1c ($F = 4.3$; $p < 0.005$) whereas the reverse was true for visits to a psychologist ($F = 3.7$; $p < 0.005$). There was no association between HbA1c and frequency of contact with nurses, dietitians or social workers. When parents reported contact with doctors there was no significant association with HbA1c, but more contact with nurses ($f = 4.9$; $p < 0.005$), dietitians ($F = 4.2$; $p < 0.01$) and psychologists ($F = 10.1$; $p < 0.001$) were associated with higher HbA1c. There was a significant correlation between parent ($r = 0.20$) and adolescent ($r = 0.21$) reports of their perceived ideal HbA1c level and actual results. There was a stronger association between what parents ($r = 0.39$) and adolescents ($r = 0.4$) report as the HbA1c they would be happy with and actual result. There were significant differences between centers on both parent and adolescent reports of ideal HbA1c levels and the result they would be happy with ($8.1 < F > 17.4$; $p < 0.001$). Adding these variables as co-variates substantially reduces the

effect of center on HbA1c (center alone F = 12.3; controlling for co-variates center effect F = 3.27).
Conclusion: The provision of a 24-h hotline or the number of contacts with healthcare professionals overall has a weak association with glycemic outcome. However, target setting may well play a more important role in outcome.

P1

A one hundred per cent increase in incidence of type 1 diabetes over a 5-year period at a large paediatric centre – no support for the accelerator hypothesis

M. O'Connell, S. Donath, S. Vidmar & F. J. Cameron
Royal Children's Hospital, Melbourne, Victoria, Australia

Background: Our diabetes clinic provides care for a demographically and ethnically diverse population in Melbourne Australia. Throughout the 1980's and early 1990's our clinic diagnosed approximately 70–80 children and adolescents with type 1 diabetes annually. Between 1999 and 2003 there was a 100% increase in incidence to 150 patients per year. There have been no demonstrable changes in referral patterns to our institution and these increases are coincident with a sustained statewide increase in incidence of 9.3% per year. The 'Accelerator Hypothesis' suggests that this increase should be associated with younger and more overweight newly diagnosed patients.
Aim: The aim of this study was to test the validity of the Accelerator Hypothesis in the context of a major and sustained increase in incidence in type 1 diabetes in our clinic.
Methods: Clinical data from all children and adolescents diagnosed with T1DM between the years of 1999–2003 at our institution were reviewed. To allow for weight loss secondary to dehydration and catabolism at the time of diagnosis, auxology and BMI data were collected for all subjects from their initial outpatient clinic review (3 weeks–3 months post diagnosis).
Results: Data was available for 512 newly diagnosed patients between 1999–2003. Over the 5-year study period the median age at diagnosis increased from 9.8 to 10.1 years. The overall median BMI Z score showed no clinically significant increase: it decreased by 0.22 between 1999 and 2001 and increased thereafter by 0.27 to 2003. When patients were analysed according to three age-groupings (0–4.99, 5.00–9.99 and >10.00 years) there was no consistent upward trend of mean BMI Z score in any age groupings.
Conclusion: The recent major increase in incidence of type 1 diabetes seen in our clinic was not associated with changes in age or body mass that would support the Accelerator Hypothesis.

P2

Cardiovascular mortality and age at onset of childhood-onset type 1 diabetes – a nationwide population-based study

T. Skrivarhaug, L. C. Stene, H. J. Bangstad, L. Sandvik, K. F. Hanssen & G. Joner
Department of Pediatrics, Diabetes Research Centre, Ullevål University Hospital, Oslo, Norway

Introduction: We have earlier reported a high cardiovascular mortality in childhood-onset type 1 diabetes (SMR ≈10 for both genders). Individuals with pubertal onset (10–14 years) had a significant increased all-cause mortality rate compared to those with prepubertal onset (0–9 years), (RR = 1.70, 95% CI: 1.15–2.51).
Aims: To study the impact of age at onset on the risk of cardiovascular death in a nationwide population-based cohort with childhood-onset type 1 diabetes.
Methodology: All Norwegian type 1 diabetic patients who were diagnosed between 1973 and 1982 and <15 years of age at diagnosis were included (n = 1906). At diabetes onset: 1036 individuals were <10 years and 870 were 10–14 years. Mortality was recorded from diabetes-onset until 31 December 2002. The highest age attained among deceased subjects was 40 years. The maximum diabetes duration in the cohort was 30 years (range 19–30). Mean age at 31 December 2002 was 34 years (range 21–45). Cause of death was ascertained by reviews of death certificates, autopsy protocols and medical records. Cases classified as cardiovascular death included ICD 10: I20-I25, I44-I49, I60-I67 (all cardiac and cerebrovascular death).
Results: At a maximum follow-up of 30 years, 103 patients were dead; 42 with prepubertal and 61 with pubertal diabetes-onset. In 15/1906 (0.79%) the cause of death was cardiovascular; two (2/1036, 0.19%) in the prepubertal group and 13 (13/870, 1.49%) in the pubertal group (Log-rank, p = 0.001). This remained significant after adjusting for gender (Cox-regression analysis, p = 0.005).
Conclusion: With a median duration of 24 years with childhood-onset type 1 diabetes, individuals with pubertal onset had a significant increased risk of dying a cardiovascular death compared to individuals with prepubertal onset.

P3

Diabetes incidence and metabolic control in New Zealand: Data from Starbase 1993–2005

C. Jefferies[1], W. Hunter[2], P. Hofman[2], P. Carter[2] & W. Cutfield[2]
[1]Auckland District health Board, Auckland, New Zealand, [2]University of Auckland, Auckland, New Zealand

Aims: Starbase is a prospective database of children with diabetes in from nine centres in New Zealand.
Methods: Each participating centre collected data on their clinic population; files are encrypted and sent electronically to the central Starbase held in Auckland, by emailing txt files. Data was downloaded for appropriate statistical analysis. Data on the following is recorded on each visit: HbA1c, Height, weight, insulin doses, current dose (unit/kg/day) frequency of testing, type of insulin, complications screening, and frequency of hypo and diabetic ketoacidosis.
Results: More than 900 children are registered in Starbase, with ~9000 individual clinical assessments. There was a tripling of incidence of new type 1 diabetes from 1993 to 2005. There were no children with Type 2 diabetes in 1993 but in Auckland (the main centre) by 2005 represented ~5% of all new cases. The overall grand mean HbA1c was 8.6%, and was shown to increase with both current age and length duration of diabetes. Maori and Pacific Island children with Type 1 diabetes had poorer glycaemic control than European children (p < 0.001). There was a wide variation of HbA1c amongst centres, the lowest at 7.9% and the highest at 9.7%: presumably reflecting resource and geographical difficulties at these sites. Intricate detail on the impact of multiple insulin on BMI and HbA1c is being performed.
Conclusions: Starbase is a useful clinical tool to compare and contrast geographically distant centres. There are significant differences in glycaemic control between ethnic groups and between centres, which requires further investigation. The ongoing collection of Starbase data is important at local and

national levels for monitoring the current state of health of children and young people with Type 1 and 2 diabetes in New Zealand, and could easily be used internationally.

P4

High incidence of type 1 diabetes mellitus in the Liguria region (Italy) in 0 to 14-year age-group from 1999 to 2004

P. Barbieri[1], G. d'Annunzio[1], L. Minicucci[1], N. Minuto[1], A. Pistorio[2] & R. Lorini[1]

[1]Department of Pediatrics, G. Gaslini Institute, Genoa, Italy, [2]Epidemiology and Biostatistics Section, Scientific Directorate, G. Gaslini Institute, Genoa, Italy

Introduction: In a previous 10-year survey (1989–1998) on type 1 diabetes mellitus (T1DM) incidence during childhood (0–14 years) in Italy, we already demonstrated the high incidence (12.6/100 000 per year) in the Liguria Region as compared to other Regions of Peninsular Italy (8.0–8.8/100 000 per year). In the same survey in the Sardinia island was observed a more than 4 fold increased incidence (36.9/100 000 per year).
Aims: To confirm these data, the T1DM epidemiology in Liguria has been continued. We report a further 6-year period (1999–2004).
Methodology: Assuming that all patients at T1DM diagnosis were admitted to local hospital for insulin therapy, case ascertainment was sought via two alternative sources. All the departments of Pediatrics, Endocrine and Metabolic Sciences, or Internal Medicine of the four Liguria Provinces (Genoa, La Spezia, Savona, Imperia) were considered as primary source. The secondary source were prescription registries from the Liguria National Health Service offices. Because of new legislative rules to protect subjects' privacy, information obtained from the secondary source was strongly hampered. An adjustment of the possible underreporting due to the new law was then made by comparing these data with that of the previous study. Underreporting was estimated at 9%. Incidence rates per year (IR) were standardized based on the year 2000 world population statistics and reported as cases per 100 000 children. The independent effect of age, sex, residence, and calendar year was estimated with a Poisson regression model.
Results: Overall, 124 new T1DM new cases were diagnosed in Liguria for a IR of 12.2. The corrected value adjusted for underreporting was 136 cases for an IR of 13.4. Rates were higher among males (14.3) than among females (12.2). Moreover, the age group with higher incidence was the 10–14 years among males (16.7) and the 5–9 years among females (13.7).
Conclusions: These data confirm that in the Liguria Region the IR of T1DM still remains high.

P5

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

O. A. Malievsky[1], D. S. Nurmukhametova[2] & D. U. Allaberdina[2]

[1]1Bashkir State Medical University, Ufa, Russia, [2]Republican Children Hospital, Ufa, Russia

Introduction: In most world countries a rise of prevalence of the type 1 diabetes mellitus (DM) in children has been observed.
Aim: To evaluate prevalence of the type 1 diabetes mellitus in children aged 0–14 years in the Republic Bashkortostan, Russia, for 14 years (between 1992 and 2005).
Methodology: Data about all cases of the type 1 diabetes mellitus were recorded in the State Registry of diabetes mellitus. In this Registry, the following data were recorded for each case: patient's name, address, date of birth, date of first insulin injection, insulin dose, auxological characteristics, results of laboratory analyses, complications of the disease. The source of information about the diabetic children was data from Endocrinology Department of the Republican Children Clinical Hospital, from local practicing pediatricians, and from State Epidemiology Statistical institutions. Prevalence of the type 1 diabetes mellitus as well as 95% confidential interval (CI) were calculated per 100 000 children aged 0–14 years.
Results: Prevalence of the type 1 diabetes mellitus in 1992 amounted to 33.91 (CI95% 30.41–37.71), in 1993 – 34.53 (31.00–38.36), in 1994 – 35.38 (31.79–39.27), in 1995 – 36.79 (33.11–40.77), in 1996 – 38.15 (34.38–42.21), in 1997 – 43.70 (39.66–48.04), in 1998 – 48.16 (43.83–52.80), in 1999 – 48.30 (43.90–53.02), in 2000 – 52.08 (47.42–57.07), in 2001 – 45.84 (41.39–50.64), in 2002 – 49.62 (44.88–54.72), in 2003 – 50.73 (45.85–55.99), in 2004 – 49.11 (44.20–54.41), in 2005 – 52.42 (47.24–58.02) per 100000 children. For the last 3 years, prevalence of the type 1 diabetes mellitus in children has not changed. Prevalence of the type 1 diabetes mellitus rose with age. In 2005, it amounted to 14.33 in the 0 to 4-year old children, to 56.61 in the 5 to 9-year old children, and to 79.33 in the 10 to 14-year old children per 100 000 children of the corresponding age.
Conclusion: Prevalence of the type 1 diabetes mellitus in children in the Republic Bashkortostan, Russia, for 14 years rose 1.5 times (from 33.91 cases per 100 000 children in 1992 to 52.42 cases in 2005).

P6

Mortality among children with type 1 diabetes mellitus diagnosed from 1989 to 1999

W. M. Mladenov, V. I. Iotova & V. T. Tzaneva

Clinic of Pediatric Endocrinology, Department of Pediatrics, Medical University, Varna, Bulgaria

Introduction: Despite the improvement in the treatment of the patients with type 1 diabetes the disease is still supposed to carry a higher mortality risk.
Aims: The aim of the present study is to establish the mortality rate among children with type 1 diabetes diagnosed at age below 15 between 1989 and 1999.
Methodology: Patients with type 1 diabetes aged under 15 at the time of diagnosis and registered at the Diabetes Incidence Registry of our clinic were included. End of follow-up was 31st of March 2004. Active follow-up was performed. The causes of death were ascertained by reviewing the death certificates. The overall deaths, expected deaths and SMR were calculated. Person year at risk analysis was applied. The observed deaths were divided into sub-groups according to age at diagnosis, gender, cause of death.
Results: From the included 443 patients 10 deaths were observed. The expected deaths were 2.1. The SMR was 4.7. The most common causes of death were DKA, severe infections and accidents. We came across a disturbing fact – 3 uncertain causes of death (two in rural areas), suspicious of ceasing of insulin by the parents or other authorized by them people.
Conclusions: The current study reveals the mortality rate among children with diabetes for the 1st time in our country. The prevention of the acute complications of diabetes and adequate treatment of the infections seem to be a resource for decreasing the mortality risk. Care should be taken for better education of parents

and family doctors for preventing discontinuation of the insulin therapy.

Acknowledgements: This study is a part of the EURODIAB ACE Mortality Sub-study.

P7

Prognosis of young IGT patients found by urine glucose screening test for school children

K. Shiga, N. Kikuchi & E. Tokuhiro

Yokohama City University Medical Center, Yokohama, Japan

Background: Impaired glucose tolerance (IGT) is recognized as a risk factor for the development of type 2 diabetes in adult patients. In recent years, the morbidity of IGT found by urine glucose screening test for school children has increased. We examined young IGT patients to evaluate the prognosis of IGT.

Aim: To evaluate the prognosis of young IGT patients.

Method: Thirty-three IGT patients (14 males and 19 females, age 13.7 ± 1.6 years) found by urine glucose screening test for school children in Yokohama were examined. Their follow up duration was 19.9 ± 10.7 m. Both anti GAD antibody and IA-2 antibody were negative in all subjects. Analysis of data was performed using Kaplan-Meier method.

Result: About 34% of IGT patients developed to type 2 diabetes after 5 years from diagnosis. Obesity group showed significantly high incidence of developing diabetes ($p = 0.0038$), and all of the diabetic patients showed worsening of obesity at the point of onset of diabetes. Higher total cholesterol group also showed high incidence of developing type 2 diabetes ($p = 0.027$). There was no significant difference in incidence of developing diabetes between higher and lower insulinogenic index groups, but higher basal insulin level group showed significantly high incidence of developing diabetes ($p = 0.008$).

Conclusion: IGT patients of obese and high basal insulin level are the high risk group of developing type 2 diabetes, and the incidence of developing diabetes may accelerated by increasing of obesity. Lifestyle intervention in individuals with IGT would seem to prevent prognosis to type 2 diabetes.

P8

Relationship between seasonality at birth and development of diabetes mellitus type 1 (dm-1) in our country

M. Rodríguez Rigual[1], E. Sáez de Adana[1], G. M. Lou Francés[1], M. Suso[1], V. Borrás[2], M. Gussinyé[2], C. Castel[2], A. L. Gómez[3], J. P. López[3], E. García[3], S. Bernal[3], R. Espino[3], F. Hermoso[4], M. Oyarzabal[5], C. Luzuriaga[6], R. Barrio[7], I. Rica[8] & M. J. López[9]

[1]Hospital Universitario Miguel Servet, Zaragoza, Spain, [2]Salud Publica, Cataluña, Spain, [3]Hospital Infantil Virgen del Rocío, Sevilla, Spain, [4]Hospital Clinico Universitario, Valladolid, Spain, [5]Hospital Virgen del Camino, Pamplona, Spain, [6]Hospital Marquez de Valdecilla, Santander, Spain, [7]Hospital Ramon y Cajal, Madrid, Spain, [8]Hospital de Cruces, Bilbao, Spain, [9]Hospital Clinico Universitario, Valencia, Spain

Introduction: Studies about seasonality and DM-1 show children who develop DM-1 are born in different seasons than normal population. This support the hypothesis that viral infections would initiate the autoimmune process against pancreatic β cells in the perinatal period.

Objectives: To study the seasonality at birth of children with DM-1. To elucidate if grouping with seasonality at birth is higher than seasonality at onset of DM-1. To identify factors that influence in this relationship.

Methods: We analysed 5.177 patients with DM-1 born from 1980 who developed DM-1 before 18 years. We've studied: birth date, date at onset of DM-1, gender, age at onset of DM-1 (age < ó (de 7 years), birthplace.

Results:

SEASONALITY VARIATION INDEX (*100)	Winter	Spring	Summer	Autumn
General birth Population	97,335	100,707	102,346	99,611
DM-1 birth Population	98,287 (RR: 1,014)	96,838 (RR: 0,953)	107,025 (RR: 1,069)	97,849 (RR: 0,963)
Onset of DM-1	116,914	91,853	87,730	103,502

RR= Relative Risk of DM-1 development.

SEASONALITY VARIATION INDEX AT BIRTH (*100)	Winter	Spring	Summer	Autumn
Male	93.089	103,963	100,793	102,208
Female	103,095	102,492	104,200	90,213
Age at onset < 7 years	106,297	99,498	103,161	91,044
Age at onset ≥ 7 years	94,115	99,891	105,507	100,487
North	98,868	101,335	103,678	96, 118
South	101,160	95,659	104,797	98,385
SEASONALITY VARIATION INDEX AT ONSET (*100)				
Male	115,169	95,857	87,834	101,140
Female	112,035	96,663	104,182	87,121
Age at onset < 7 years	106,804	96,787	106,967	89,441
Age at onset ≥ 7 years	127,979	90,780	78,712	102,529
North	112,855	92,846	94,026	100,273
South	114,681	112,018	74,434	98,867

Conclusions: (1) It's estimated a higher grouping at onset of DM-1 than at birth date. (2) We've observed the typical relationship described previously in the literature. (3) Birth date in a specific season of the year doesn't show a risk for developing DM-1 either in the total group or in our study population.

P9

Relatively higher BMIs in younger children at presentation

C. Gardner, M. Kaseem & J. M. Robinson

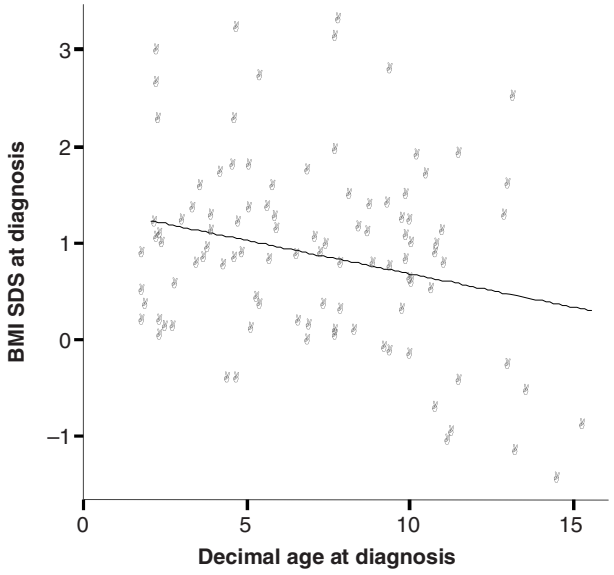
NHS, Wigan, UK

Introduction: The fat accelerator hypothesis seeks to link the rise in childhood insulin dependent diabetes mellitus to the rise in obesity. Accordingly children who were younger at diagnosis might therefore have a relatively higher BMI.

Aims: To study our local population to ascertain whether a link exists between younger age at diagnosis and BMI.

Methods: A retrospective analysis of 102 children from local clinic. BMI recordings between 4 and 8 weeks after diagnosis were used so as to allow for full re-hydration but before very significant re-feeding might occur. A further nine children were excluded:

maturity onset diabetes of the young (3), no relevant height recordings (3), renal failure (1), trisomy 21(1) and non-insulin dependent diabetes mellitus (1). The BMI SDS scores were calculated using the method described by Cole et al (ADC 1995).
Results: The diagram below illustrates the relationship between BMI and decimal age shortly after diagnosis. There is a significant correlation (Pearsons r = –0.25, p = 0.011).



Conclusion: We have shown a correlation between younger age at diagnosis and higher BMI SDS. This supports the fat accelerator hypothesis.

P10

Spatio-temporal trends and age-period-cohort modelling of the incidence of type 1 diabetes among children aged <15 years in Norway 1973–1982 and 1989–2003

G. Aamodt[1], L. C. Stene[2] & G. Joner[3]

[1]Akershus University Hospital, Nordbyhagen, Norway, [2]Norwegian Institute of Public Health, Oslo, Norway, [3]Ullevål University Hospital, Oslo, Norway

Introduction: Many studies have investigated time trends and regional variation, but few have simultaneously modelled the effects of age, period, cohort and location, on the incidence of type 1 diabetes.
Aim: To investigate age-period-cohort effects and spatial and temporal trends for the incidence of type 1 diabetes mellitus among 0-14 years old children in Norway.
Methods: Children diagnosed with type 1 diabetes in Norway during 1973–1982 and 1989–2003 were included. The age, calendar period, and birth cohort effects were studied using Poisson regression, including Holford's method of parameterisation to model the dependencies between age, period and cohort effects. To study the spatial distribution of incidences and temporal effects, a spatio-temporal scan statistic was used.
Results: The overall incidence rate was 22.7 cases per 100 000 (95% CI: 22.5–22.9), showing an average annual increase of 1.2% (95% CI: 0.7–1.5%) during the study period. Two specific areas with 40% and 50% increased incidence rates were identified in the southern part of Norway during 1976–80 and 2000–2003 (both P = 0.001). Also, children born during 1969–1971 in some specific municipalities in the southern part of Norway and children born during 1987–1988 in some specific municipalities in the northern part of Norway showed 60% and 50% increased incidence rates compared to the remaining municipalities (P = 0.001 and P = 0.024).
Conclusions: The incidence of type 1 diabetes among children increased during the study period. Birth cohort effects were detected only when geographic location was taken into account. The spatio-temporal scan method showed regional differences for both calendar period and birth cohorts. Such effects within the relatively homogenous Norwegian population, suggests the influence of non-genetic etiological factors.

P11

The epidemiology of childhood diabetes mellitus in Beijing, China

C. X. Gong, B. Y. Cao, J. Mi, B. Sun, J. P. Liang & Y. C. Li

[1]Beijing children's hospital affiliated of the Capital University of Medical Science, Beijing, China, [2]The Capital Institute Of Paediatrics, Beijing, China

Objective: To describe the epidemiologic characteristics of schoolchildren in Beijing, to assess the difference of age, gender and district.
Methods: A cross-sectional screening program was carried out in 19593 schoolchildren from March 2004 to October 2004, the screening test is fasting capillary blood glucose (FCBG). According to the diagnostic criteria of World Health Organization (WHO), Diabetes mellitus (DM) is assumed if FCBG ≥ 6.1 mmol/l, impaired fasting glucose (IFG) is assumed if 5.6 mmol/l ≤ FCBG < 6.1 mmol/l.
Results: There are 19 121 cases with complete data from 19 593 people including 9522 males and 9599 females. The median age for the study population was 12.56 years (range 6.03–18.99 years). The aggregate age-adjusted prevalence of DM and IFG was 0.56% and 1.35%, respectively. There were significant differences between males and females in prevalence of DM (0.76% vs. 0.36%, p = 0.0005) and IFG (2.68% vs. 1.13%, p < 0.0001). The DM, IFG prevalence of different districts ranged from 0.20% to 0.86%, and from 0.75% to 2.74%, respectively. Dong Cheng District has the highest prevalence of DM and IFG, Ping Gu District has the lowest, consistent with the higher rate of obesity in Dong Cheng district than Ping Gu district (28.68% vs. 12.75%, p < 0.0001). The gender-adjusted prevalence of DM among different age group was rising with age, the highest prevalence of IFG is in the age group 10–15. Among males, the highest prevalence of DM and IFG was in the age group 16–18 and 10–15, respectively, the highest prevalence of female DM and IFG were both in the age group 10–15.
Conclusions: The prevalence of DM and IFG has significant discrimination according to age, gender and district. Age, gender, puberty maturation, obesity and sedentary life style are contribute to the development of DM. DM and IFG is prevalent in Beijing now, paediatrician should attach importance to this phenomenon, earlier to intervene, earlier to treat, postulating the chronic complication for adults.

P12

Update of Sardinian Eurodiab register

C. Putzu, A. Casu, The Sardinian IDDM Epidemiology Study Group & M. Songini

S.C. Diabetologia-Azienda Ospedaliera Brotzu, Cagliari, Italy

The aim of the present study was to update the incidence trend of T1D in Sardinia from 1989 to 2004. All newly diagnosed T1D

patients aged 0–29 from Sardinia were recorded according to the Eurodiab ACE criteria. Total, sex- and age-specific (0–14 and 15–29 years) incidence rates were estimated for each calendar year and province. A subanalysis was done for babies who developed T1D within 1-year of age. From 1989 to 2004 a total of 1781 (1039 M/742 F) newly T1D patients aged 0–14 years and 1131 (687 M/444 F) aged 15–29 years were recorded. The incidence rate in Sardinian children (0–14 years) was 42.4/100 000 person-years (95% C.I. 40.5–44.4) 47.9 in M (95% C.I. 45.0–50.8) and 36.6 in F (95% C.I. 34.0–39.2). In adults aged 15–29 years the incidence rate was 18/100 000 (95% C.I. 17.0–19.1) 21.5 in M (95% C.I. 19.8-23.1) e 14.4 in F (95% C.I. 13.1-15.8). Twenty-five babies developed T1D within 1-year of age and eight of them were below 6 months. A significant increase of incidence was observed over time in the 0–14 age group (linear regression $p = 0.020$) and a decrease were observed in the older age group. The increase of incidence was higher among females compared to males especially in the 0–4 age group, even if the incidence itself was higher among males. Thus, the male to female ratio decreased in the most recent years. In the 0–14 age group the highest incidence was recorded in Oristano province (51.4 95% C.I. 44.3–58.6) then in Cagliari (45.5 95% C.I. 42.5–48.5), Nuoro (41.7 95% C.I. 36.8–46.3) and Sassari (34.9 95% C.I. 31.4–38.3). A similar picture was observed in the oldest age group. The T1D incidence rates in Sardinia is still very high and it is still increasing particularly in young females in most recent years.

P13

Why is diabetes in childhood more common in areas with low levels of mercury, lead and/or calcium oxide?

U. S. Samuelsson

Division of Pediatrics, Department of Molecular and Clinical Medicine, University hospital, Linköping, Sweden

Previous studies from the South-east region of Sweden (42 356 km^2) has shown geographical variation between municipalities and parishes in the incidence of type 1 diabetes. In connection with another study, which explores how socio-economic factors contribute to the geographical variation in this region, there was an opportunity, as a pilot study, to relate some geological data to the incidence of diabetes. All 1871 children diagnosed with Type1 diabetes and residing in the study area between 1977 and 2001 in the south-east part of Sweden were included and allocated x- and y- coordinates in the national grid. The Population at risk, comprising all children 0–16 years of age, aggregated in 82.000 200 meter squares covering the study area was geocoded likewise. The geochemical analysis were done on brook water plants on 6929 places in the region, samples were also taken from moraine, 1 m (3.28 feet) underground, in 6029 places. The incidence of Type 1 diabetes was 9/100 000 in areas with levels of bao (bariumoxide) in the moraine $>$90th percentile and 47.9 in areas with levels $<$10th percentile. The levels of cao (calcium oxide) showed an opposite pattern with incidence of 61.4 and 10.9, respectively. The incidence was 81/100 000 in areas with low levels of Hg (mercury) in brook water plants and 20.3/100 000 in areas with high levels. The same pattern was seen for Pb (lead), 26.4 in areas with low and 19.8 in areas with high levels. It is not easy, in the writing moment, to explain these findings. The results could be random or caused by confounding factors but since areas with the same pattern often overlap each other it could be of some etiological importance and imply that local environmental factors may play a role in the process leading to the disease

P14

Recent trend toward decrease in incidence of children with type 2 diabetes in the Tokyo metropolitan area

T. Urakami, S. Morimoto, Y. Nitadori, M. Owada & T. Kitagawa

Department of Pediatrics, Nihon University School of Medicine, Tokyo, Japan

Objective: We previously reported that the annual incidence of type 2 diabetes children in the Tokyo metropolitan area after 1981 was significantly higher than that before 1980. This study examined recent changes in the annual incidence of children with type 2 diabetes in the Tokyo metropolitan area.

Methods: From 1974 to 2004, a total of 9 242 259 school children were tested for glucosuria to detect diabetes. A total of 236 students were diagnosed as having type 2 diabetes through this screening program. We compared annual incidences of type 2 diabetes for 5-year durations throughout this period.

Results: The overall incidence of type 2 diabetes was 2.55/100 000. Overall, 83.9% of children with diabetes were obese. Junior high school children had a significantly higher incidence than primary school children (0.75 vs. 6.27/100 000). The annual incidences over the 5-year periods from 1974 to 2004 were 1.73, 3.23, 3.05, 2.90, 2.70 and 1.41/100 000, respectively. The incidences in 1974–1980 and 2001–2004 were significantly lower than those in 1981–1985, 1986–1990 and 1991–1995, because primary school children in 1974–1980 had a significantly lower incidence (0.27/100 000), and junior high school children in 2001–2004 had a somewhat lower incidence (3.66/100 000) than during 1981–2000.

Conclusions: After 1980, the tendency toward childhood obesity rapidly increased in primary and junior high school children in Japan contributing to the increase in incidence of childhood type 2 diabetes. This trend has recently weakened, and children's lifestyle and eating habits have gradually improved, possibly contributing to the trend toward decrease in the incidence of type 2 diabetes in 2001–2004 in the Tokyo metropolitan area.

P15

Screening for type 2 diabetes mellitus in children: lessons from a clinic database

J. C. Agwu

Sandwell and west Birmingham NHS trust, West midlands, UK

Children with type 2 diabetes (T2D) have been identified in the last decade. Prior to contemplating a community based screening project, we retrospectively reviewed our clinic experience of diagnosing and opportunistically screening for childhood T2D.

Methods: Case notes of all children aged $<$19 years who had an oral glucose tolerance test or fasting blood glucose (between 2000–2005) to screen or diagnose T2D were reviewed. Demographic data, presence of risk factors and clinical course were extracted. Any abnormalities of glycaemia (AG) was noted. The effectiveness of using either the ADA screening strategy (fasting blood sugar on pre-selected high risk children) or presence of glycosuria as screening tools was studied.

Results: Sixty-one children were identified. Mean age 12.05 years. 60.6% were of ethnic minority origin. All were either obese or overweight. Six patients had glycosuria on presentation. 21/61 (34.4%) had abnormalities of glycaemia during the period of study. Three children initially had impaired glucose tolerance (IGT), two of these later developed T2D. Thirteen were initially diagnosed with T2D, two of these later converted to IGT on retesting. Five other patients had impaired fasting glucose (IFG). Children who had abnormalities of glycaemia had significantly more risk factors than those without any abnormalities (3.8 vs. 3.0) $p = 0.025$. Applying ADA screening strategy to our cohort would have missed

four children with abnormalities of glycaemia. The sensitivity of using only the ADA risk criteria was 90.4% whilst specificity was low at 25.6%. The positive predictive value was 39.5%. Glycosuria as a screening tool had a high specificity (97.5%) though sensitivity was poor (25%).
Conclusion: The state of glucose tolerance in children appears to be dynamic. Repeated testing of at risk children with OGTT is important to detect this. Currently recommended screening strategies may not be effective for use in community based screening projects.

P16

The prevalence of obesity and body mass index distribution in Shanghai children and adolescents aged 6–18 years

F. Luo, S. Shen, Y. Tu, H. Xia, D. Zhi & Q. Hong
Children's Hospital of Fudan University, Shanghai, China

Background: The Chinese children obesity and BMI distribution profile aged from 6 to 18 years old haven't been published.
Aims: To investigate the prevalence of obesity and BMI distribution profile of children and adolescents aged from 6 to 18 years old.
Methods: One district in urban area and one district in suburb area were randomly selected. 70 431 students were screened. Body weight and height were measured. Standardized prevalence was calculated and statistical difference was tested.
Results: (1) The standardized prevalence of obesity was 3.30%. The standardized prevalence of overweight was 12.95%. (2) The prevalence of obesity and overweight was significantly higher in urban district than suburb and also was significantly higher in male than female. (3) The prevalence of both obesity and overweight decreased with the increasing of age ($p < 0.001$). (4) From the 5th percentile to 95th percentile, all the BMI values in boys were higher than that of girls. (5) P_{85} and P_{95} of BMI were 25. 0 kg/m^2 and 28.2 kg/m^2 in boys and 23.3 kg/m^2 and 25.7 kg/m^2 in girls, respectively, at 18 years old in Shanghai. (6) BMI was increased with the increasing of ages, which was evident among the 7–16 years old, then the increasing rate diseased with age. (7) When comparing with the CDC BMI charts, the 85th and 95th percentile were high in Shanghai children before sixteen years old and it became lower afterwards.
Conclusion: The prevalence of obesity was decreased with the increasing of age which was different from the obesity trend in the western countries. The BMI distribution profile of Shanghai children and adolescents was different from the American CDC BMI charts especially after sixteen years old. It is essential to establish the Chinese based BMI standard in the future children and adolescents obesity study.

P17

Comparison of clinical characteristics between South Asians and White Caucasians with T1DM

S. D. Shenoy[1], D. Cody[1], P. G. F. Swift[1], M. J. Davies[2], I. G. Lawrence[2] & N. T. Raymond[3]
[1]*Children's Hospital, Leicester Royal Infirmary, Leicester, UK,* [2]*Department of Diabetes & Endocrinology, Leicester Royal Infirmary, Leicester, UK,* [3]*Warwick Medical School, University of Warwick, Coventry, UK*

Background: A significant increase in incidence of T1DM among the South Asians (SA) has been described in several UK communities.
Aim: To compare the clinical characteristics of T1DM between SA and White Caucasians (WC) to evaluate potential ethnic heterogeneity.
Methodology: Retrospective study involving 300 children (WC 253: SA 47) diagnosed in a single centre during 1990–99. Ethnicity was assigned by manual analysis of names by the staff familiar with the families. Index of multiple deprivation 2004 was used as proxy for social deprivation and expressed in fifths (lowest fifth Q1 being most deprived). Follow-up data were collected in 2004 with time from diagnosis ranging from 5 to 15 years.
Results: There was no significant difference between the two groups for mean age at diagnosis (WC 9.0 ± 3.9 years vs. 9.6 ± 3.5 years, $p = 0.36$) or gender (WC 53% boys vs. 55% SA). Of SA 72% were from most deprived status (Q1 + Q2) compared with 29% WC ($p < 0.001$). While a family history of T1DM was similar (WC 23% vs. SA 20%), there was a significantly increased family history of T2DM rate among SA (WC 11% vs. SA 31%, $p = 0.001$). 20% of the overall cohort presented in DKA at diagnosis with no significant difference in the rate or severity in the two groups across all age groups. There was no significant difference in insulin regimen or insulin dose requirement at diagnosis. At follow-up, mean age (WC 17.7 ± 4.6 years vs. SA 18.9 ± 4.0, $p = 0.15$) and time from diagnosis (WC 9.0 ± 2.8 vs. SA 9.5 ± 2.3, $p = 0.30$) were similar. Although BMI SDS at first clinic visit after diagnosis was significantly higher in WC (WC 0.25 ± 1.0 vs. SA –0.14 ± 1.3, $p < 0.05$), there were no significant differences in the rates of overweight/obesity(WC 38% vs. SA 49%, $p = 0.90$) at follow-up across all age groups. Glycaemic control was identical with HbA1c of 9.1% ± 1.8 among WC and 9.1% ± 1.4 among SA ($p = 0.90$) even after adjusting for the effect of deprivation. There were no statistically significant differences in the rates of microvascular complications, hypertension or dyslipidaemia.
Conclusion: Despite significant differences in the family history of T2DM, deprivation status and BMI at diagnosis, there is little evidence of ethnic heterogeneity in other clinical or metabolic characteristics either at diagnosis or follow-up.

P18

Continuous glucose monitoring shows progressive fluctuations in interstitial glucose during development of type 1 diabetes

J. Lähde[1], K. Ranta[1], T. Salonsaari[1], P. Keskinen[1], J. Ilonen[3], O. Simell[4] & M. Knip[2]
[1]*Department of pediatrics, Tampere University Hospital, Tampere, Finland,* [2]*Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland,* [3]*Immunogenetics Laboratory, University of Turku, Turku, Finland,* [4]*Department of Pediatrics, University of Turku, Turku, Finland*

Introduction: Data on changes in glucose homeostasis during prediabetes, i.e. the time between the emergence of signs of beta-cell autoimmunity and diagnosis of clinical type 1 diabetes (T1D), is sparse. The Medtronic Continuous Glucose Monitoring System (CGMS), which is in widespread use in the follow-up of children with T1D, offers a possibility to monitor fluctuations in interstitial fluid glucose concentrations also in non-diabetic children.
Aims: In a substudy of the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) study, we are conducting repeated CGMS recordings in a group of children at high genetic risk for T1D to find out whether the progression of prediabetes correlates with trends seen in CGMSs. Here we report preliminary results based on four consecutive CGMS recordings performed in a prediabetic child.

Methodology: The study subject was a 6-year old boy observed in the DIPP study. By the age of 4 yrs, he had developed three diabetes-related autoantibody reactivities and had a subnormal first-phase insulin response (?? mU/l). Four CGMS recordings (1–3 days each) were performed at 3 to 8-month intervals. Immediately after the last recording he was diagnosed with T1D.
Results: The first CGMS showed only slight variability in tissue glucose, which remained within the normoglycemic range. On later recordings, glucose excursions, which appeared approximately at the same time each day (after breakfast and after bedtime) became progressively more pronounced, briefly exceeding the limit of diabetic hyperglycemia (11.1 mmol/l).
Conclusions: Our recordings showed a clear trend towards higher glucose excursions during the morning and early night time. If confirmed in other prediabetic subjects, the observation suggests that such children have their weakest glucose tolerance at those time points. These time periods would be the most appropriate for measuring blood glucose in a child who is at the verge of presenting with clinical T1D.

P19

Does body composition influence type 1 diabetes in children?

P. Fichna[1], K. Majewska[1], B. Skowronska[1], M. Zakrzewska[2] & W. Stankiewicz[1]
[1]Department of Pediatric Endocrinology & Diabetes, University of Medical Sciences, Poznan, Poland, [2]Institute of Psychology, University of Poznan, Poznan, Poland

Body composition seems to interplay with type 1 diabetes.
Aim: To evaluate body components in diabetic children in relation to their disease and to compare them with healthy coevals.
Patients: A total of 116 children (72 girls & 44 boys) suffered from type 1 diabetes (T1DM) for 4.5 ± 3.4 (range: 0.1–15) years and receiving daily insulin dose of 38 ± 20 (range: 8–103) IU, which was divided into 4.8 ± 2.0 doses daily, had HbA1c 8.3 ± 1.9 (range: 5.5–14.5)%; insulin daily dose/body mass was 0.8 ± 0.3 IU/kg. Control group consists of 14 healthy girls and 13 boys). Bioimpedance was estimated with AkernBIA-101 and following markers (kg) were considered: BW-body weight, BCM-body cellular mass, ECW-extra cellular water, MM-muscle mass, FM-fat mass, FFM-free fat mass and their percentage in total body mass, BMI-body mass index, BMR-basal metabolic rate (kcal). Results were statistically analysed with: Kolomogorov-Smirnov, Student's t, Levene's, UNIANOVA tests and Pearson's correlations.
Results: Differences in body composition were not significant between diabetic and control patients (table). However, girls had lower results in both groups for: BCM (p 0.005), BCM% (p 0.029), ECW (p 0.013), MM (p 0.006), MM% (p 0.000), FFM (p 0.017), FFM% (p 0.000) and higher for FM (p 0.054), FM% (p 0.000). Analyses indicated on highly positive correlations for: age, diabetes duration, total insulin dose and dose/kg and number of doses/day to all (with FM two exceptions) absolute body composition parameters, when HbA1c didn't correlated significantly with them and was negative to BCM% only. ECW negative correlation to age was found in both groups.

Group	AGE	BW	BCM	ECW	MM	FM	FFM
T1DM	12.2 ± 3.4	45.7 ± 16.8	16.4 ± 6.6	11.6 ± 3.9	20.4 ± 8.1	11.4 ± 6.5	34.2 ± 12.7
Control	12.3 ± 3.7	45.5 ± 14.2	17.3 ± 6.4	12.0 ± 3.7	21.5 ± 7.9	10.4 ± 4.0	35.1 ± 12.0
	BMR	BMI	BCM%	ECW%	MM%	FM%	FFM%
T1DM	1093 ± 268	19.0 ± 3.6	47.4 ± 3.9	44.2 ± 5.1	44.5 ± 5.6	24.7 ± 7.9	75.3 ± 7.9
Control	1145 ± 259	18.2 ± 3.0	49.0 ± 3.6	44.0 ± 4.0	46.8 ± 5.6	23.2 ± 6.8	76.8 ± 6.8

Conclusion: Selected markers of body composition could be related to insulin dosage but not to disease control in diabetic children.

P20

Effect of MMF and/or antiCD25 on prevention of autoimmune diabetes in the DRBB rat

F. Ugrasbul, J. Popovic, W. V. Moore & K. L. Kover
Children's Mercy Hospital, Kansas City, USA

Abstract withdrawn.

P21

Factors of low-grade inflammation in type 1 diabetes children and adolescents

E. Pankowska, A. Szypowska, M. Lipka & L. Groela
Medical University in Warsaw, Warsaw, Poland

Introduction: Fibrinogen and C-reactive protein are the markers of inflammation and its slightly elevated plasma level in subject with type 2 diabetes indicates a risk for cardiovascular events. Pathogenesis of subclinical inflammation in type 1 diabetes it has still been poorly investigated.
Aim: The aim of study was to determine the CRP and fibrinogen plasma level in metabolically stable, free from microangiopathy type 1 young diabetics and analysis of significant factors low-grade inflammation.
Material and method: We analyzed 190 type 1 diabetes (92 female/98 male), mean age 11.54 SD 4.13 years; mean diabetes duration 4.47 SD 3.96 years (0.1–17.6) mean GlyHbA1c8.46 SD 2.18% (4.9–19). During schedules visits clinical and biochemical parameters: CRP, Fibrinogen, GlyHbA1c, Total-, LDL-, HDL-cholesterol, triglyceride, C-peptide, antibody TPO, TG, IgA_{EmA}, IA_2, GAD were assessed. After examinations subjects with severe hypoglycaemia, DKA (ketoacidosis), infections or endocrine diseases were excluded.
Results: Seventeen percent of study population had plasma fibrinogen level above age-related range, this group present significantly higher C-reactive protein (0.5 mg/dl vs. 0.167 respectively $p = 0.019$), but metabolic control, BMI, diabetes duration and age was comparable to group with normal fibrinogen range. After adjustment for age, diabetes duration, gender, BMI, total-, LDL-, HDL-cholesterol, positive fibrinogen correlation with antibody TPO ($r = 0.22$ $p = 0.0045$), TG ($r = 0.12$ $p = 0.0022$) was found. Additional analyzes in group with increased risk of microvascular complications (HbA1c > 8.5% and diabetes duration > 5 years) did not revel correlation with fibrinogen and CRP plasma concentrations.
Conclusion: This preliminary analysis indicates that low-grade inflammation parameters correlate with non metabolic and diabetes related factors in children with type 1 diabetes. Autoimmune thyroid process is a significant factor involved into this pathology.

P22

Increased prevalence of positive skin prick test in type 1 diabetes: an indicator of impairment of T-cell regulatory function?

R. Cardani, A. Saporiti, P. Marino, S. Arrigo, S. Salvatore, A. Salvatoni & L. Nespoli

Pediatric Clinic University of Insubria, Varese, Italy

Introduction: Type 1 diabetes results from an abnormal T-cell mediated autoimmune response, thought to be primarily of the TH type 1 cells. By contrast, TH type 2 cells predominate in allergic diseases. Because it is known that TH1 and TH-cells reciprocally counteract each other it can be speculated that the prevalence of TH2 mediated disease is lower in patients with TH1 mediated disease.
Aims: To determine whether type 1 diabetes children have significant different prevalence of allergy skin test compared to normal control.
Methodology: Fifty-four Type 1 diabetes children free of allergic symptoms (28 boys) aged 13.9 ± 5.0 years and 54 healthy controls matched for age and gender without allergic symptoms (M 24, F 30, mean age 82,7 months) were enrolled. All children underwent skin-prick tests for common aero and alimentary allergens. Parents of children compiled a questionnaire on allergic disease and atopic familiar history.
Results: The results are summarised in the table. Our study showed a significant higher prevalence of positive skin prick test in type 1 diabetes children compared to control despite a significantly lower positive familiar history for allergies.

		Prick positivity			Allergy familiar history
Groups	N	Inhalants	Alimentary	Total	
Diabetics	54	18/54 (33%)	7/54 (13%)	21/54 (39%)	10/54 (19%)
Controls	54	9/54 (17%)	0/54 (0%)	9/54 (17%)	26/54 (48%)
χ^2 p		4.00 < 0.05	7.50 < 0.01	6.01 < 0.025	11.173 < 0.001

Conclusions: This date do not confirm previous studies reporting decreased prevalence of atopic disease in T1DM and they support the hypothesis of an impaired T-cell regulatory function causing an alteration on Th2 to Th1 switching.

P23

Islet autoantibodies at birth is associated with reduced prevalence of islet autoantibodies in newly diagnosed type 1 diabetic children born to non-diabetic mothers

M. Elfving[1], B. Lindberg[2], K. Lynch[3], G. Sundkvist[3], M. Månsson[2], Å. Lernmark[3] & S-A. Ivarsson[2]

[1]Department of Clinical Sciences, Pediatric Unit, Lund University, University Hospital, Lund, Sweden, [2]Department of Clinical Sciences, Pediatric Unit, Lund University, Malmö University Hospital, Malmö, Sweden, [3]Department of Clinical Sciences, Unit of Diabetes and Celiac disease, Lund University, Malmö University Hospital, Malmö, Sweden

Introduction: A recent study suggested that fetal exposure to islet autoantibodies in children born to mothers with type 1 diabetes may be protective against future islet autoimmunity and diabetes.
Aim: We investigated islet cell autoantibodies in an unselected population of children with type 1 diabetes, born to non-diabetic mothers, by comparing autoantibodies in their cord blood serum samples with a sample taken at the time of clinical diagnosis.
Methodology: Serum samples at birth and at the time of diagnosis were available from 141 children who developed type 1 diabetes between 1.3–18.8 years of age (median 9.0 years; male/female ratio 83/58). Children born to mothers with type 1 diabetes or any other form of diabetes were excluded. The samples were tested for autoantibodies against glutamic acid decarboxylase (GAD65Ab), islet-associated antigen 2 (IA-2Ab), insulin (IAA) by radiobinding assays as well as to islet cell antibodies (ICA) by indirect immunofluorescence.
Results: The frequency of islets autoantibodies in cord blood was 11% (15/141), (ICA 4%, GAD65Ab 6%, IA2-Ab 1% and IAA 1%) compared to 91% (129/141) (ICA 76%, GAD65Ab 61%, IA2-Ab 69% and IAA 44%) at diagnosis. Children with fewer islet autoantibodies (Abs) at diagnosis were more likely to have had autoantibodies in their cord blood sample. Of children with no Abs at diagnosis 25% had autoantibodies in cord blood, 1 Ab 21%, 2 Ab's 17% and ≥3 Ab's 5% ($p < 0.01$) demonstrating a significant inverse relationship (trend, $p < 0.001$). Cord blood autoantibodies were most strongly associated with absence of ICA at diagnosis [OR (95%CI) 6.06 (1.97–18.60) $p = 0.0016$] even after adjusting for other islet autoantibodies at diagnosis [OR (95%CI) 4.86 (1.23–19.2) $p = 0.02$].
Conclusion: Our data support the notion that cord blood islet autoimmunity may induce immunological tolerance and explain why some type 1 diabetes children are islet autoantibody negative at the time of clinical diagnosis.

P24

The role of islet antibodies in type 1 diabetes prediction

S. Eising[1], A. Nilsson[2], D. M. Hougaard[3], B. Nørgaard-Pedersen[3], F. Pociot[1], J. Nerup[1] & Å. Lernmark[2]

[1]Steno Diabetes Center, Gentofte, Denmark, [2]Lund University, Department of Clinical Sciences, Malmø, Sweden, [3]Staten Serum Institut, Department of Clinical Biochemistry, Copenhagen, Denmark

Background: It is still unknown if diabetes-related autoantibodies at the time of birth impact the development of type 1 diabetes(T1D). A reason for current controversies is the lack of sufficiently large investigations at time of birth of subjects who later developed T1D.
Aims: To determine GAD65 and IA-2 autoantibodies at time of birth in a large unselected population-based case-control population of newborns using Dried Blood Spot(DBS) collected 5 days after birth. We test the hypothesis that islet autantibodies at birth predict T1D.
Samples: DBS of 2028 Danish T1D patients from the birth cohorts of 1981–2002, and two controls per patient were selected. Patient and control samples were matched by place and date of birth. The samples had been stored for 3–24 years at -25ordm; at Statens Serum Institut, Copenhagen, Denmark.
Methods: A radiobinding assay was performed on 3.2-diameter DBS punch-out samples, simultaneously detecting autoantibodies to GAD65, IA-2, or both. Autoantibody positive samples (by 99% percentile) are re-analyzed for IA-2 autoantibodies alone to distinguish the possible role of GAD65 from IA-2 autoantibodies. Conditional logistic regression was used to estimate hazard ratios of diabetes occurrence from the matched case control data.
Results: In the case group, 70/2028(3.45%) were autoantibody positive compared to 21/4021(0.52%) in the control group ($p < 0.0001$). The 99.5% percentile in the control population was used as a cut-off point. Proportional Hazard Regression Model in cases compared to their matched controls showed a Hazard Ratio of 2.54 (confidence limits 2.002–3.242) for every 10-fold increase in relative units (an expression of autoantibody levels) ($p < 0.0001$). Antibody positive compared to negative patients did not differ with respect to age at diabetes diagnosis, birth weight, birth length, or gestational age (determined by regression analysis). Only 2/70 (2.86%) autoantibody positive cases were born to mothers with known T1D.

Conclusion: Detection of islet autoantibodies against GAD65 and IA-2 at the time of birth is a prediction marker of T1D diagnosed before 24 years of age.

P25

Analysis of genetic factors predisposing to type 1 diabetes in children under 5 years of age

A. Skorka[1], E. Pankowska[1], A. Szypowska[1], M. Choim[1], G. Kostrzewa[1], M. Szalecki[2], L. Korniszewski[1] & R. Ploski[3]

[1]Department of Diabetology, Neonatology and Birth Defects, Medical University of Warsaw, Warsaw, Poland, [2]Department of Diabetology and Endocrinology, Children Hospital, Kielce, Poland, [3]Department of Medical Genetics, Medical University of Warsaw, Warsaw, Poland

Type 1 diabetes is a multifactorial disease. The genetic contribution involves many loci. Recently it has been claimed that the incidence of type 1 diabetes has increased in many countries including Poland. The highest increase occurred in children under 5 years of age. There are data suggesting that the type 1 diabetes in very young children may have different genetic background. The aim of the study was to compare the frequencies of several genetic factors in two groups of children: diagnosed under 5 years of age and the group of older children.

Materials and methods: The study group consisted of 357 children with type 1 diabetes aged from 0.33 to 18.2 (mean age 8.34, SD 4.61). There were 101 children under 5 years of age. We analysed the following markers: DRB1 alleles, CTLA-4 gene polymorphism (+49A/G, CT60, MH30), six polymorphism of Il-10 gene (592 C/A, 819 C/T, 1082 G/A, 2763 C/A, 2849 G/A, 3575 T/A), polymorphism 1085 C/T of PTPN22 gene, polymorphism –23HpHI of INS gene, polymorphism –1260 C/A of CYP27B1 gene, polymorphism rs 1544410 A/G of VDR gene and polymorphism rs 10774671 A/G of OAS1 gene. PCR-RFLP or SnapShot minisequencing method was used.

Results: There were no statistically significant differences in frequencies of studied polymorphisms between children with diabetes diagnosed under 5 years and those diagnosed later. For haplotypes of CTLA-4 polymorphism $p = 0.31$, for haplotypes of Il-10 SNPs $p = 0.41$, for 1085C/T of PTPN22 gene $p = 0.58$, for INS gene polymorphism $p = 0.31$, for CYP27B1 $p = 0.73$, for VDR $p = 0.59$, for OAS 1 gene $p = 0.29$.

Conclusions: The youngest children with type 1 diabetes do not differ genetically from children diagnosed at later age. The increasing incidence of type 1 diabetes in children under 5 years of age is due to some environmental factors that operate early in prenatal or infancy period.

P26

Association of IL6 serum levels but not of the IL6-174G/C polymorphism with age, sex and islet-autoantibody titres, during the remission period in children and adolescents with newly diagnosed type 1 diabetes

S. Poerksen[1], L. B. Nielsen[1], C. Pfleger[2], N. C. Schloot[2], P. Hougaard[3], R. Holl[4], P. Swift[5], H. B. Mortensen[1] & L. Hansen[6]

[1]Glostrup University Hospital, Glostrup, Denmark, [2]German Diabetes Research Institute, Düsseldorf, Germany, [3]University of Southern Denmark, Odense, Denmark, [4]University of Ulm, Ulm, Germany, [5]Leicester Royal Infirmery, Leicester, UK, [6]Novo Nordisk A/S, Bagsvaerd, Denmark

Introduction: Islet-autoantibodies (ICA, GADA, IA-2A) are associated with the development and progression of T1D. Negative correlation of cytokines to auto-antibody titres in adults with new onset T1D have been reported. The single nucleotide polymorphism IL6 -174G/C in the promoter of the IL-6 gene has been suggested as a T1D susceptibility gene in young females.

Aims: Our aim was to investigate the correlation between the IL6-174G/C variant, IL-6 serum levels, autoantibody titres, and age of onset in children during the first year of newly diagnosed T1D, and to evaluate if differences in IL-6 serum levels or age at onset could be influenced by the genetic variant IL6-174G/C.

Methodology: A total of 256 patients (134 females, 122 males, age 9.6, range 0.2–16.8) with newly diagnosed T1D were recruited from 18 paediatric centres and followed for 12 months. At 1, 6, and 12 months after diagnosis serum IL6 levels were measured by ELISA together with autoantibody titres. Genotyping was carried out by PCR-RFLP.

Results: IL6 levels negatively associated with ICA ($p = 0.056$) at 1 month and IA-2A ($p = 0.011$ and $p = 0.042$) and GADA ($p = 0.012$ and $p = 0.026$) at 1 and 6 months. IL6 ($p = 0.023$) levels at 1 month also correlated negatively with age mainly due to significantly higher IL-6 ($p = 0.035$) levels in young females (< 10 years). We found no association of the IL6-174G/C-polymorphism with age, sex or IL6 serum levels, autoantibodies, or age of onset.

Conclusions: We conclude that IL-6 as part of the systemic immunoregulation may contribute to a more aggressive disease progression and shorter remission period in children and especially young females with T1D. In our study we were not able to attribute the findings on IL6 serum levels and age of onset in females to genetic variation within the IL6 gene, possibly due to a limited sample size.

P27

Better Diabetes Diagnosis (BDD): A country-wide registry of incident patients suggests an altered HLA genotype distribution from 1986–87

A. Carlsson, L. Blom, G. Forsander, S-A. Ivarsson, A-K. Karlsson, A. Kernell, Å. Lernmark, B. Lindblad, J. Ludvigsson, C. Marcus, A. Nilsson & H. Rastkhani & I. Zachrisson

[1]Clinical Science, Lund, Sweden, [2]Clinical Science, Malmö, Sweden, [3]Clinical Science, Göteborg, Sweden, [4]Clinical Science, Malmö, Sweden, [5]Clinical Science, Göteborg, Sweden, [6]Karolinska University Hospital, Stockholm, Sweden, [7]Clinical Science, Malmö, Sweden, [8]Clinical Science, Göteborg, Sweden, [9]Division of Pediatrics and Research Centre, Faculty of Health Sciences, Linköping, Sweden, [10]Karolinska University Hospital, Stockholm, Sweden, [11]Clinical Science, Malmö, Sweden, [12]Clinical Science, Malmö, Sweden, [13]Karolinska University Hospital, Stockholm, Sweden

Introduction: Sweden has the second highest incidence rate of Type 1 diabetes in the world and the age at onset has been shown to decrease.

Aims: The aim of the present study was to test the hypothesis that HLA-typing at time of diagnosis would better diabetes diagnosis and improve classification and thereby treatment.

Methodology: A case-control study of patients developing type 1 diabetes in 1986–87 ($n = 430$) was the baseline reference study for HLA. The Better Diabetes Diagnosis (BDD) project was initiated in May 2005. Almost all 42 Paediatric clinics in Sweden participate by preparing Dried Blood Spots (DBS) of blood samples taken on the day of specific diagnosis. HLA DQA1-B1 genotypes were determined by PCR on the DBS using allele specific probes detected by time-resolved fluorescence.

Results: A total of 491 incident patients have been analyzed about nine months into the BDD study. The most common HLA DQA1-B1 genotype, DQB1*0501-0201/0301-0302, which was 36% in 1986–87 had decreased in frequency to 27% (130/491) in 2005–2006. The DQ A1*–B1* genotype 0301-0302/0301-0302 had increased from 8% to 28%. The homozygous genotype 0501-

0201/0501-0201 increased from 3% in 1986–87 to 11% (56/491). DQB1* was not present in any child 1968–87 but in BDD 6 of 491 0602-positive children have developed diabetes.
Conclusions: It is concluded that there is a temporal change in HLA genotype distribution. We speculate that the change in HLA distribution may reflect adaptation of triggering infectious agents(s) to specific HLA.

P28
Clinical and molecular findings in an atypical case of IPEX-Syndrome

B. Rami[1], O. Bodamer[1], B. Item[1], A. Heitger[2], O. Haas[2], W. D. Huber[1] & E. Schober[1]

[1]Medical University Vienna, Department of Pediatrics, Vienna, Austria, [2]St. Anna Children's Hospital, Vienna, Austria

Introduction: IPEX-Syndrome (immunodysregulation, polyendocrino-pathy, and enteropathy, x-linked) is a rare disorder, which usually results in death during the first months of life. The clinical features include early onset diabetes mellitus, chronic diarrhoea with villous atrophy, eczema, anaemia, thrombozytopenia, thyreoiditis and recurrent infections. Mutations in the *FOXP3* gene (Xp11.23-q21.1) are pathogenic for IPEX-Syndrome.
Aims: We describe an unusual clinical course of a patient with IPEX-Syndrome.
Results: The now 20-year-old male presented with dystrophy and diarrhoea at the age of 7 months, the histological result of the small bowel biopsy showed a subtotal villous atrophy. The endomysial antibodies were negative. At the age of 2 years an allergy to hen's egg was diagnosed. An autoimmune-hepatitis was diagnosed (liver-biopsy) at the age of 4 years, when he showed clinical symptoms of an icterus. Subsequently therapy with cortison and azathioprin was initiated and continued until today. At the age of 18 years he was diagnosed with type 1 diabetes mellitus, due to the typical clinical symptoms (polyuria, polydipsia and weight loss) and positive GAD-antibodies (IAA- and IA2-Ab were negative). The combination of enteropathy, autoimmune-hepatitis and diabetes mellitus led us to suspect the diagnosis of IPEX-Syndrome, which was confirmed by a mutation analysis in the *FOXP3*-gene (R347H). The brother of this patient suffered from enteropathy and died due to a catheter-sepsis during the first year of life. Most likely, he also had IPEX-Syndrome, but due to a lack of genetic material we were unable to confirm the diagnosis. Interestingly our patient presented with mild clinical symptoms, which contradict previous reports in the medical literature.
Conclusions: We speculate that an unknown, immunological factor ameliorates the otherwise fatal clinical course in our patient with atypical IPEX-Syndrome.

P29
Genetic and immunologic basis of diabetes in an extended consanguineous Bedouin family

A. Peretz[1], S. Israel[2], E. Hershkovitz[1], N. Loewenthal[1], Y. Abu-Rabiah[3], T. Chechik[1], O. Birk[4] & E. Leiberman[1]

[1]Pediatrics, Endocrinology & Metabolism Unit, Soroka Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel, [2]Tissue Typing Unit, Hadassah-Hebrew University Hospital, Jerusalem, Israel, [3]Clalit Health Services - Rahat, Ben-Gurion University of the Negev, Beer-Sheva, Israel, [4]The Genetics Institute Center, Soroka Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Introduction: Diabetes incidence among the Bedouin population has been increasing. Genetic understanding of diabetes is dependent on large population studies. The closed society and consanguineous marriages of the Bedouins provide an opportunity to examine the genetic and immunologic basis of diabetes. This study is a genetic-immunologic research dealing with diabetes among the Bedouin population.
Aims: To describe the immunological and genetic characteristics of a Bedouin population highly prevalent with diabetes.
Methodology: *Study population:* An extended Bedouin family (~80 individuals) highly prevalent with diabetes. HLA control group encompassing ~220 unrelated healthy (no known diabetes or any other autoimmune diseases) of Bedouin origin. Biochemical and immunologic markers to differentiate between the different types of diabetic syndromes have been obtained. HLA oligotyping on all subjects.
Results: We identified type 2 diabetics with an overlap of diabetic markers of autoimmunity. 14% of family members have diabetes (type 1 or 2). 22% have at least 1 marker of autoimmunity (either pancreas or celiac antibodies). 36% of childbearing women had gestational diabetes. We compared HLA typing of a Bedouin control group and HLA of individuals from families affected with diabetes and autoantibodies. There is an aggregation of DRB1*07 DRB1*10 in these families while DRB1*04 is lower compared to the controls. Seven of 12 individuals with autoantibodies, are adults and did not develop T1D. They carry either DQB1 or DRB1 alleles, which are negatively associated with T1D.
Conclusions: These families have a genetic background with susceptibility to developing either T1D or T2D. The presence and absence of relevant HLA alleles is responsible for interruption of the outcome to T1D in the individuals with the autoantibodies. Analysis of HLA in the group with autoantibodies strengthens this possibility. Presence of 'protective' or 'deleterious' HLA with autoantibodies among families with genetic susceptibility may prevent or promote development of T1DM.

P30
Kir6.2 impact of mutation and treatment on diabetes and neurology

A. S. Slingerland[1], R. Nubour[2], M. Hadders-Algra[3], A. T. Hattersley[1] & G. J. Bruining[4]

[1]Institute of Biomedical and Clinical Science, Exeter, UK, [2]Meander Medical Center, Amersfoort, The Netherlands, [3]Department of Neurodevelopment, University Medical Center, Groningen, The Netherlands, [4]Department of Diabetes, Erasmus Medical Center, Rotterdam, The Netherlands

Introduction: Activating mutations in the KCNJ11 gene encoding the Kir6.2 subunit of the pancreatic beta cell's KATP channels were a common cause of neonatal diabetes. One third of patients also have developmental delay believed to arise from mutated KATP channels in muscle, nerve and brain. Sulfonylurea can replace insulin injections in these patients. Long-term treatment or the impact on neurodevelopmental features has not been described.
Aim: We aimed to study the long-term impact of sulfonylurea treatment on neonatal diabetes and neurology.
Methodology: We studied glucose homeostasis and neurology on standardised scales in the patient with longest follow up, and who also had the V59M mutation that is associated with Intermediate Developmental delay Epilepsy and Neonatal Diabetes syndrome.
Results: Sulfonylurea treatment was started at 1 year and 10.5 months. This resulted in insulin being discontinued, improved mean premeal glucoses (9.8 mmol/l–6.4 mmol/l), reduced daily fluctuations in glucose (9.2 mmol/l–3.6 mmol/l) and reduced hypoglycaemia. Good control (HbA1C 6.5%) was maintained despite a reduced glibenclamide dose (0.41–0.11 mg/kg/day). His motor development also improved markedly as assessed by the Bayley Scales of Infant Development II, starting to walk 1 month after initiation of treatment. There was no improvement of mental function and he developed absence seizures on treatment.
Conclusion: This case highlights in patients with KCNJ11 mutations sulfonylurea can result in prolonged excellent

glycaemic control and may improve motor but not mental features suggesting a predominantly peripheral, rather than a central, site of neurological action. Early molecular diagnosis is vital in patients with neonatal diabetes and neurological features.

P31

Neonatal diabetes in children from central Poland: catch up effect for body weight and a novel mutation in glucokinase gene

W. Mlynarski[1], B. Mianowska[1], O. Wegner[1], A. Gach[1], M. Zawodniak Szalapska[1], J. Nazim[2], M. Borowiec[1], M. Malecki[2] & J. Bodalski[1]

[1]Medical University of Lodz, Lodz, Poland, [2]Jagiellonian University, Cracow, Poland

The literature suggests that neonatal diabetes is genetically determined with mutations within the genes, which encode for proteins involved in regulation of beta cell function, e.g. *KCNJ11*, glucokinase or *SUR1*. The study aimed to evaluate clinical and genetic characteristics of patients with neonatal diabetes from central Poland registry. Between 1992 and 2004 we found 10 children who were diagnosed for diabetes before the 12-month of age; median age at onset 2.25 (0.1–6.2) months; F/M 6/4. Mean C-peptide level at onset was 0.12 ± 0.10 ng/ml. Six of these patients were positive for at least one type of the islet autoantibodies. Interestingly, the antibody positive patients were older at onset, median 3.6(0.1–5.2) months as compared to antibody negative individuals, median 0.35 (0.15–1.25), however, the difference was not statistically significant ($p = 0.3$). Only nine of these patients were available for follow-up; median age at follow-up 7.0 (4.0–7.0) years. The comparison of the body weight at birth and at follow-up stratified by hbd, age and gender (standard deviation score, SDS) revealed higher values at follow-up –1.5(–3.2 to –1.1) vs. –0.1(–0.6 to 1.3); $p = 0.04$ in nonparametric analysis. Observed catch up effect points to defective insulin secretion among studied individuals, which resulted in relatively low body weight at birth. Thus, we decided to perform genetic analysis of the glucokinase gene as a possible defective factor within beta cells. Direct sequencing of the gene revealed that one of the children (age at onset 6.5 months) is heterozygous for a unique combined genotype with four mutations located in the beta cell specific promoter and the 5'UTR of glucokinase gene (-282C/T, -194 A/G, -30 G/A, +403 C/G). Only the -30 G/A polymorphism is known as relatively common in general Caucasian population. Further functional studies and family screening is needed to confirm that these DNA sequence differences contribute to the neonatal diabetes in this individual. Additional studies are in progress for screening of the *KCNJ11* gene.

P32

No association of new polymorphism in PTPN22 region (rs 3789604 C/A) with type 1 diabetes in Polish population

A. Skorka[1], E. Pankowska[1], A. Szypowska[1], M. Choim[1], G. Kostrzewa[1], M. Szalecki[2], L. Korniszewski[1] & R. Ploski[3]

[1]Department of Diabetology, Neonatology and Birth Defects, Medical University of Warsaw, Warsaw, Poland, [2]Department of Diabetology and Endocrinology, Children Hospital, Kielce, Poland, [3]Department of Medical Genetics, Medical University of Warsaw, Warsaw, Poland

An individual's predisposition to insulin-dependent type 1 diabetes mellitus (T1D) is largely determined by complex interactions between several genetic loci and other, nonheritable factors. The disease is characterised by the autoimmune destruction of β-cells in the pancreas by cytotoxic CD8+ T cells. PTPN22 gene on chromosome 1p13, which encodes a lymphoid protein tyrosine kinase (LYP), is a negative regulator of T-cell activation and seems to be the best example of a non-MHC common susceptibility allele for autoimmunity with its R620W SNP consistently associated with increased risk for T1D, RA, SLE and Graves disease. Recently additional SNPs in the region of PTPN22 gene have been implicated in pathogenesis of RA (Am J Hum Genet 2005; 77:567-581) with SNP rs 3789604 C/A defining one of the two major risk haplotypes for the disease.

Objective: The purpose of the study was to investigate in a Polish population the frequency of two polymorphisms in the region of PTPN22 gene: 1858C/T (R620W) and rs 3789604 C/A and to determine its association with T1D.

Materials and methods: A cohort of 361 children with T1D and 373 healthy controls was genotyped by a PCR-RFLP method. The distribution of PTPN22 alleles and genotypes among patients and controls were compared using chi-square test.

Results: Genotype frequencies are reported below.

PTPN22 1858 C/T	CC	CT	TT
Controls (n = 349)	76.7%	22.0%	1.3%
T1D (n = 310)	61.0%	34.1%	4.9%

($p < 0.00001$)

rs 3789604 C/A	AA	AC	CC
Controls (n =361)	66.2%	30.6%	3.2%
T1D (n = 373)	64.6%	30.7%	4.7%

($p = 0.572$)

Conclusions: Our results indicate that PTPN22 1858'T' allele is associated with T1D in Polish population whereas we found no association of SNP rs 3789604 C/A with T1D in our population.

Acknowledgement: Supported by State Committee for Scientific Research grant No 2PO5E 054 26

P33

Rapid HLA-DQ genotyping and HLA-DRB1*04 subtyping using real-time PCR with sequence-specific primers

O. Cinek[1], K. Rakova[1], O. A. Fuglesang[2] & K. S. Ronningen[2]

[1]Motol University Hospital, Charles University, Prague, Czech Republic, [2]The Norwegian Institute of Public Health, Oslo, Norway

Background: Current studies on pathogenesis of type 1 diabetes usually select individuals based on their genetic risk. This requires use of high-throughput HLA-genotyping techniques that frequently have to rely on alternative sources of DNA, as mouth swabs, dry blood spots or saliva. These sources usually provide DNA of inconstant quantity and quality. From these samples, HLA typing methods based on an end-point detection of the PCR product may yield results that are difficult to interpret.

Aims: We set out to develop a real-time PCR-based HLA typing method that gives results independent on the quantity of DNA in the reaction.

Methodology: We selected and tested sets of six reactions identifying the HLA-DQA1*01 to DQA1*05, twelve reactions covering the HLA-DQB1 alleles associated with diabetes, and ten reactions sorting the HLA-DRB1*04 into eight subtypes. Each allele-specific reaction contains an allele-specific primer set, a fluorescent probe detecting all alleles at the respective HLA locus, and a primer-probe set to detect an internal control. The internal control secures against a PCR failure. Alleles are called using the difference between the allele-specific signal and the generic reaction signal.

Results: Effective allele identification is enabled by the size of the difference in threshold cycles between the true and false positivity. It ranges from approximately eight cycles (some of the DQB1 reactions), 10 cycles (DRB1*04 subtyping) to infinity (DQA1 reactions). The method is now being used in a two-step screening

using mouth swabs as the source of DNA. In the first step, individuals having the HLA-DQA1*03/05 genotype are identified, among whom the carriers of the highest-risk HLA-DQB1 are found in the second step.
Conclusions: The HLA typing based on real-time PCR detection seems to offer a valid alternative to end-point methods, especially when high-quality DNA is not available.

P34

Sulfonylurea instead of insulin in PNDM patients with activating mutation in the gene KCNJ11 encoding the Kir6.2 subunit led to significant improvement of DM compensation

M. Paskova
Childreńs Uni Hospital, Kosice, Slovakia

Introduction: It is known, that activating mutations in the gene KCNJ11 encoding the Kir 6.2 subunit of the ATP sensitive potassium channel can be cause of permanent neonatal diabetes. This new fact results in different treatment approach of PNDM.
Aim: Two cases of PNDM with different mutations will be presented, whereas one mutation is novel.
Cases: First patient (Pt.1) has most common mutation R201H in the KCNJ11 gene. He developed manifestation of DM in age of 6 weeks with low level of C-peptide – 0.25 pmol/l, ICA negative. He was treated with intensified insulin regimen for 10 years. GAD and IA2 were negative in last couple of years. The second one (Pt.2) has novel mutation H46Y/N in the KCNJ11 gene. Diabetes was diagnosed at age of 4 months with C - peptide 0.21 pmol/l, ICA negative, AD and IA2 negative for the last years. This patient expressed slight dysmorphic features – a mild bilateral blepharoptosis and also mild degree of mental retardation. She was treated with intensified insulin regimen for 12 years. Due to the genetic finding mentioned above we gradually started with administration of sulfonylurea (SU) in dose 0.1 mg/kg and simultaneous decrease of insulin. Sulfonylurea dose 0.8 mg/kg enabled to withdraw insulin completely.
Results: Exchange of the medication was started in October 2005 in both patients. Level of C-peptite was dramatically increases immediately after the introduction of SU, in Pt. 1 from 0.5 pmol/l to 1350 pmol/l, in Pt.2 from 11.5 pmol/l to 800 pmol/l, after 2 h of administration. After half year of treatment with SU is improvement in DM compensation remarkable. HbA1c decreased from 8.1 to 4.7% in Pt. 1 and from 9.6 to 4.5% in Pt. 2. Both patients are without hypoglycaemic episodes. Their glycaemic profiles range between 3.8 and 9.6 mmol/l. C-peptide is still in normal range.
Conclusions: It seems, due to the presented clinical experience, that in compare with insulin is monotherapy of sulfonylurea more effective treatment of PDMD with activating mutation in the gene KCNJ11.

P35

Clinical remission of type 1 diabetes mellitus in children – relation to insulin secretion and insulin sensitivity

A. Szadkowska, A. Zmyslowska, I. Pietrzak & J. Bodalski
Department of Pediatrics, Medical University, Lodz, Poland

The aim of the study was to estimate the relationship between prevalence of clinical remission of type 1 diabetes mellitus (T1DM) in children and adolescents and insulin secretion and insulin sensitivity.
Materials and methods: Sixty-seven patients at the age 13 ± 2.7 years with newly diagnosed T1DM were recruited into the study. The patients were observed for 6 months. Clinical remission was recognized when daily dose of insulin was below 0.3 U/kg and HbA1c < 6.5%. Insulin secretion was estimated on the base of the serum C-peptide concentration in glucagon test: C-peptide-0' fasting and C-peptide – 6 ' in the 6th minute after stimulation by glucagon. Euglycemic-hyperinsulinemic clamp was performed to assess insulin resistance. Glucose disposal rate (M index) determined during the last 30 min of the test estimated insulin resistance. HbA1 was examined by HPLC.
Results: The remission was recognized in 13 (19.4%) T1DM children and adolescents. The patients with remission had better residual insulin secretion than patients without remission at the onset of diabetes and at the 6th month (onset: C-peptide-0' – 0.18 ± 0.02 vs. 0.27 ± 0.04 pmol/l, p = 0.06; C-peptide –6' – 0.32 ± 0.09 vs. 0.50 ± 0.04 pmol/l, p = 0.03; 6 month: C-peptide-0' – 0.39 ± 0.05 vs. 0.25 ± 0.02 pmol/l, p = 0.029; C-peptide –6' – 0.66 ± 0.09 vs. 0.47 ± 0.04 pmol/l, p = 0.046). At the onset of T1DM there was no difference in insulin sensitivity between groups (M index 6.91 ± 0.34 vs. 7.07 ± 0.74 mg/kg/min, p = 0.84). But at the 6th month better insulin sensitivity was observed in the patients with remission than in children without it (M index – 10.39 ± 0.82 vs. 7.95 ± 0.38 mg/kg/min., p = 0.035).
Conclusion: In type 1 diabetic children and adolescents the prevalence of clinical remission depends on their own residual insulin secretion and improvement of insulin sensitivity.
Acknowledgement: Supported by Medical University of Lodz – 503-127-3.

P36

Partial remission phase and its effect on long-term glycaemic control and microvascular complications in type 1 diabetes mellitus

S. D. Shenoy[1], D. Cody[1], P. G. F. Swift[1], M. J. Davies[2], I. G. Lawrence[2] & N. T. Raymond[3]
[1]Children's Hospital, Leicester Royal infirmary, Leicester, UK, [2]Department of Diabetes & Endocrinology, Leicester Royal infirmary, Leicester, UK, [3]Warwick Medical School, University of Warwick, Coventry, UK

Aims: To evaluate the characteristics of partial remission (PR) phase in children with T1DM and its relation to glycaemic control and rates of microvascular complications during follow-up.
Method: Retrospective study involving 300 children diagnosed with TIDM under the age of 16 years (mean age 9.1 ± 3.8 years) during 1990–1999 in a single centre. PR, defined as insulin requirement of <0.5 units/kg/day, was evaluated at 3, 6, 12, 18 and 24 months after diagnosis by comparing differences in insulin requirement and HbA1c levels. Follow-up data were collected in 2004 (time from diagnosis range 5–15 years).
Results: Data on PR were available in 263 (88%). 112 (43%) showed some period of PR during the 24 months after diagnosis. Rate of PR was most marked at 3 months (37%) with 5% (n = 12) still in remission at 24 months. Mean estimated duration of remission from diabetes diagnosis was 8.2 ± 5.7 months. Throughout the 24 months, insulin requirement and HbA1c in remitters were significantly lower than non-remitters (p < 0.0001, p < 0.005, respectively). Significantly lower rates of remission were found in girls and with presence of DKA at diagnosis (p < 0.001, p < 0.05, respectively). There was no statistically significant difference in the PR rates in any particular age band, ethnic background (South Asian vs. White Caucasian) or deprivation status. Of those treated at home at diagnosis 52% remitted vs. 40% of those requiring hospital admission albeit not statistically significant (p = 0.08). Follow-up data were available in 224 (75%) with mean age at follow-up 17.9 ± 4.5 years. There were no statistically significant differences between remitters and non-remitters in glycaemic control, insulin requirement or rates of microvascular complications at 5, 10 or 15 years.

Conclusion: PR phase is associated with significantly reduced insulin requirement and HbA1c but its favourable effect on later glycaemic control and rates of microvascular complications is questionable.

P37

A Glargine + Aspart + NPH regimen is associated with better prediction of nocturnal hypoglycaemia from routine capillary glucose readings, in pre-pubertal T1DM children on 3x daily insulin regimen

E. Froehlich-Reiterer, K. Ong, F. Regan, C. Acerini & D. Dunger

University Department of Paediatrics, Cambridge, UK

Introduction: In prepubertal T1DM children on a 3x daily insulin injection regimen, we previously reported that compared to conventional insulin therapy (using long-acting NPH), a regimen combining Glargine + Aspart + NPH was associated with reduced risk of nocturnal hypoglycaemia, and lower and more stable pre-breakfast blood glucose readings.

Aims: To explore whether the prediction of nocturnal hypoglycaemia assessed by continuous glucose monitor (GCMS, Minimed) from routine capillary blood glucose readings is improved on Glargine + Aspart + NPH, compared to the conventional NPH-long-acting regimen.

Methodology: Seventeen pre-pubertal children with T1DM (10 boys), median age 10.2 years (range 6–12.4), HbA1c 8.8% (6.8–11.5) took part in an open-label, randomised, crossover study. After a 2-week run-in period (with NPH *pre-bed*), every child received three different 3-week Glargine treatment blocks in randomized order. Treatment block 3 consisted of insulin Aspart + NPH in the morning, insulin Aspart *pre-tea*, and Glargine *pre-bed* and led to reduced nocturnal risk for hypoglycaemia. CGMS was applied for 3 days at the end of each treatment period. Nocturnal hypoglycaemia was defined as a sensor glucose value of <3.5 mmol/l for >15 min, and prolonged hypoglycaemia >60 min.

Results: On Glargine + Aspart + NPH, a low pre-breakfast capillary glucose reading (<4.0 mmol/l) was seen following 5/10 (50%) of all nocturnal hypoglycaemic nights compared to 0/35 (0%) of non-hypoglycaemic nights. Pre-bed glucose readings (8–9 pm) <10 mmol/l were recorded prior to all 5/5 (100%) of nights with prolonged hypoglycaemia >100 mins, compared to 45% of other nights. In comparison, on the NPH-long-acting regimen, a low pre-breakfast glucose reading (<4.0 mmol/l) was seen following 21% of nocturnal hypoglycaemic nights and 3% of non-hypoglycaemic nights. Pre-bed glucose readings <10 mmol/l were recorded prior to 44% of nights with prolonged hypoglycaemia, and on 34% of other nights.

Conclusion: Compared to conventional 3x daily insulin regimens, Glargine + Aspart + NPH is associated with less variable blood glucose levels, and therefore increased prediction of nocturnal hypoglycaemia from daytime capillary glucose readings.

P38

A randomized clinical trial comparing breakfast and bedtime administration of insulin glargine in children and adolescents with type 1 diabetes

D. Goksen, B. Yildiz, G. Asar & S. Darcan

Department of Pediatric Endocrinology and Metabolism, Ege University Faculty of Medicine, Izmir, Turkey

Introduction: Insulin glargine provides effective glycemic control when administered at bedtime in adults.

Aim: This study investigated whether insulin glargine is equally effective if administered in the morning or at bedtime in combination with preprandial anologue insulin.

Methodology: Twenty-eight patients that have been treated with an intensified insulin regimen for at least one year were randomized to insulin glargine injection at breakfast (06:00–09:00)(12 patients), bed-time (21:00–24:00) (16 patients), plus mealtime anologue insulin. Glucose data from each day were analyzed at four different times: between 9:00 and 21:00 (t1), between 21:00 and 24:00 (t2), between 24:00 and 04:00 (t3), 04:00 and 09:00 (t4) by the Minimed continuous glucose monitoring system.

Results: Baseline characteristics were similar in the two groups. The sensor values were lower before breakfast in the bed time group (180.5 ± 49.0 vs. 223.8 ± 47.3 mg/dl, $p = 0.03$). There were 13.7 events/patient/day in the bed time group and 6.9 events/patient/day in the breakfast group in which glucose levels fell below 60 mg/dl ($p = 0.3$). There were 121.6 events/patient/day in the bed time group and 162.4 events/patient/day in the breakfast group in which glucose levels exceeded 180 mg/dl ($p = 0.05$). Night-time hypoglycemia only reached to a statistical significance in between the two groups in between 24:00 and 04:00. There were no significant correlations between the duration of nocturnal hypoglycemia, age, duration of diabetes, gender and HbA1c levels.

Conclusion: Breakfast group is hyperglycemic during the day and hyperglycemia starts in the morning at 04:00. There is no significant difference in the frequency or duration of hypo/hyperglycemia during the day and night irrespective of the timing of glargine injection except pre breakfast levels are significantly better in the bed-time group and hypoglycemia occurs in between midnight and 04:00 in the bedtime group.

P39

To determine practices for insulin initiation, identifying the most common care environment at diagnosis, the most commonly used insulins, regimens and delivery systems, and factors/criteria that influence the decision-making process

L. M. Lowes

Cardiff University, Cardiff, UK

Introduction: Little is known about clinical practice and decision-making in relation to insulin initiation in children with type1diabetes across the UK.

Aims: To determine practices for insulin initiation, identifying the most common care environment at diagnosis, the most commonly used insulins, regimens and delivery systems, and factors/criteria that influence the decision-making process. Methodology:

Questionnaires were distributed to paediatric diabetes specialist nurses (PDSNs) ($n = 247$) across the UK. Descriptive analysis using SPSS was undertaken with quantitative data, and thematic analysis with qualitative data.

Results: Response rate 45% ($n = 112$). Median caseload/PDSN WTE was 103 (49–660) children with median number of new cases annually 18 (3–52). Home management was practiced by 37 (33%) PDSNs, with a median hospital stay of 2 (1–5) days for clinically-well hospitalised children. Fifty-one of 75 (68%) PDSNs not practicing home management would do so with improved resources/staffing. Diabetes knowledge by ward staff (medical/nursing) was frequently problematic. The most common regimen at diagnosis was BD insulin (92%) but regimens varied in 65% of cases with age (57%) the most common influencing criterion. Calculation (83%) and protocols (73%) were the most common criteria influencing decisions about insulin dosage, with doctors usually making the final decision. Reusable pens were the device most frequently used at diagnosis (86%), with guidelines (92%)

and protocols (78%) informing the decision, which was usually made by PDSNs (54%). Transfer to the adult service took place most commonly (59.5%) when children were 16–18 years of age.
Conclusions: Insulin initiation practice is variable across the UK, with many factors/criteria influencing the decision-making process. NICE supports home care at diagnosis where appropriate, a recommendation frequently not met due to a lack of resources particularly in relation to the PDSN/caseload ratio. Only 8% PDSNs in this survey held caseloads ≤70 children, as recommended by the RCN and Diabetes UK.

P40

Changes of insulin dose per weight and %BMI during growth in type 1 diabetic children – effect of onset age

I. Yokota[1], Y. Kotani[2], K. Shinahara[2], S. Kagami[2], S. Amemiya[3], N. Matsuura[4] & N. Sasaki[3]

[1]Kagawa National Children's Hospital, Kagawa, Japan, [2]Tokushima University, Tokushima, Japan, [3]Saitama Medical College, Saitama, Japan, [4]Seitoku University, Chiba, Japan

Introduction: Insulin dose per body weight (INS/BW, U/kg) changes during the growth of type 1 diabetic children. Long-term subcutaneous insulin injection may influence body composition, especially those treated since younger age.
Aim: An aim of this study is to compare the changes of Ins/BW and relative rank of BMI at each age (%BMI) between groups with different onset ages.
Methodology: One-thousand-sixty-nine Japanese T1DM children (416 boys and 653 girls) diagnosed during 1990–2000 and registered in Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes were participated in this study. The subjects were categorized into three groups according to onset age (< 5 years; group Y, 5< <10 years; group M, <10 years; group O). Cross-sectional changes of Ins/BW (U/kg) and %BMI were compared among these three groups.
Results: In group Y, Ins/BW raised up to 13 years (1.3 ± 0.2U/kg) and then gradually decreased. Group M or O had significantly lower Ins/BW compared with group Y during several years after onset. In group Y, %BMI gradually decreased during prepubertal age, reached to 50% or below in both boys and girls and then elevated to 70% during puberty only in girls. Similar pattern of elevation in girls during puberty was observed in group M and O.
Conclusion: Ins/BW is different between groups even in same age, probably because of the degree of residual beta-cell function. The mechanism of the elevation of %BMI during puberty in girls, which is independent to onset age, needs to be clarified.

P41

Efficacy of insulin glargine in adolescents with type 1 diabetes

G. Salzano, F. Lombardo, E. Pustorino, M. Foti, V. Manzo & F. De Luca

Department of Pediatrics, University of Messina, Messina, Italy

Insulin glargine (Lantus®) is known as a long-acting and peakless insulin analogue. In several clinical studies in people with type 1 diabetes mellitus (T1DM), insulin glargine has been demonstrated to improve pre-breakfast blood glucose levels and to reduce the frequency of hypoglycaemic episodes, in comparison with NPH. However, glargine has not yet been shown to improve HbA1c, especially in children and adolescents. The aim of this study was to review the effects of glargine therapy in terms of HbA1c, insulin requirement and frequency of hypoglycaemic events during a 2-year follow-up in a group of 124 adolescents (67 girls, 57 boys) with T1DM, previously treated with NPH (three daily injections of short analogue before meals + 1 injection of NPH at bedtime). They switched from NPH to insulin glargine between September 2003 and March 2004. Subjects' mean age at the study start was 14.3 ± 0.3 years (their mean age at disease onset was 8.8 ± 3.2 years). Mean HbA1c was 9.7 ± at the time of the switch was 9.7 ± 0.5%. Mean HbA1c dramatically decreased six months after glargine therapy start (7.2 ± 0.1%; $p < 0.0001$) and resulted to be significant lower even after 18 months (8.8 ± 0.9%; $p < 0.001$) and 24 months (8.6 ± 0.7; $p < 0.05$). We did not find significant differences in terms of daily insulin requirement either 1 year before or 2 years after the switch. Referred hypoglycaemic episodes significantly decreased, especially the nocturnal ones. The rate of the decrease was from average 4 times per month to less than once per month ($p < 0.001$) after starting glargine therapy. As compared to NPH, insulin glargine is more effective in improving metabolic control and it is associated with reduced rates of nocturnal hypoglycaemia.

P42

Improved glycemic control after introduction of insulin glargine in children and adolescents

R. L. Thorisdottir, R. Bjarnason, E. Konradsdottir & A. V. Thorsson

[1]Department of Pediatrics, Landspitali University Hospital, Reykjavik, Iceland, [2]GP-GRC, Sahlgrenska University Hospital, Göteborg, Sweden

Objective: Long acting insulin analogs have since ther introduction been used in in increased frequency in pediatric care. The aim of the study was to evaluate change of insulin therapy from NPH to insulin glargin in children and adolescents.
Subjects and study methods: Data from 59 patients (34 girls, 25 boys), were collected for 6 months before and 12 months after insulin glargine therapy. The numbers of severe hypoglycemic events, HbA1c values (DCA 2000), and daily insulin dose were recorded.
Results: Subjects mean age (±SD) at initiation of glargine therapy was 13.9 ± 3.2 years. After 6 months, the average HbA1c level in the entire cohort dropped from 9.5 ± 1.5 to 8.8 ± 1.3% ($p < 0.001$). After 12 months of therapy the average HbA1c had dropped to 8.6 ± 1.0% ($p < 0.001$). The greatest response was observed in subjects with HbA1c above 10.5, in this group HbA1c levels decreased by 1.5 ± 0.4%. Eleven episodes (37.3/per 100 pat years) of hypoglycemia occurred the first half year after initiation of insulin glargine therapy but 15 episodes (50.8/per 100 pat years) had occurred the last half year before glargine therapy. There were no significant changes in insulin doses 6 months before and after initiation of glargine ($p > 0.5$).
Conclusion: Introduction of insulin glargine significantly improved glycemic control in children and adolescents with type 1 diabetes. Greatest improvement was seen in the oldest children and those who had the worst glycemic control. Fewer hypoglycemic events were observed after introduction of insulin glargine.

P43

Initiating insulin detemir improves glycaemic control and reduces hypoglycaemic episodes in children with type 1 diabetes: results from a German subgroup of the PREDICTIVE™* study

B. Gallwitz, S. Maxeiner, R. Ackermann & H-J. Lüddeke

[1]Universitätsklinikum Tübingen, Tübingen, Germany, [2]Diabetologische Schwerpunktpraxis Bosenheim, Bad Kreuznach, Germany, [3]Novo Nordisk A/S, Bagsværd, Denmark, [4]Praxis Lüddeke/Trauner, Munich, Germany

Background: A challenge in the treatment of children with diabetes is attaining glycaemic goals without increasing the risk of hypoglycaemia.

Aims: PREDICTIVE™ is a large multi-national, prospective, observational study, assessing the safety and efficacy of insulin detemir in clinical practice. We report analysis of a subgroup of paediatric patients from the German arm of the study.
Methods: A total of 113 children and adolescents (11% 0–11 years; 89% 12–18 years) with type 1 diabetes [65% female; mean age 15.4 years; diabetes duration 5.6 years; glycosylated haemoglobin A1c (HbA_{1c}) 8.5%; body mass index (BMI) 22.5 kg/m^2] were followed up for 14.5 weeks after initiation of insulin detemir. The primary endpoint was safety. Secondary endpoints included change in: HbA_{1c}; weight; fasting blood glucose (FBG); and within-subject FBG variability, calculated as the SD of FBG.
Results: No serious adverse drug reactions were reported. Hypoglycaemic episodes were significantly reduced from 35.7/patient year in the 4 weeks prior to study start to 10.5/patient year at follow-up (–25.2, $p < 0.001$). The reduction in hypoglycaemia included a significant decrease in nocturnal episodes (7.8–1.4/patient year; $p < 0.001$). Glycaemic control significantly improved, with reductions in mean HbA_{1c} (0.6%; $p < 0.001$), FBG (32 mg/dl; $p < 0.001$) and within-subject FBG variability (11 mg/dl, $p < 0.01$). Weight remained stable (+0.23 kg; $p < 0.43$). Total insulin daily dose also remained stable (+0.07 IU/kg). At follow-up, there was a reduction in the number of children receiving >2 basal injections (20.7–3.7%).
Conclusions: These data show that insulin detemir-based therapy provides good glycaemic control in association with a lower risk of hypoglycaemia and weight neutrality in paediatric patients with type 1 diabetes.
*Predictable Results and Experience in Diabetes through Intensification and Control to Target: An International Variability Evaluation.

P44

Insulin allergy in two 9-year-old boys: Desensitisation with simultaneous intravenous insulin infusion (III) and CSII

K. A. Neville, B. K. Wainstein, C. F. Verge, H. J. Woodhead, J. B. Ziegler & J. L. Walker

[1]Sydney Children's Hospital, Sydney, NSW, Australia, [2]University of NSW, Sydney, NSW, Australia

Persistent allergic reactions to insulin are rare. Treatment of insulin allergy with CSII is reported, but a rational approach to CSII introduction is missing in the literature. We report two unrelated atopic 9-year-old boys presenting simultaneously with probable Type 1 systemic allergic reactions to insulin. Urticaria following each subcutaneous injection of regular (Actrapid) and NPH (Protaphane) insulin was initially localised to injection sites but became generalised after 2–3 months. Reactions were refractory to multiple changes in insulin type and treatment with antihistamines. Intradermal testing was positive for all insulin preparations in one boy but only Actrapid and Protaphane in the other, with negative insulin and latex specific-IgE in both. Rapid desensitisation with hourly subcutaneous Actrapid and Protaphane, increasing from 1/10 000 dilutions to usual bolus doses over 8–10 h was unsuccessful. When rapid desensitisation (12–24 h) with CSII (Lispro), commencing at 0.1 U/h resulted in allergic reactions and ketosis, III was started with no reactions. Under III cover for basal requirements and meal boluses, the rate of CSII was increased initially in increments of 0.05 U/h every 4–12 h, once any new reactions resolved. Hundred percent basal rate insulin delivery by CSII was achieved 138–144 h after III initiation. Bolus subcutaneous insulin for meals and corrections was initially given over 3 h, reducing to immediate boluses by 48 h with no or minimal reaction. Both boys remain on antihistamines with only occasional rash/pruritus but no urticaria. Intravenous infusion of insulin in Type 1 diabetic patients with allergy to subcutaneous insulin appears to be well tolerated and allows desensitisation to occur without ketosis using CSII over the variable time required by individuals to achieve tolerance.

P45

PREDICTIVE: a global, prospective, observational study to evaluate insulin detemir treatment – baseline characteristics from paediatric patients in the European cohort

A. Robinson, S. Sreenan, M. Honka, S. Smirnov & A. Dornhorst

[1]The Royal Bolton Hospital, Bolton, UK, [2]Connolly Hospital, Dublin, Ireland, [3]Fakultni nemocnice s poliklinikou Ostrava, Ostrava, Czech Republic, [4]Novo Nordisk A/S, Bagsværd, Denmark, [5]Imperial College, London, UK

Background: Observational studies are valuable in confirming clinical trials outcomes in clinical practice.
Aims: PREDICTIVE is a large observational study assessing the safety and efficacy of insulin detemir in diabetes. We report baseline data from children and adolescents included in the European cohort.
Methods: A total of 668 type 1 patient's ≤ 18 years requiring basal insulin were enrolled in the study after being prescribed insulin detemir. Patients will be followed up for 12, 26 and/or 52 weeks. The primary endpoint is incidence of serious adverse drug reactions, including major hypoglycaemia. Secondary endpoints are change in: HbA_{1c}; weight; FBG; and within-subject FBG variability (calculated as SD of FBG).
Results: Baseline characteristics are provided in the Table. The main reasons physicians chose to enroll patients were: to improve glycaemic control (>75%); and reduce hypoglycaemic risk (>40%).

Parameter	0–11 years n = 189	12–18 years n = 479
Gender M/F, %patients	51/49	45/55
Mean age, years (±SD)	8.7 (±2.1)	15.3 (±2.1)
Mean diabetes duration, years (±SD)	3.1 (±2.4)	5.7 (±4.0)
Mean BMI, kg/m^2 (±SD)	18.1 (±3.5)	22.2 (±3.7)
Mean HbA_{1c}, %(±SD)	8.8 (±2.2)	9.2 (±2.1)
Mean FBG, mmol/l (±SD)	10.6 (±3.2)	10.6 (±3.6)
Mean within-subject FBG variability (±SD)	4.3 (±2.4)	3.3 (±2.1)
Mean hypoglycaemic events, in 4 weeks prior to study		
All events (±SD)	3.2 (±5.7)	2.5 (±5.1)
Major events (±SD)	0.2 (±0.7)	0.2 (±0.7)

Conclusion: Data from a subgroup of paediatric patients in the PREDICTIVE study clearly indicates that metabolic control is not optimal and that there is a need for improved treatment options. The majority of patients were switched to insulin detemir with the expectation of improving glycaemic control and reducing hypoglycaemic risk; follow-up data will provide valuable insights to the impact of insulin detemir in paediatric diabetes management.

P46

Pre-meal insulin treatment during basal-bolus regimen in young children with type 1 diabetes

V. Cherubini[1], A. Iannilli[1], D. Iafusco[2], F. Cardella[3], M. S. Giamprini[1] & S. Nobile[1]

[1]Polytechnic University of Marche, Department of Pediatrics, Ancona, Italy, [2]Second University of Napoli, Department of Pediatrics, Napoli, Italy, [3]University of Palermo, Department of Pediatrics, Palermo, Italy

The introduction of insulin analogues in clinical practice suggests updating therapeutic schemes in subjects with type 1 diabetes.

Rapid-acting analogues offer unquestionable advantages, however they need great accuracy in dosage, above all in young children. Aims of this study were to evaluate metabolic effects in pre-puberal children treated with glargine and regular or rapid-acting insulin, using the carbohydrate-count system (CHC). We recruited 30 children aged 8.1 ± 1.8 years with type 1 diabetes, having basal C-peptide <0.1 nmol/l, mean diabetes duration 5.2 ± 2.0 years. Children were shifted from NPH to glargine insulin and randomized into two groups: A, receiving regular insulin (breakfast, lunch and supper) and B, rapid-acting insulin. Children in B-group received an additional insulin shot before the afternoon snack. Parents were instructed on CHC and received a personalized diet. Changes in percentage of A1C over the 18-week period were analyzed by using repeated measures ANOVA. Fasting blood glucose (FBG) levels were similar at baseline (group A, 171 ± 38 mg/dl; B, 173 ± 37 mg/dl) and decreased more in group A (–22 ± 30 mg/dl, $p < 0.05$) than in group B (–3.3 ± 40). A1C decreased from 7.5 ± 0.8 to 7.0 ± 0.4 % ($p < 0.05$) and from 7.5 ± 1.4 to 7.4 ± 0.5% in group A and B, respectively. The mean afternoon BG at baseline was higher in group A than in group B, whereas they were similar by the end of the study (165 ± 49 to 160 ± 52 mg/dl, A vs. B, respectively, p = ns). Hypoglycaemic episodes (BG < 70 mg/dl and BG < 50 mg/dl) were not statistically different between groups. FBG and A1C decreased in pre-puberal children receiving regular insulin, even though the pre-snack insulin shot was not used. Glargine insulin was very helpful in minimizing nocturnal hypoglycaemia, without differences among children on regular or rapid-acting insulin.

P47

To evaluate the variations in metabolic control in very recent years since insulin lente analogues was introduced in clinical practice

S. Zucchini, R. Santoni, D. Elleri, I. Bettocchi, M. Scipione, G. Maltoni, A. Cicognani & S. Salardi

S.Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Despite strenuous efforts (new insulins, multiple-dose insulin therapy, intensive education), a nonsignificant improvement in metabolic control is often reported by many authors also in Italy (MCDC-Italy Group, 2005).

Aim: To evaluate the variations in metabolic control in very recent years since insulin lente analogues was introduced in clinical practice. We therefore compared the HbA1c values of 2002 with those of 2005 in our diabetic outpatient Clinic Patients. 149 children and adolescents with type 1 diabetes diagnosed at mean age 7.0 ± 4.0 years were regularly examined every 3–4 months in the last 3 years. At entry age was 13.8 ± 5.7 years, duration of disease 6.9 ± 5.2 years and mean HbA1c values 7.9 ± 1.2%. Seventy-six patients were changed during follow-up from traditional insulin lente to insulin lente analogues (Glargine), while 72 continued the old insulin regimen. The two groups were not different at entry for age, disease duration, daily insulin dosage (IU/kg), while differed for mean HbA1c values, that were significantly ($p = 0.003$) higher in the group treated with glargine (8.1 ± 1.1%) than in the traditionally treated group (7.6 ± 1.2%).

Results: In 2005 mean HbA1c values were significantly ($p < 0.0001$; paired t-test) higher than in 2002 in the whole group, in the group treated with traditional lente insulin and in the group treated with glargine. Subdividing the patients according to age, the increase in HbA1c values was significant for the patients below 20 years of age, but not over. During the 3 years of follow-up the percentage of patients with HbA1c values ≥ 8.5% significantly increased ($p = 0.012$) in the group treated with glargine (from 60% to 70%), but not in the group treated with the traditional lente (from 40% to 30%). In both groups daily insulin dose remained unchanged.

Conclusions: In agreement with most of the literature, we obtained this distressing result of a slow but progressive worsening of metabolic control also in the last few years, despite the use of new insulins. Hypotheses of this unsatisfactory trend may be too many therapeutic choices, excessive freedom and flexibility, not suitable for patients under 20 years of age not yet mature adults.

P48

The addition of rosiglitazone to insulin in adolescents with type 1 diabetes and poor glycaemic control: a multicentred, randomised, placebo controlled trial

M. L. Stone[1], M. E. Craig[2], K. C. Donaghue[2], P. Crock[3], D. Anderson[3], J. Walker[1], D. Chisholm[4] & C. F. Verge[1]

[1]Sydney Children's Hospital, NSW, Australia, [2]The Children's Hospital at Westmead, Sydney, NSW, Australia, [3]The John Hunter Children's Hospital, Newcastle, NSW, Australia, [4]The Garvan Institute and St Vincents Hospital, Sydney, NSW, Australia

Aims: To improve the glycaemic control of adolescents with T1DM using an insulin sensitizer to overcome the insulin resistance of puberty.

Methodology: Randomised, double blind, placebo controlled crossover trial of rosiglitazone (4 mg twice daily) vs. placebo (24 weeks each, separated by a 4-week washout period). Entry criteria were diabetes duration > 1 year, age 10–18 years, puberty (> Tanner breast stage 2 or testicular volume > 4 ml), insulin dose ≥ 1.1 units/kg/day, and HbA1c > 8%. Responses to rosiglitazone were compared to placebo using paired *t*-tests.

Results: Thirty-six subjects were recruited, 28 completed the trial (17 male). At baseline, mean ± SD; age was 13.6 ± 1.8 years, HbA1c 8.9 ± 0.96%, BMI-SDS 0.94 ± 0.74, insulin dose 1.5 ± 0.3 u/kg/day. Rosiglitazone resulted in decreased insulin dose (2.9% vs. 8% increase on placebo, $p = 0.05$), less increase in BMI-SDS (+0.01 vs. +0.02, $p = 0.03$), increased serum adiponectin (9.4% vs. 5.5% decrease, $p < 0.01$), increased cholesterol (+0.5 mmol/l vs. no change, $p = 0.02$), but no significant change in HbA1c (decrease of 0.23 vs. 0.06, $p = 0.63$). Insulin stimulated glucose uptake improved on rosiglitazone vs. placebo in 5/7 subjects who underwent euglycaemic hyperinsulinaemic clamps. There were 13 subjects who had a positive response to rosiglitazone, their median reduction in HbA1c was 1.3 (range –0.7 to 2.3). None of the following were predictive of a positive response: compliance (estimated by tablet count as 68% overall), order of entry into the trial, baseline pubertal stage, BMI-SDS, HbA1c, insulin dose, cholesterol, triglycerides or adiponectin level. There were no adverse effects attributable to rosiglitazone.

Conclusion: The use of rosiglitazone in adolescents with T1DM resulted in a decrease in insulin dose and increase in serum adiponectin, however, no significant improvement in HbA1c. There was no significant weight gain with rosiglitazone.

P49

Blood glucose and beta-hydroxybutyrate responses when the insulin pump is stopped in children and adolescents

R. Hanas, K. Lundqvist & L. Windell

Uddevalla Hospital, Uddevalla, Sweden

The small insulin depot when using pump therapy increases the risk of ketosis and ketoacidosis when insulin supply is interrupted. Patients often forget to check ketones and to give extra insulin with a pen or syringe when there is unexplained hyperglycemia. As a

clinical routine, we have performed a pump stop lasting 6–8 h at the day care ward. Blood glucose (BG) and ketones are checked hourly. When the pump is started again, the patient takes 0.1 U/kg extra with a pen. The aim of the present study was to evaluate this procedure. Data was available for 22 patients aged 13.2 ± 2.6 years with a diabetes duration of 7.2 ± 4.5 years. Pump therapy was started 5.3 ± 4.0 years after diabetes diagnosis. Rapid-acting insulin was used in all pumps. 9/22 patients experienced nausea but none vomited. PH was >7.35 in all cases. The lowest base excess was –5.0 mmol/l. Eleven patients with partial remission defined as C-peptide of >0.1 nmol/l, <0.5 U/kg/day or <2 years diabetes duration were analyzed separately. The mean BG rise/hour of the remaining 11 patients was 2.0 mmol/l/h and for beta-hydroxybutyrate (B-OHB) 0.2 mmol/l/h. Peak levels of BG was 20.2 ± 1.6 mmol/l and B-OHB 1.8 ± 0.3 mmol/l. The patients in partial remission had lower BG increase (1.1 mmol/l/h.) and B-OHB rise (0.1 mmol/l/h.) with peak BG of 14.9 ± 3.6 mmol/l and B-OHB of 0.8 ± 0.4 mmol/l. We conclude that pediatric pump patients can be without insulin for 6–8 h without any risk of ketoacidosis if a pump failure occurs. There is a rather linear rise in B-OHB. Thus, the level of B-OHB can be used as an indicator to estimate for how long there has been a deficit of insulin in a pump patient.

P50

Continuous subcutaneous insulin infusion with insulin aspart in preschool children: superior caregiver satisfaction vs. multi-injection therapy

E. Pankowska, M. Szalecki, G. Wiedermann, J. Nazim & M. Urban

[1]Department of Paediatric Diabetology and Birth Defects Medical University in Warsaw, Poland, [2]Independent Health Center, Gliwice, Poland, [3]The University Children's Hospital, Krakow, Poland, [4]The Specialist Paediatric Hospital, Kielce, Poland, [5]Children's Clinical Hospital by Medical Academy, Bialystok, Poland

Children with type 1 diabetes often receive multi-injection therapy (MIT) with human insulin, but a timing mismatch between food and insulin absorption, and unpredictable exercise and eating patterns, place this group at risk of frequent, severe hypoglycemia, neuropsychological development. Rapid-acting insulin analogues, and continuous subcutaneous insulin infusion (CSII) more closely approximate physiological insulin delivery.

Aim: To compare the efficacy, safety and career quality of life when insulin aspart (IAsp) is used in multi-injection therapy (MIT) or continuous subcutaneous infusion (CSII) in preschool age children with type 1 diabetes, using human insulin as a comparator.

Methodology: Sixty-one children (mean age = 5.2–5.7 years; mean HbA1c = 7.4–7.7) after a 3-week human MIT run-in, subjects were allocated to CSII (n = 20), or randomized to MIT with SHI (n = 21) or IAsp (n = 20), plus NPH, for 26 weeks.

Results: ANOVA of mean HbA1c at 26 weeks showed no change from baseline in all groups, and no difference between groups (7.7% for CSII; 7.6% in both other groups). The glucose AUC over 24 h demonstrated equivalency in all groups (mean = 200.1–219.8 mmol/l*h). Three major episodes in the CSII group and one in the IAsp MIT group were noted; Caregiver quality of life (QoL) questionnaires, total scores indicated superior QoL with CSII (4.0 vs. 2.2 and 0.3 for IAsp MIT and SHI MIT, respectively; p = 0.04), and notable satisfaction with low hypoglycemic frequency (CSII score + 0.9 vs. -0.6 and -1.1 in SHI and IAsp MIT groups, respectively; p = 0.0002).

Conclusions: After 26 weeks of treatment with IAsp CSII, IAsp MIT or HI MIT, all glycaemic control parameters remained unchanged and equivalent, but a significant advantage to carer QoL was demonstrated when children received IAsp CSII pump therapy, particularly with respect to frequency of hypoglycaemia.

P51

Contribution of basal insulin on daily dose is related to c-peptide secretions in diabetes children treated with continuous subcutaneous insulin infusion

A. Szypowska, E. Pankowska & M. Lipka

Medical University in Warsaw, Warsaw, Poland

Introduction: Continuous subcutaneous insulin infusion has becoming an increasingly used option for type 1 diabetes children management. This advanced technology providers the most precise insulin administration and also allows to keep the records delivered insulin doses over the period of last 12 weeks. The analysis of registered data gives an opportunity to review obligatory algorithms of insulin adjustment in intensive therapy.

Aim: To investigate the insulin requirement, basal contribution on total insulin daily dose (TIDD) and analysis determinant factors for basal to bolus proportion in TIDD.

Material and methods: Seventy-eight (35 female/43 male) well controlled type 1 diabetes children were included; mean age 10.19 ± 4.19 years (1.05–17.91), mean diabetes duration 3.38 ± SD 2.7 years (0–12.7), GlyHbA1c 6.75 ± 0.84%, BMI 17.93 ± SD 2.78 kg/m^2. During hospital visits pumps memory data was downloaded; clinical and biochemical: fasting c-peptide, GlyHbA1c were assessed. Patients with DKA, SH or infection diseases during last 3 months were excluded.

Results: The average requirement for insulin was 0.75 ± 0.21 U/kg/d not significantly different in age groups: it was comparably in prepubertal group and pubertal children (0.71 ± 0.17 vs. 0.79 ± 0.24 U/kg/d) but basal contributions were statistically lower in prepubertal patients than in pubertal (22.35 ± 8.76 vs. 31.23 ± 14.82% p < 0.05). Analysis of factors of basal contribution on TIDD shows significant correlation with age (r = 0.33, p 0.05), diabetes durations (r = 0.54, p < 0.0001) and BMI (r = 0.325, p < 0.0037) but inversely correlated with c-peptide (r = –0.349, p = 0.0017). However, c-peptide did not significantly correlated with TIDD.

Conclusions: The basal to bolus insulin is below 50% in children with type 1 diabetes. The basal contribution on TIDD in growing-up population should be differentiated by the age, diabetes duration and BMI. Remission phase clinically is expressed by contribution of basal insulin on TIDD but not by insulin amounts per kg of body mass per day.

P52

Insulin pump therapy in youth with type 1 diabetes mellitus: a retrospective paired study

R. Nimri, N. Weintrob, H. Benzaquen, R. Ofan, G. Fayman & M. Phillip

Schneider Children's Medical Center of Israel, Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Petah Tikva, Israel

Introduction: In the last 5 years, use of pump therapy has grown steadily. Previous pump studies show inconsistency regarding safety and efficacy.

Objective: To compare continuous subcutaneous insulin infusion (CSII) to multiple daily injections (MDI) in youth with type 1diabetes treated in our institute for metabolic control and adverse events.

Design and Methods: The charts of 249 patients with type 1 diabetes who switched from MDI to CSII between 1998 and 2003 were reviewed for glycemic control, body mass index (BMI) and

adverse events. Patients were divided by age: 23 prepubertal, 127 adolescent, and 129 young adults. The data collected a year preceding CSII was compared to the period following onset of CSII (ranged 1–6 years).
Results: A significant decrease in HbA1c was demonstrated after onset of CSII use, for the entire cohort (–0.51%, $p < 0.001$), prepubertal (–0.48%, $p < 0.05$), adolescents (–0.26%, $p < 0.05$), and young adults (–0.76%, $p < 0.001$) groups. There was a significant interaction between the change in HbA1c level and HbA1c value at initiation of CSII (–1.7% for patients with HbA1c ≥ 10%, +0.2% for patients with HbA1c ≤ 7%; $p < 0.001$), and between the decrease in HbA1c levels and duration of CSII therapy for the first 3 years ($p < 0.001$ for each additional year). The rate of severe hypoglycemic episodes decreased significantly in the adolescent group, from 36.5 to 11.1 events per 100 patient-years ($p < 0.01$), and in the young adult group, from 58.1 to 23.3 ($p < 0.05$). There was no significant change in the rate of diabetic ketoacidosis between the two periods. The young adults showed a significant decrease in BMI SDS (–0.08 ± 0.37, $p < 0.05$).
Conclusions: CSII improves glycemic control in youth with type 1diabetes, especially those with a history of poor glycemic control. This improvement is associated with a decrease in the rate of severe hypoglycemia, in the absence of weight gain.

P53

Insulin pump treatment in children with type 1 diabetes: a study of patient preferences, satisfaction and metabolic control

B. S. Olsen, M. M. Andersen & H. B. Mortensen
Department of Pediatrics, Glostrup University Hospital, Glostrup, Denmark

Background: Insulin pump treatment in childhood has become increasingly popular. The results on metabolic control are however conflicting.
Aim: To investigate the influence of insulin pump treatment on quality of life, patient preference and metabolic control in children aged 6–12 years.
Methodology: Twenty children (13 boys), mean age (± SD) 9.3 (±2.0) years, mean diabetes duration (±SD) 4.9 (±2.1) years and mean HbA1c 7.6 (±0.5)%, were randomised to either 3 months of insulin pump treatment or 3 months of pen treatment, and then switched to the opposite treatment arm for 3 months. Eight-point blood glucose profiles were performed every fortnight and CGMS four times during the study. Children and parents filled in questionnaires of satisfaction three times and a preference questionnaire at study end (WHO-DTSQ).
Results: After the trial all patients continued with pump treatment and there was a higher patient satisfaction ($p < 0.01$) during the pump period. HbA1c decreased significantly during pump treatment [mean (SE) 7.35 (0.10)] % vs. [mean (SE) 7.67 (0.10)]% ($p = 0.0273$). The total mean of the 8-point blood glucose profiles were lover during pump treatment mean (SE) 8.07 (0.56) mmol/l vs. 10.68 (0.53) mmol/l, and CGMS showed more readings in the interval 5–10 mmol/l during pump treatment ($p = 0.0387$). Patients on pen received more insulin than those on pump [mean (SE) 0.94 (0.02) U/kg/24 h] vs. [mean (SE) 0.80 (0.02) U/kg/24 h], while patients on pump were treated with significantly more bolus insulin [mean (SE) 0.55 (0.02) U/kg/24 h] vs. [mean (SE) 0.35 (0.02) U/kg/24 h] (pen group) compared to the pen group. There were no episodes of ketoacidosis, but two episodes of severe hypoglycaemia (convulsions and unconsciousness) (1/20 patient years) in each study arm.
Conclusion: Young Danish TID patients prefer insulin pump treatment. Pump treatment improves quality of life and is associated with improved glycaemic control.

P54

Insulin pumps vs. multiple injections from the onset of type-1 diabetes in children

L. Krogvold, K. Dahl-Jørgensen, H. Bjørndalen & H. J. Bangstad
Paediatric department, Ulleval University hospital, Oslo, Norway

Introduction: Continuous subcutaneous insulin infusion (CSII) has become increasingly popular in children with type-1 diabetes. Still there remains evidence showing improved metabolic control when comparing CSII with multi-injection treatment (MI) from the onset of diabetes.
Aims: We wanted to investigate whether treatment of children from the onset of type 1 diabetes with CSII is feasible and if children treated with CSII achieve a better metabolic control compared to children treated with MI.
Methodology: Two cohorts of patients were compared: the 29 children with type 1 diabetes diagnosed in 2003–2004 (24 months) all treated with CSII and 11 children in the Hvidore study diagnosed between December 1999 and November 2000 (12 months) treated with MI. The groups went through the same education programme with the same diabetes team and were followed regularly in the outpatient clinic. HbA1c (4.3–6.1%) was measured every third month and a Sustacal stimulated C-peptide test was performed at 6 and 12 months after diagnosis.
Results: Eleven children (mean age 8.8 years, CI 6.2–11.5) from 1999–2000 and 29 patients (9.0, 7.4–10.5) from 2003–2004 were enrolled in the study. HbA1c at three months was in the CSII-group 7.3% and in the MI-group 7.4%, similar numbers at six months were 7.1/7.9, 9 months 7.4/8.3, 12 months 7.9/8.1, 15 months 7.5/8.7, 18 months 7.9/8.7, 21 months 7.8/9.0 and at 24 months 8.1/8.5. In spite of the consistently lower HbA1c-values in the CSII-group, the difference was statistically significant only at 15 months ($p = 0.03$). No statistical difference was found in median stimulated C-peptide, the values at 6 months where 410 (CSII) and 284 (MI), and at 12 months 225 (CSII) and 207 (MI).
Conclusion: This study shows that treatment with CSII from the onset of type-1 diabetes in children is feasible and indicates that CSII results in better metabolic control than treatment with multiple injections in the first 2 years of diabetes.

P55

Is there a benefit of continuous glucose monitoring on insulin pump dosing in children and adolescents with type-1 diabetes?

D. Deiss[1], R. Hartmann[1], J. Hoeffe[1], R. Lauterborn[1] & O. Kordonouri[2]
[1]Clinic of General Pediatrics, Otto-Heubner-Centrum, Charité, Humboldt-University, Berlin, Germany, [2]Diabetes Center for Children and Adolescents, Children's Hospital at the Bult, Hannover, Germany

Introduction: Although insulin pump therapy (CSII) is frequently used in pediatric patients with type-1 diabetes, no age-dependent standard scheme for an initial insulin dosing is available. Aim of this randomized clinical trial was to investigate variations of insulin dosing at the start of CSII and after 6 weeks depending on the preceding use of continuous glucose monitoring system (CGMS) or conventional self-monitoring of blood glucose (SMBG).
Patients and methods: Thirty-one patients (11 boys, 20 girls) were included into the study to receive CSII. Median age was 12.1 years (range 1–18) and median diabetes duration 3.3 years (0.3–10.2). 15 patients were randomized to perform ambulatory CGMS (MedtronicMinimed) over 3 days immediately before CSII was