Poster Session II: Diabetes Genetics, Immunology

P/190/FRI

Methyline tetrahydrofolate gene polymorhism in type 1 diabetes mellitus: relationship to microvascular complications

M. Aboelasrar[1], E. El-Sobky[2], A. Al-Saeed[1] & M. Saied[1]
[1]*Ain Shams University, Pediatrics, Cairo, Egypt,* [2]*Ain Shams University, Genetics, Cairo, Egypt*

Objectives: To study the relationship between methylene tetrahydrofolate reductase (MTHFR) gene polymorphism and microvascular complications in Egyptian adolescents with TIDM.
Methods: A total of 99 type 1 diabetic patients with disease duration more than 5 years aged 11–18 years participated in the study over 10 months period. History taking, physical, neurological and fundus examination were performed. Laboratory investigations included mean glycated hemoglobin concentration in the last year, urinary albumin excretion, serum creatinine, testing for peripheral neuropathy were assessed by nerve conduction velocity and MTHFR genotype by DNA extraction, polymerase chain reaction (PCR), enzyme digestion.
Results: Our results revealed that 54.5% of our patients had normal MTHFR genotype (C/C) group, 36.4% had heterozygous MTHFR gene polymorphism (C/T) group and 9.1% had homozygous MTHFR gene polymorphism (T/T) group. No significant difference was found between the three groups as regard age and disease duration. C/T subgroup showed significantly lower HbA1c when compared with T/T subgroup ($P = 0.002$).T/T subgroup showed significantly higher number of patients with microalbuminuria when compared with C/C subgroup ($P < 0.001$) and C/T subgroup ($P = 0.001$).C/C subgroup showed significantly lower number of patients with fundus changes when compared with C/T subgroup ($P = 0.027$) and T/T subgroup ($P < 0.001$). On the other hand T/T subgroup showed significantly higher number of patients with fundus changes when compared with C/T subgroup ($P < 0.001$).T/T subgroup showed significantly higher number of patients with nerve conduction abnormalities when compared with C/C subgroup ($P < 0.001$) and C/T subgroup ($P < 0.001$). Multivariate forward stepwise logistic regression analysis revealed that MTHFR gene polymorphism to be the most important variable risk factor for microvascular complications.
Conclusion: MTHFR gene polymorphism may be a risk factor for microvascular complications in T1DM.

P/191/FRI

A multicenter study on the genetic base of neonatal diabetes mellitus and the effect of sulfonylurea therapy

Z. Zhao[1], F. Luo[1], X. Chen[1], S. Shen[1], T. Li[2], L. Chen[3], M. Hu[4], H. Du[5], L. Cao[6] & S. Ellard[7]
[1]*Department of Endocrinology and Metabolism, Children's Hospital of Fudan University, Shanghai, China,* [2]*Department of Pediatrics, The Affiliated Hospital of Medical College Qingdao University, Qingdao, China,* [3]*Department of Pediatric Endocrinology, Soochow University Affiliated Children's Hospital, Soochow, China,* [4]*Jiaxing Maternity and Child Health Care Hospital, Jiaxing, China,* [5]*Department of Pediatric Endocrinology, Children's Hospital of Haerbin, Haerbin, China,* [6]*Children's Hospital of Fudan University, Institute of Pediatrics, Shanghai, China,* [7]*Department of Molecular Genetics, Royal Devon & Exeter NHS Hospital, Wonford, United Kingdom*

Objectives: Neonatal Diabetes Mellitus (NDM) is a rare special type diabetes mellitus. It is classified as permanent neonatal diabetes mellitus and transient neonatal diabetes mellitus. Many genes participate in its pathogenesis. Although there are occasional case reports, no genetic clues and clinical follow-ups has been disclosed about NDM in Chinese population.Our objective was to evaluate the contribution of the responsible gene and delineate their clinical treatment.
Methods: Fourteen NDM patients were followed up. Six of them agreed for molecular analysis. The exons of KCNJ11, ABCC8, INS gene with adjacent intron-exon junctions in 6 patients diagnosed with NDM were analyzed using sequence method.
Results: A molecular basis for NDM was found in 4 patients: three(D209E (c.627C>A), L39V(c.115C>G)), I544T (c.1631T>C)) in ABCC8, one (V59M (c.175G>A)) in KCNJ11 and one (L39V (c.115C>G)) in INS. The other patients were unknown. Eight NDM patients were in good glycemic control after sulfonylurea treatment, except one INS mutation. The 88.9% (8/9) patients were substituted with SU. Other five patients, who were treated with insulin, were lost or died.
Conclusion: KCNJ11, ABCC8 and INS mutation are major causes of NDM in Chinese patients. Our study suggested that NDM are able to transfer from insulin onto sulfonylurea treatment with an improvement in glycemic control. Though NDM, who were treated with insulin, were in good glycemic control, most of them died. The research should be performed in multiple centers to form a perfect treatment of NDM because Neonatal diabetes is a rare disorder.

P/192/FRI

A novel mutation in an infant with congenital hyperinsulinism

M.A.K. Salem[1], S. Abdel Hay[2], J.H. Labib[1], S. Ellard[3] & S. Flanagan[3]
[1]*Ain Shams University, Pediatrics, Cairo, Egypt,* [2]*Ain Shams University, Pediatric Surgery, Cairo, Egypt,* [3]*Universities of Exeter and Plymouth, Royal Devon & Exeter NHS Foundation Trust, Exeter, United Kingdom*

Objective: To report a case of novel mutation of autosomal recessive congenital hyperinsulinism.
Methods: We present a case of 5-month old male infant who presented early in the neonatal period with repeated convulsions due to severe hypoglycemia that was treated with bolus IV glucose and was maintained on IV glucose infusion 10–15 mg/kg/min, in addition to artificial milk feeding every 2 hours regularly. The patient had 2 elder siblings who died, a female sib who had similar attacks of hypoglycemic convulsions and died at the age of 2 months and a male sib who died at the age of 3.5 years and had recurrent hypoglycemic convulsions too.
Results: The biochemical diagnosis of congenital hyperinsulinism was established with concomitant fasting high insulin level and severe hypoglycemia (less than 30 mg/dl), Insulin / glucose ratio (0.5), absent urinary ketones during attacks of hypoglycemia and physiological levels of growth hormone and serum cortisol. The pelviabdominal MRI revealed mild hepatomegaly and normal size of the pancreas. After failure of medical treatment with subcutaneous octereotide, distal subtotal pancreatectomy was done. Pathologic examination revealed diffuse sheets of hypertrophic cells with giant nuclei and multiple Islet-like cell clusters. There was immunohistochemical evidence of insulin expression. Molecular genetic analysis revealed that the patient is homozygous for a novel missense mutation that has not been reported previously.
Conclusion: Congenital hyperinsulinism is an uncommon pancreatic disorder, with an incidence of 1 in 50,000 live births

per year in USA. No known genetic abnormalities have been found in approximately half of the patients studied, suggesting the existence of mutations that have not yet been described. This case is unique in its genetic mutation and encourages scientists to continue studying all cases of congenital hyperinsulinism to discover all underlying genetic mutations.

P/193/FRI

Evaluation of subclinical thyroiditis among Egyptian type 1 diabetic patients

M.H. El Hefnawy, A. Bassyouni, M. Abdel-Kareem, N. Abdel Rahman, M. Aziz & I. Emara
[1]*National Institute for Diabetes & Endocrinology, Pediatric, Cairo, Egypt*

Autoimmune thyroiditis (AIT) is a group of inflammatory thyroid disorders with either hyperthyroid, euthyroid or hypothyroid state. The aim of this study was to detect the subclinical thyroiditis among the Egyptians type 1 diabetic patients and to study the relation of the thyroid antibodies to different metabolic control indices of diabetes. The study group consisted of 50 type 1 diabetic patients aged from 8–18 years. They were selected from the out-patient daily clinics of National Diabetes Institute (NIDE). The control group consisted of 20 healthy subjects comparable for age, sex and socioeconomic classes of study group. Both groups were having no signs or symptoms of thyroid dysfunction. They were subjected to the following: Quantitative determination of free T3 & free T4 in serum, quantitative determination of TSH in serum, estimation of thyroid auto-antibodies using enzyme-linked immunosorbent assay (ELISA) for the semiquantitative detection of thyroglobulin antibodies (TG-AB), and thyroid peroxidase antibodies (TPO-AB) or microsomal autoantibodies. The results of this study revealed that 1.5% of the type 1 diabetic patients were with strong positive of both thyroid auto-antibodies and the same percentage were for diabetic patients with strongly positive T-antibodies, while 22% were positive for M-antibodies. The number of diabetic patients, with weak positive TG-antibodies, were 9 patients (18%) and 14 patients (28%) for TPO-Abs. While the weak positive results for both antibodies were 6 patients (12%). It could be concluded that thyroid antibodies should be done periodically for every type 1 diabetic patient. Patients with positive antibodies should be monitored for TSH elevation at yearly intervals.

P/194/FRI

Levels of soluble seceptor for advanced glycation end products correlate with age, HLA-DR genotype and metabolic state in children with newly diagnosed type 1 diabetes

K. Salonen[1], S. Ryhänen[1], J.M. Forbes[2], P.-H. Groop[3,4] & M. Knip[1]
[1]*Children's Hospital, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland,* [2]*Baker IDI Heart & Diabetes Institute, Melbourne, Australia,* [3]*Folkhälsan Institute of Genetics, Folkhälsan Research Center, Biomedicum Helsinki, Helsinki University, Helsinki, Finland,* [4]*Department of Nephrology, Department of Medicine Helsinki University Central Hospital, Biomedicum Helsinki, Helsinki, Finland*

Objectives: To assess the relationship between levels of soluble receptor for advanced glycation end products (sRAGE) and the phenotype of children with newly diagnosed type 1 diabetes (T1D) including age, metabolic state at diagnosis, HLA genotype and number and titers of diabetes-associated autoantibodies.
Subjects and methods: The subjects (n = 2116) were derived from the Finnish Pediatric Diabetes Register and Biobank. Mean age at diagnosis was 7.96 years (range 0.28–14.99). Levels of sRAGE were analyzed using Quantikine® Human RAGE Immunoassay kit. The statistical analyses were performed with the *t*-test and Pearson (r) and Spearman (r_s) correlation tests using the SPSS statistical software package.
Results: There was a positive correlation ($r = 0.10$; $P < 0.001$) between age at diagnosis and sRAGE levels. Children under the age of 2 years had reduced concentrations of sRAGE (mean difference 149 pg/ml [95%CI 74–225 pg/ml]; $P < 0.001$) than the rest of the subjects. Children younger than 10 years had lower sRAGE concentrations (mean difference 58 pg/ml [95% CI 18–97 pg/ml]; $P = 0.004$) than older children and adolescents. Subjects carrying the HLA DR3 risk allele had lower sRAGE levels (mean difference 41 pg/ml, 95% CI 4–78 pg/ml; $P = 0.03$). There was no significant correlation between sRAGE and number of diabetes-associated autoantibodies detectable. However, there was a weak positive correlation between levels of sRAGE and ZnT8A titers ($r_s = 0.078$; $P < 0.001$) and a weak inverse correlation between sRAGE and IA-2A titers ($r_s = -0.075$; $P = 0.001$). Diabetic ketoacidosis defined as a pH <7.30 was associated with decreased levels of sRAGE (mean difference 109 pg/ml, 95% CI 60–157 pg/ml; $P < 0.001$).
Conclusions: sRAGE concentrations increase with age in diabetic children. The aggressiveness of humoral beta-cell autoimmunity does not correlate with sRAGE concentrations. The state of metabolic decompensation at diagnosis and the HLA DR3 allele were related to lower sRAGE concentrations.

P/195/FRI

Evaluation of serum vitamin D in young type 1 diabetic patients

M.H. El Hefnawy[1], A. Bassyouni[2], A. Ismaiel[3] & I. Emara[4]
[1]*National Institute for Diabetes & Endocrinology, Pediatric, Cairo, Egypt,* [2]*National Institute for Diabetes & Endocrinology, Departments of Internal Medicine, Cairo, Egypt,* [3]*National Institute for Diabetes & Endocrinology, Clinical Pathology, Cairo, Egypt,* [4]*National Institute for Diabetes & Endocrinology, Biochemistry, Cairo, Egypt*

Background: Recent evidence suggests a role for vitamin D in pathogenesis and prevention of diabetes mellitus.
The aim of this study is to investigate the serum levels of 25-hydroxyvitamin D in young type 1 diabetic patients.
Subjects and methods: The study group consisted of 200 type 1 diabetic children that were attending the outpatient pediatric clinic. They were subdivided into 150 type 1 diabetic children with duration of diabetes ≥1 year and a second 50 type 1 diabetic patients with a recently discovered type 1 diabetes (<1 year duration). There was another 50 comparable healthy children as a control group. All groups were subjected to estimation of serum 25-hydroxyvitamin D & serum Ca and Ph levels.
Results: The serum levels of serum 25-hydroxy vitamin D levels in diabetic children showed that there was a highly significant statistical difference between old type 1 diabetic patients with duration of diabetes ≥1 year and recent type 1 diabetic patient, and between recent type 1 diabetic patients and control healthy group. There was no statistical difference between old type 1 diabetic patients, with duration of diabetes ≥1 year, and control healthy group. As regarding serum Ca levels, there was a significant difference between old type 1 diabetic patients with duration of diabetes ≥1 year and recent type 1 diabetic patients; and between old type 1 diabetic patients with duration of diabetes ≥1 year and control healthy group. While there was no statistical significant difference between recent cases with duration of type 1 diabetes <1 year and control healthy group.
It could be concluded that there is a great link between vitamin D levels and the occurrence of type 1 diabetes. We could recommend starting more advanced trials on the role of giving vitamin D in the prevention of type 1 diabetes.

P/196/FRI

Coxsackie virus (CV) RNA in peripheral blood mononuclear cells (PBMCs) in newly diagnosed type 1 diabetic children

E.M. Sherif[1], N.M. Fahim[2] & F.M. Ali[2]
[1]*Faculty of Medicine, Ain Shams University, Pediatric, Cairo, Egypt,* [2]*Ain Shams University, Microbiology and Immunology Department, Cairo, Egypt*

Objectives: To study the occurrence and frequency of CV infection in newly diagnosed type 1 diabetic children by detection of CV-RNA in PBMCs and to clarify any possible association between such infection and induction of autoantibodies to islet cells (ICA).
Methods: The study comprised 80 newly diagnosed type 1 diabetic children (within 10 days of diabetes onset), with a mean age of 5.84 ± 3.53 years and 40 healthy children, age and sex matched, as controls. CV-RNA (group A and B) was detected in PBMCs by reverse transcriptase polymerase chain reaction (RT-PCR). ICA were estimated by immunoflurescence technique, at onset of diabetes and 6 months after diagnosis in 52 patients (convalescent stage).
Results: It was found that 44/80 (55%) of type 1 diabetic children were positive for CV-group A versus none of the controls, the difference was highly significant (P = 0.00). CV-group B was detected in 36/80 (45%) of type 1 diabetic children versus 12/40 (30%) of controls. There was no statistically significant difference in the frequency of CV-group B between diabetics and controls (P = 0.42).ICA were detected in 12/80 (15%) of type 1 diabetic children at onset versus 32/52 (61.5%) in the convalescent stage. The frequency of ICA was significantly higher in the convalescent stage than in the acute stage (P = 0.00). Seroconversion in ICA occurred in 46% (24/52) of type 1 diabetic children. CV-group A positive patients were more associated with ICA than group B positive patients (P = 0.056 and P = 0.92 respectively).
Conclusion: The detection of CV-RNA in a majority of newly diagnosed type 1 diabetic children supports the possible association between CV infection and the development of type 1 diabetes. The significant difference seen with group A but not with group B might indicate the existence of diabetogenic strains. In addition CV infection might be capable of inducing a process of autoimmune beta-cell damage. A putative CV vaccine might be relevant in primary prevention of type 1 diabetes.

P/197/FRI

Prevalence of diabetes-associated antibodies and impaired insulin response to glucose in first degree relatives of diabetic patients

M.H. El Hefnawy, A. Bassyoni & M. Aziz
National Institute for Diabetes & Endocrinology, Pediatric, Cairo, Egypt

Type 1 diabetes is a chronic autoimmune disease with a subclinical prodromal period characterized by the presence of circulating antibodies to various islet cell proteins. Our main objective is to estimate the prevalence of diabetes-associated autoantibodies in a group of 1st[t] degree relatives, compared to healthy control subjects. Also, we tried to assess the insulin secretory capacity in subjects having multiple antibodies using First Phase Insulin Response (FPIR) to intravenous glucose.
Eighty children and adolescents of the first degree relatives of diabetic patients attending the outpatient clinic in the diabetic institute participated in our study. They were (34 boys and 46 girls, 50 siblings and 30 offspring of diabetic parents, aged 8–20 years with mean age 13.23 + 3.6). 20 age and sex matched control subjects with negative family history of diabetes were enrolled from the child health clinic in the NRC. Sera of all subjects and controls were monitored for: islet cell antibodies (ICA), anti-insulin autoantibodies (IAA) and glutamic acid decarboxylase antibodies (GAD) using ELIZA technique, and (IA-2) antibodies using radioligand binding assay. It was found that: according to the considered cut off point for positivity, 23 out of the 80 relatives (28.75%) showed positive ICA. 21 out of 80 relatives (26.25%) showed positive IAA. 17 out of 80 relatives (21.25%) showed positive GAD antibodies. 5/80 relatives (6.25%) showed positive IA-2 antibodies. It was found that only two subjects of the study group (2.5%) had three positive antibodies, 10% had positive ICA and IAA, 3.75% had positive ICA and anti-GAD. The same percent of the study group had positive IAA and anti-GAD. Those subjects showing more than one positive antibody underwent IVGTT to determine FPIR to predict subjects at high risk for developing type 1 diabetes. One subject was found to be at risk and four subjects were found to be at high risk for developing type 1 diabetes.

P/198/FRI

Islet autoimmunity and c-peptide levels in children with high risk for type 1 diabetes

L. Åkerman, J. Ludvigsson, U. Swartling & R. Casas
Linköping University, Div of Pediatrics, Dept Clin Exp Medicine, Linköping, Sweden

The diagnosis of Type 1 diabetes (T1D) is supposed to be preceded by an autoimmune process, but with sufficient insulin secretion to keep normal glucose tolerance just until the clinical diabetes. We hypothesize that beta cell function and glucose tolerance is gradually deteriorating.
Methods: ABIS (All Babies In South-east Sweden) included 17055 Swedish children born 1997–1999. So far 80 of them have developed T1D. Based on 2 or more autoantibodies (GADA, IA2A, IAA) on at least 2 sampling occasions (at 1, $2^{1/2}$, 5 and 8 years of age), 45 children were identified as T1D high risk individuals. At age 12, 22/45 had developed T1D. The remaining 23 were asked to continue their prospective follow-up study with shorter intervals (6 months) for analysis of autoantibodies (GADA, IA2A, IAA, and 3 different ZnT8), fasting blood glucose, c-peptide and HbA1c, with OGTT every 12 months. The families are also studied from an ethical/psychological perspective. ABIS children (n = 17) without diabetes-related autoantibodies and age matched children with T1D (n = 8, 1 month duration) were included as controls.
Results: Children with IA2A (n = 13) had lower c-peptide compared to IA2A negative children (n = 10, P = 0.018). In comparison with age-matched controls, fasting C-peptide was lower in high risk children (0.39 pmol/ml) than children without risk (0.49 pmol/ml, P = 0,034), but higher than in type 1 diabetic children (0.19 pmol/ml, P = 0.003). Increasing autoantibodies correlated to lower c-peptide level (r = -0.38; P = 0.074) During the last year, 7/23 high risk children have got T1D diagnosed by OGTT without clinical symptoms.
Conclusions: Islet autoimmunity in healthy children seems to be accompanied by gradually decreasing c-peptide levels, long before clinical manifestation of T1D.

P/199/FRI

Withdrawn by author

P/200/FRI

Triple-specificity of ZnT8 autoantibodies in relation to HLA and other islet autoantibodies in childhood and adolescent type 1 diabetes

C. Andersson[1], F. Vaziri-Sani[1], A.J. Delli[1], B. Lindblad[2], A. Carlsson[3], G. Forsander[2], J. Ludvigsson[4], C. Marcus[5], U. Samuelsson[4], E. Örtqvist[5], S.A. Ivarsson[1], Å. Lernmark[1] & H. Elding Larsson[1], The BDD Study Group

[1]*Lund University/CRC, Department of Clinical Sciences, Malmö, Sweden,* [2]*The Queen Silvia Children Hospital, Department of Pediatrics, Göteborg, Sweden,* [3]*Lund University, Department of Pediatrics, Lund, Sweden,* [4]*Linköping University, Department of Pediatrics, Linköping, Sweden,* [5]*Karolinska University Hospital, Department of Pediatrics, Stockholm, Sweden*

Objectives: To test whether autoantibodies to all three ZnT8RWQ variants along with GADA, IA-2A and IAA in combination with HLA define clinical heterogeneity in newly diagnosed type 1 diabetes (T1D) children and adolescents.
Methods: We analyzed 3.165 T1D patients in the Better Diabetes Diagnosis (BDD) study for all six autoantibodies (ZnT8RA, ZnT8WA, ZnT8QA, GADA, IA-2A, IAA) and HLA-DQ genotypes.
Results: ZnT8RA was found in 54%, ZnT8WA in 47% and ZnT8QA in 32% resulting in at least one ZnT8A in 65% of the patients. Together with GADA (56%), IA-2A (73%) and IAA (33%), 93% of the T1D patients had one or several islet autoantibodies. All three ZnT8RWQA were less frequent in children under 5 years of age ($P < 0.0001$). ZnT8QA was not found as a sole islet autoantibody. Kappa agreement analysis showed moderate agreement between all three ZnT8RWQA, fair agreement for ZnT8RA and IA-2A as well as for ZnT8WA and IA-2A and slight agreement for all other combinations. All three ZnT8RWQA were associated with DQA1-B1*X-0604 ($P < 0.0001$). ZnT8WA ($P = 0.0001$) and ZnT8QA ($P = 0.02$) were associated with DQA1-B1*03-0302 (DQ8). All ZnT8RWQA were negatively associated with DQA1-B1*05-02 (DQ2) ($P < 0.0001$) and DQA1-B1*05-02/03-0302 (DQ2/8) ($P < 0.05$). GADA was associated with DQ2 ($P < 0.0001$) and DQ2/8 ($P < 0.006$) and negatively associated with DQ8 ($P = 0.0005$) and DQA1-B1*X-0604 ($P = 0.03$). IA-2A was associated with DQ8 ($P < 0.0001$) and negatively associated with DQ2 ($P < 0.0001$) and DQA1-B1*X-0604 ($P = 0.02$). IAA was associated with DQ8 ($P = 0.001$) and DQ2/8 ($P = 0.002$).
Conclusions: This study revealed that ZnT8RA was the most common ZnT8RWQA. Agreement between autoantibody pairs was most obvious for the three ZnT8RWQA. ZnT8RA, ZnT8WA and ZnT8QA were all associated with DQA1-B1*X-0604 and negatively associated with DQ2 and DQ2/8. ZnT8WA and ZnT8QA were also associated with DQ8. The ZnT8A therefore strongly contributes to the diagnostic sensitivity of autoimmune diabetes.

P/201/FRI

The DiViD-study: a pancreatic biopsy study of newly diagnosed type 1 diabetes patients

L. Krogvold[1], B. Edwin[2], T. Buanes[3], M.C. Eike[4], G. Frisk[5], H. Hyöty[6], O. Korsgren[5], J. Ludvigsson[7], K. Hanssen[8] & K. Dahl-Jørgensen[9]

[1]*Divison of Pediatrics, Oslo University Hospital Ullevål, Oslo, Norway,* [2]*Oslo University Hospital Rikshospitalet, Intervention Centre, Oslo, Norway,* [3]*Department of Gastroenterological Surgery, Oslo University Hospital Ullevål, Oslo, Norway,* [4]*Department of Medical Genetics, Oslo University Hospital, Oslo, Norway,* [5]*Department of Immunology, Uppsala University Hospital, Genetics and Pathology, Uppsala, Sweden,* [6]*University of Tampere, School of Medicine, Tampere, Finland,* [7]*Divison of Pediatrics, Linköping University, Linköping, Sweden,* [8]*Oslo University Hospital Aker, Oslo Diabetes Research Center, Oslo, Norway,* [9]*Oslo University Hospital, Faculty of Medicine, Oslo, Norway*

Objectives: The objectives of the DiViD (Diabetes Virus Detection) study are in part to describe the immunological processes in the pancreas of young adults with newly diagnosed type 1-diabetes (T1D), and to search for viruses. Biopsies from organ donors for pancreatic islet transplantation are used as controls.
Methods: GAD-vaccination is part of the protocol. In addition to blood samples, laparoscopic pancreatic biopsy is obtained under general anaesthesia. Islets are isolated in fresh samples, T-cells sampled and classified by flow cytometry, and stored. Virus detection is done by immunohistochemistry, in situ hybridization, PCR and high-throughput sequencing. The study is approved by the governmental regional ethics committee.
Results: So far (May 2011), two cases are enrolled in the study. In case 1 (female, age 25), pancreatic biopsy was performed four weeks after diagnosis, in case 2 (male, age 23) two weeks after diagnosis. Islets were isolated and T-cells cultivated from both patients. In both cases islets were found in different stages of pathological development. Some islets were completely normal. In other islets β-cells were present together with different T and B-cells (CD3, CD4, CD8, and CD20) as well as macrophages (CD68). Some islets had a complete loss of β-cells with no signs of inflammation. In both cases enterovirus capsid protein VP1 positive cells were found. Isolated islets from both cases showed impaired insulin secretion upon glucose stimulation, partly restored when stimulated with glucose and theophylline. Controls had completely normal islets.
Conclusions: Preliminary analyses show different stages of immune cell infiltration in the pancreas and functional defects of living ß-cells. VP1 positive cells were detected by immunohistochemistry. The presence of virus needs to be confirmed by other methods. Recruitment of new cases continues.

P/202/FRI

ICA, anti-GAD and IA2/ICA512 antibodies in children with autoimmune hepatitis (AIH)

A. Chobot[1], K. Wyka[2], W. Mlynarski[2], J. Kwiecien[1], G. Deja[3] & J. Polanska[4]

[1]*Clinical Hospital No1, Zabrze, Poland,* [2]*Medical University of Lodz, Lodz, Poland,* [3]*Medical University of Silesia, Katowice, Poland,* [4]*Silesian University of Technology, Gliwice, Poland*

Objectives: AIH and type 1 diabetes (T1DM) are both autoimmune diseases, however their concomitance is rarely reported. The aim was to assess the incidence of characteristic for T1DM autoantibodies in children with AIH.
Methods: The study covered 13 patients (9♀) aged 3.8–17.2 year (12.6 ± 4.8) with AIH duration 0–15.2 years (10.2 ± 5.8; 1 case of

newly diagnosed AIH). Data concerning the course and treatment of AIH as well as concomitant autoimmune diseases was collected. Hemoglobin A1c (HbA1c) level, fasting blood glucose (FBG) and ICA, anti-GAD, IA2/ICA512 antibodies concentrations were examined and an oral glucose tolerance test (OGTT) was performed. The antibodies results were compared to those of 68 (33♀) healthy siblings (aged 11.1 ± 4.9 years) of patients with T1DM.

Results: Elevated antibodies concentrations were found in 6 children (5♀): anti-GAD in 1 girl (5% of cases), IA2/ICA512 in 5 patients (38%) (4♀). ICA antibodies were not detected in any of the children. Higher IA2/ICA512 concentrations [28.59 (12.25÷44.94) vs. 11.57 (-1.74÷24.89), P = 0.042], in three cases exceeding normal range, were found in patients with concomitant autoimmune diseases (celiac disease – 2 cases, autoimmune hemolytic anemia – 1, thrombocytopenia – 1). HbA1c (mean 5.1 ± 0.6%) and FBG (85.8 ± 7.6 mg/dl) results were normal in all cases. OGTT could be performed in 10 children – the results being within normal range (glycemia after 120 minutes: 116.6 ± 14.9 mg/dl). Higher, but normal, HbA1c [4.9 (4.57÷5.23) vs. 5.80 (0.72÷10.88); P = 0.033) was observed in patients with positive family history (1st and 2nd degree relatives) of autoimmune diseases (2 cases). Comparison of IA2 incidence between AIH patients and healthy siblings of T1DM patients showed significant difference between these groups [38.5% (36.12÷83.18) vs. 8.8% (3.61÷17.07), P < 0.05).

Conclusions: AIH and beta cell destruction (T1DM pre-diabetes) seem to be two independent immunologic processes.

Partially supported by MNiSW grant NN519579938.

P/203/FRI

HLA-associated phenotypes in youth with autoimmune-related diabetes

M.H. Black[1], J.M. Lawrence[1], C. Pihoker[2], L. Dolan[3], C. Davis[4], B. Rodriguez[5], S.M. Marcovina[6], E.J. Mayer-Davis[7] & D. Dabelea[8]
[1]*Kaiser Permanente Southern California, Research and Evaluation, Pasadena, United States,* [2]*Children's Hospital and Regional Medical Center, Seattle, United States,* [3]*Department of Pediatrics, University of Cincinnati School of Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, United States,* [4]*Division of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, United States,* [5]*Pacific Health Research Institute, Honolulu, United States,* [6]*Department of Medicine, University of Washington, Seattle, United States,* [7]*Department of Nutrition, University of North Carolina School of Public Health, Chapel Hill, United States,* [8]*Department of Epidemiology, School of Public Health, University of Colorado Denver, Aurora, United States*

Objectives: We examined the distribution of HLA-DRB1 alleles within a multiethnic cohort, and assessed their association with clinical characteristics of diabetes onset.

Methods: The sample was composed of 1,668 youth from the SEARCH for Diabetes in Youth Study (10% Black, 13% Hispanic, 77% non-Hispanic White (NHW)) who tested positive for GADA65 and/or IA2-A autoantibodies. Blood drawn at baseline was also used to measure fasting C-peptide and genotype the HLA-DRB1 locus. Age at diagnosis and race/ethnicity were obtained by self-report. DKA at diagnosis was determined from medical records. Multivariable linear and logistic regression models stratified by race/ethnicity were used to estimate the association between presence of DRB1 alleles and clinical characteristics.

Results: The distribution of DRB1 alleles varied widely by race/ethnicity. Of the susceptibility alleles, the frequency of DRB1*03 ranged 27–29% in all groups; DRB1*04 was present in 23% of Black, 45% of Hispanic and 41% of NHW youth. DRB1*03 was associated with younger age at diagnosis and lower fasting C-peptide levels in only NHW youth, and increased GADA65 titers in both NHW and Hispanic youth. DRB1*04 was associated with increased IA2-A titers in all racial/ethnic groups, but also with decreased GADA65 titers in NHW and Black youth. Of the protective alleles, DRB1*16 frequency ranged 2–3% in all groups; DRB1*13 was present in 11% of Black, 8% of Hispanic and 14% of NHW youth. DRB1*16 was associated with decreased IA2-A titers among NHW only. DRB1*13 was associated with decreased IA2-A among Black youth and decreased GADA65 titers among NHW. DRB1 was not associated with DKA at diagnosis in any racial/ethnic group.

Conclusions: The distribution of DRB1 alleles and their association with onset-related characteristics of autoimmune diabetes varies across major racial/ethnic groups in the United States. This may contribute to variation in clinical presentation of autoimmune diabetes by race/ethnicity.

P/204/FRI

Rabson-Mendenhall syndrome: which is the best treatment?

S. Innaurato[1], R. Pozzato[1], V. Grasso[2], F. Barbetti[2] & C. Monciotti[1]
[1]*Department of Pediatrics, University of Padua, Padua, Italy,*
[2]*Department of Internal Medicine, University of Rome Tor Vergata, Rome, Italy*

We describe a case of a 15-month-old boy with Rabson-Mendenhall syndrome, single child to nonconsanguineous parents; family history was silent. Because of maternal gestosis, oligodramnios and IUGR, the baby was delivered at 32nd g.w., with a birth weight of 990 g (< 3rd pc), L 37 cm (< 3rd pc), HC 27 cm (<10th pc). He presented with characteristic facies, hirsutism, phallic enlargement, medullary nephrocalcinosis. Acanthosis nigricans appeared at the age of 8 months, dentition was precocious and abnormal. At birth he was admitted at the NICU for respiratory distress, presenting from birth hyperglycemia with hyperinsulinism (1100 mU/l, C peptide 13.5 ug/l). Molecular genetic screening of insulin receptor gene revealed two missense mutations, E238K and E1074Q. Insulin i.v. was started with increasing doses (up to 17 U/kg/d) to which Metformin was added at 3.5 months of life (up to 300 mg/d, b.w. 3,100 g). Because of the poor response (plasma glucose 200–450 mg/dl, HbA1c >10%), at the age of 5.5 months the combined therapy was scaled down and then stopped and IGF1-analog mecasermin was started. The dose was progressively increased up to 20 U/d (0.6 mg/kg per day) with improvement of plasma glucose and HbA1c (7.7%); consequently mecasermin was reduced progressively to 0.2 mg/kg per day (b.w 6,100 g). Continuous glucose monitoring, 10 months after mecasermin therapy was started, confirmed the improvement. Currently, growth and relationship are good; renal function, lipid and hormonal profile are normal, motor recovery with physical therapy fairly good. The patient was also able to overcome an episode of ketoacidosis during infection. Molecular genetic diagnosis provided the rational basis to start metformin and then mecasermin and the clinical response to IGF1 in our patient is at present good. However, the lack of consensus guidelines and of information about long-term effects of high doses of IGF1 makes any therapeutical choice difficult.

P/205/FRI

Tropism and ultrastructural analysis of two Coxsackie B-5 strains to human primary pancreatic cell clusters in vitro

M. Hodik, A. Lukinius, O. Korsgren & G. Frisk
Uppsala University, Immunology, Genetics and Pathology, Uppsala, Sweden

Objective: Coxsackie B viruses (CVBs) have been implicated in pancreatic diseases such as type 1 diabetes and pancreatitis. Since the access to human material is scarce, mice models have often been used to study the correlation between the virus and disease. Inoculating mice with CVB normally results in extensive destruction of the exocrine acinar cells, whereas the endocrine islet of Langerhans are spared. In humans however very little is known about the tropism of these virus strains in the pancreas. In the present study we have analyzed the tropism of two CVB-5 strains to primary human pancreatic cell clusters *in vitro*. In addition, the sub-cellular location of virus particles in infected pancreatic cells was investigated.
Methods: Endocrine and exocrine cell clusters were inoculated with two CVB-5 strains and the replication was studied by TCID50 titration, immunohistochemistry, immunofluorescence and electron microscopy.
Results: The mean virus titer increase during seven days post infection was in exocrine cell clusters: 0.5 ± 0.27 (Adr, n = 7) and 0.43 ± 0.23 (V89–4557, n = 7) log TCID 50 /200 μL and in endocrine cell clusters 2 ± 0.59 (Adr, n = 8) and 2.45 ± 0.9 (V89–4557, n = 5). The virus particles were found to replicate exclusively in the endocrine cells by IHC and IF. In the electron microscope, the replication was associated to insulin granules.
Conclusion: In humans, CVB-5 replicates only in the endocrine cells which is the opposite of that in mice. The association of virus particles with the insulin granule membranes might reflect the use of these as replication scaffolds.

P/206/FRI

Prospective study concerning the humoral immunity and metabolic markers in the infantile population with diabetogenic risk

P.I. Velea[1], C. Paul[2], I. Tamasan[3], O.A. Velea[4] & E. Gai[5]
[1]*University of Medicine and Pharmacy, Clinic II Pediatrics, Timisoara, Romania,* [2]*University of Medicine and Pharmacy 'Victor Babes', Clinic II Pediatrics, Timisoara, Romania,* [3]*Emergency Clinical County, Clinic II Pediatrics, Timisoara, Romania,* [4]*University of Medicine and Pharmacy 'Victor Babes', Faculty of Dental Medicine – Department of Periodontology, Timisoara, Romania,* [5]*Emergency Clinical County, Department of Immunology, Timisoara, Romania*

Aim: To identify the subjects at risk to develop of insulin dependent diabetes mellitus (IDDM) in childhood.
Methods: The studied lot included 41 children, divided in 4 groups: group A = 32 children (siblings of the children with overt IDDM), group B = 5 children examined for impaired fasting glycemia, group C = 1 toddler of 3 months from diabetic mother, group D = 3 cases with overt IDDM at onset. We determined: fasting glycemia, HbA1c, total cholesterol, triglycerides, HDLc, antibodies anti GAD and ICA. Of the metabolic markers we used the evaluation of C peptid concentration (normal ranges: 0.5–3 ng/ml).
Results: In group A: 3 children (9.37%) were positive for anti GAD as well as for ICA, 23 (71.87%) were positive only for anti GAD and negative for ICA, and 6 cases (18.75%) were negative for anti GAD as well as for ICA. C peptid was normal in all 6 cases negative for antiGAD and ICA and below minimal value (lower than 0.5 ng/ml) in all 3 cases positive for antiGAD as well as for ICA. In all 23 cases positive only for antiGAD the values of peptid C being outside the normal values. In group A HbA1c was normal. In group B all 5 cases were positive for anti GAD and negative for ICA, with normal HbA1c. The toddler with diabetic mother was negative for both types of antibodies, with normal fasting glycemia, normal HbA1c and normal C peptid (2.077 ng/ml). The group D were positive only for antibodies anti GAD (with titres above the upper limit of normal in all 3 cases, 2 of these having a titre higher 20-fold, but with a normal secretion of C peptid. The third case had a decreased secretion of C peptid (0.191 ng/ml). The HbA1c in all these 3 cases exceeded 12%.
Conclusions: The decreased secretion of C peptid seems to correlate only with the concomitant presence of anti GAD as well as ICA antibodies. Anti GAD antibodies seem to be significantly related with the onset of IDDM, fact proved by the significant titre in 2 of the 3 cases with IDDM at onset.

P/207/FRI

The dynamics of changes in subpopulations of dendritic cells in children with type 1 diabetes treated with vitamin D3 analogue

R. Piekarski[1], L. Szewczyk[1], J. Tabarkiewicz[2] & J. Roliński[2]
[1]*Department of Pediatric Endocrinology and Neurology, Medical University in Lublin, Lublin, Poland,* [2]*Medical University in Lublin, Clinical Immunology, Lublin, Poland*

Objectives: In type 1 diabetes dendritic cells (DC) plays an important role in the initiation and modulation of immune response against antigens of pancreatic islet β cells.
Aim: Evaluation of circulating myeloid dendritic cells (mDC) and plasmacytoid dendritic cells (pDC) in children with type 1 diabetes before and after application of the vitamin D3 analogue (Alfadiol) in both groups and compared to a group of healthy children.
Methods: The study group comprised 50 children, mean age 10 ± 5 years, with newly diagnosed type 1 DM who were randomly enrolled into two groups (treated with vitamin D3 analogue or not) and subjected to annual follow-up. In all children were assessed twice the level of 25 (OH) D3, C-peptide and anti-GAD and anti-IA2 antibodies and cell subpopulations were examined using flow cytometry. The reference group consisted of 10 healthy children. We analyzed the percentage of immature myeloid DC BDCA-1+/CD19- and plasmacytoid BDCA-2+/CD123+.
Results: In 72% of children who received Alfadiol and in 50% without Alfadiol, an increase or maintain the value of C-peptide during the annual monitoring as compared with baseline values was observed. In the blood of children with type 1 diabetes not receiving Alfadiol the average percentage of myeloid DCs was 0.79% and was significantly higher ($P < 0.05$) than in healthy children (0.26%). However, there were no differences in the percentage of BDCA1 + cells between the group receiving Alfadiol and a control group. The percentage of plasmacytoid cells did not differ significantly between groups. The dynamics of changes in the percentage of DC subsets in relation to baseline (newly diagnosed diabetes) was analyzed.
Conclusion: The demonstrated differences of the analyzed parameters and the population of immune system cells encouraging more detailed analysis of the observed dependence, because they seem to indicate certain positive elements of used vitamin D3 analogue in children with type 1 diabetes.

P/208/FRI

Ongoing pathogenic processes in pancreas at onset of type 1 diabetes

G. Frisk, O. Skog, M. Hodik & O. Korsgren
Uppsala University, Uppsala, Sweden

Objective: To study pathogenic processes in the pancreas in islet auto-antibody positive, recent onset- and longstanding type 1 diabetic (T1D) organ donors.
Methods: Pancreases were obtained from six organ donors with one or two islet autoantibodies, two organ donors at onset of T1D, two donors with long-standing T1D, and control donors. Islet function, cytokine secretion and gene expression were analyzed in isolated islets. Pancreatic sections were used for IHC and ultrastructural analysis.
Results: Pancreases obtained at onset of T1D contained a significant number of remaining β-cells, but the insulin secretion in response to high glucose was impaired. In one of these two pancreases cytotoxic T-cells and macrophages infiltrated both endocrine and exocrine parts. The other pancreas contained dilated endothelial cells and endocrine cells with a swollen appearance. Both these cases stained positive for enterovirus (EV) protein in the islets while all controls and all but one autoantibody positive controls stained negative. In one of the cases, EV positivity was confirmed by the use of a coxsackievirus-B-specific antibody and in the other case immunoflourescent staining revealed that dsRNA colocalized with insulin. Cultured isolated islets from both these donors secreted IP-10 and significantly increased levels of MCP-1. The gene encoding for RANTES was also increased in these islets. MHC class 1 was up-regulated in insulin containing islets. However, activated caspase-3, a marker for apoptosis was not seen and no apoptotic cells were discovered by electron microscopy. Instead, the ultrastructural analysis revealed widespread decomposed endocrine cytoplasm particularly in one donor, fused insulin granules, and massive cytoplasmic vacuolization.
Conclusions: The finding of EV, the precence of viral markers together with markers of an activated innate immune system in the islets strengthens the hypothesis that this virus is involved in T1D.

P/209/FRI

The stage of autoimmunity and beta cells dysfunction in children with new onset type 1 diabetes mellitus and after 1 year on vitamin D3 analogue therapy

L. Szewczyk & R. Piekarski
Medical University in Lublin, Pediatric Endocrinology and Neurology, Lublin, Poland

In the last two decades studies have been concerned on immunomodulative role of vitamin D3 and its role in prevention and treatment of autoimmune diseases like type 1 diabetes mellitus. The aim of this study was to investigate the parameters indicating the functional reserve of pancreatic beta cells and the degree of autoimmunity after annual treatment of children with type 1 diabetes by comparing their dynamics in both groups.
Material and methods: 56 children from 2–17 years old on the onset of diabetes mellitus (DM) who were randomly enrolled into 2 groups (with or without vitamin D3 analogue) were subjected to annual observations. The blood level of 25(OH) D3, c-peptide and GAD and IA2 antibodies were estimated in both groups of children on the onset and after annual observation. Children enrolled to studies with C-peptide levels below 1.1 ng/ml. and increased titers of antibodies (anti-GAD and anti-IA2).
Results: The decreased levels of vitamin D3 was observed in 85% of children with new onset diabetes mellitus (<30 ng/ml) with value of vitamin D3 which meet the criteria of deficiency (<20 ng/ml) in 56% of children. In 70% of children who received alfacalcidol and in 50% without alfacalcidol, maintain the value of c-peptide during the annual monitoring as compared to baseline was found. Decreasing trend concerning GAD and IA2 antibody titers was observed, pronounced in the group receiving alfacalcidol. After 1 year observation period the average daily insulin requirement was lower (statistically insignificantly) in the group receiving alfacalcidol.
Conclusions: The decreased levels of 25(OH) D3 are observed in children with type 1 diabetes mellitus. In children with type 1 DM who received vitamin D3 analogue after 1 year observation C-peptide levels were more frequently stable with lower titers of investigated antibodies. Vitamin D3 deficiency seems to be a risk factor of diabetes mellitus occurrence.
Grant MNiSzW N N407 3100 33

P/210/FRI

iNOS polymorphism associates to IL-1b levels at 1 month post-diagnosis in children with T1DM – results from the Hvidoere Study Group on childhood diabetes

J. Johannesen[1,2], M.L.M. Andersen[1], L.B. Nielsen[1], J. Svensson[1], P. Hougaard[3], F. Pociot[4] & H.B. Mortensen[1,2], Hvidoere Study Group on Childhood Diabetes
[1]*Department of Paediatrics, Herlev University Hospital, Herlev, Copenhagen, Denmark,* [2]*Copenhagen University, Copenhagen, Denmark,* [3]*University of Southern Denmark, Odense, Denmark,* [4]*Glostrup Research Institute, Glostrup University Hospital, Copenhagen, Denmark*

Objective: A mutation in exon 16 (E16) in the inducible nitric oxide synthase gene (iNOS) has been associated to the development of T1DM in a Danish family-based nationwide cohort. Activation of iNOS has been described as one of the main effector pathways in cytokine mediated beta-cell destruction. Here, we evaluate whether this putative functional mutation associates to interleukin-1b levels and metabolic control during the remission phase.
Materials and methods: The International Hvidoere cohort, year 1999–2000: 275 children from 22 paediatric centers. DKA at onset was recorded. All patients went through a 90-minute Boost-test at 1, 6, 12 months post-diagnosis to characterize the residual beta-cell function. All samples were centrally analyzed. The E16 mutation in the iNOS gene was tested in all participants and was analysed for association to serum IL-1b levels and residual beta-cell function as assessed by stimulated c-peptide, HbA1c and calculated IDAA1c.
Results: The iNOS polymorphism was not associated to DKA status at diagnosis, stimulated c-peptide, measured HbA1c levels or the calculated IDAA1c at any time point during the first 12 months post-diagnosis. However, at 1 month post-diagnosis the serum IL-1b levels was significant higher in wild type individuals ($P = 0.03$), an effect that was not present at 6 and 12 months post-diagnosis.
Conclusion: The previous reported iNOS polymorphism associated to T1DM development may be involved in post-diagnosis IL-1b levels in the early remission phase. However, this polymorphism does not seem to influence the metabolic outcome in the remission phase.

P/211/FRI

Body building baby? An incidental finding of muscular hypertrophy leading to the diagnosis of a rare cause of insulin resistance

A. Salam, G. Hann & P. Kapila
North Middlesex University Hospital NHS Trust, Paediatrics, London, United Kingdom

An 8-month-old girl born to non-consanguineous Ghanaian parents was referred to the paediatric team with a 2 day history of high temperature and cough. She was otherwise well in herself and a diagnosis of a simple viral illness was quickly established. However on routine examination of the child, she was noted to have marked loss of subcutaneous fat with striking muscular hypertrophy associated with acromegaloid facial features. There was also distinct acanthosis nigricans. There were no signs of virilisation. Her systems examination was otherwise normal. Bloods demonstrated insulin levels of 40 mU/l (3–17 mU/l), triglyceride 3.3 mmol/l with normal liver and renal function tests. A liver ultrasound scan did not show any fatty changes. After being reviewed in clinic, a clinical diagnosis of Berardinelli Seip Congenital Lipodystrophy (BSCL) was made which was later confirmed on genetic testing. BSCL is a rare inherited disorder of adipose tissue leading to insulin resistance and widespread metabolic abnormalities. Treatment has thus far been mainly aimed at symptom control, but a greater understanding of the endocrine importance of adipose tissue has led to novel hormonal therapies that may lead to a vastly improved therapeutic outcome.

P/212/FRI

The diabetes prevention-immune tolerance (DiAPREV-IT) study at baseline

C. Nilsson[1], I. Hansson[1], C. Andersson[1], A. Carlsson[2], E. Cederwall[3], G. Hansson[4], J. Hemmendal[4], B. Jönsson[5], K. Larsson[6], A. Lernmark[4], J. Neiderud[7], A. Nilsson[4], A. Shalouie[4], A. Winqvist[4] & H. Elding Larsson[4], for the DiAPREV-IT Study Group
[1]*Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden,* [2]*Lund University, Lund, Sweden,* [3]*Department of Pediatrics, Ängelholm, Sweden,* [4]*Lund University, Malmö, Sweden,* [5]*Department of Pediatrics, Ystad, Sweden,* [6]*Department of Pediatrics, Kristianstad, Sweden,* [7]*Department of Pediatrics, Helsingborg, Sweden*

Objectives: Recent onset T1D children have been given Alum-GAD65 (Diamyd™) without treatment related adverse events. Since only a fraction of the β-cell function is left at diagnosis, it would be important to test Diamyd™ before clinical onset. The investigator-initiated diabetes prevention-immune tolerance (DiAPREV-IT) is the first placebo-controlled, double-blinded prevention study aiming to evaluate safety and efficacy of Diamyd™ in non-diabetic children with islet autoantibodies.
Methods: Non-diabetic children with GAD65 autoantibodies (GADA) and at least one more islet autoantibody (IA-2A, IAA, ZnT8RA, ZnT8WA or ZnT8QA) are offered to participate. Children (n = 50) aged 4–17.99 years are treated with placebo (n = 25) or Diamyd™ (n = 25) in two doses of 20 μg. At baseline the children were evaluated for HLA-DQ genotypes, islet autoantibodies, OGTT and IvGTT.
Results: Children (n = 43; 22 boys), with a median age 5.5 years (4–17.8) were included as of May 2011: 13/43 (30%) had a T1D first degree relative. Participants had GADA with one (11/43; 26%), two (6/43; 14%), three (11/43; 26%), four (9/43; 21%) or five (6/43; 14%) additional islet autoantibodies at varying titres. Glucose control, measured as fasting C-peptide (median 0.17 nmol/L (range 0.10–0.70)), first phase insulin response (median 44 mU/L (8–223)), K-value (median 1.94 (1.1–3.6)), 2 hour stimulated glucose (median 6.6 mmol/L (3.1–13.6)) and HbA1c (median 35 mmol/mol (27–40)) varied significantly at screening. Decreased glucose control was evident in 21/43 (49%). HLA-DQ2/8 was found in 19/43 (44%), DQ 8/8 or 8/X (X is not 2) in 20/43 (46%) and DQ 2/2 or 2/Y (Y is not 8) in 4/43 (9%). Genotypes or number of antibodies were not associated with glucose control. No serious adverse events were reported.
Conclusion: Baseline data in DiAPREV-IT indicate that included children have widely varying glucose control, which may be associated with factors other than number of islet autoantibodies and HLA-DQ genetic risk.

P/213/FRI

Examination of human pancreatic tissue and isolated pancreatic islets from organ donors with diabetes-associated auto-antibodies

O. Skog, M. Hodik, O. Korsgren & G. Frisk, VIDIS
Uppsala University, Immunology, Genetics and Pathology, Uppsala, Sweden

Objectives: The notion that development of type 1 diabetes is a slow process progressing over several years is supported by the appearance of autoantibodies against islet antigens years before clinical presentation. It is not known what triggers this humoral response, nor whether it is a cause or a consequence of the disease. In this study we had the opportunity to examine pancreases from 10 autoantibody-positive (AAb+) and 10 control multiorgan donors.
Methods: Insulin, immune cell, and enterovirus (EV) stainings were performed on formalin-fixed samples from the pancreas head. Insulin/DNA ratio, glucose-stimulated insulin release, and chemokines were measured in isolated islets. PCR was used to detect EV nucleic acid.
Results: Islets from AAb+ donors did not differ significantly from control donors in respect to immunopositivity to insulin, glucose-stimulated insulin release, or insulin/DNA (3.7 ± 2.9 in AAb+ and 4.9 ± 2.0 in controls). Islet content of chemokines IL-6, IL-8 and MCP-1 was not altered in AAb+ donors. T cells and macrophages infiltrated the pancreatic tissue in all donors to a various extent, but no increased infiltration or accumulation in or around islets could be seen in AAb+ donors compared to controls. Islets from one donor with autoantibodies against GAD65 stained positive for EV structural protein VP1 and the presence of EV genome was confirmed with PCR. Inoculation of culture media from these islets on green monkey kidney cells induced cytopathic effect in these cells for up to four passages.
Conclusion: No pathogenic processes were found in pre-diabetic pancreata, but it cannot be excluded that B cell destruction has occurred or is ongoing in a sub-fraction of pancreatic lobules. This is one of very few cases in the world where the presence of enteroviral genome in islets has been proven by PCR and virus isolation, strengthening the link between EV and T1D and suggesting that virus may be involved even in the pre-diabetic stage of the disease.

P/214/FRI

Autoantibody status of pediatric participants enrolled in the T1D Exchange Clinic Registry

A. Gerard-Gonzalez[1], S. Gitelman[1] & K.M. Miller[2], for the T1D Exchange Clinic Network
[1]*UCSF Medical Center, Pediatric Endocrinology and Diabetes Department, San Francisco, United States,* [2]*Jaeb Center for Health Research, Tampa, United States*

Objectives: The hallmark of type 1 diabetes (T1D) is the presence of autoantibodies (AutoAbs), although these have been noted to

be absent in 10–20% of those with presumed T1D. This study aims to characterize AutoAb in T1D Exchange Registry participants (pts).
Methods: Registry enrollment is limited to patients (pts) with presumed T1D. It began in September, 2010 and includes data from pts in ~60 centers throughout the US. We compared a variety of pt characteristics in AutoAb negative (Ng) pts versus positive (Pos) pts. We also evaluated changes in AutoAb profiles over time in pts with available data from at least two sets of AutoAbs at different points in time.
Results: Of the 2243 pts < 18 years of age in the registry with AutoAb results 345 (15%) were Ng, but only 195 (57% of the 284) had ≥ 2 AutoAbs measured (excluding insulin). For the 1898 with Pos AutoAbs, 45% had ≥ 2detected. There were no observed differences between those with Pos versus Ng AutoAbs results, in most recent HbA1c, BMI Z-score, total daily insulin use, and race/ethnicity. The proportion of females among Ng AutoAb pts was 10% lower than the proportion among those with Pos AutoAbs (39% vs. 49%, P < 0.001). The mean age at diagnosis was lower in AutoAb Ng pts (6.5 years) compared with AutoAb Pos (7.5 years, P < 0.001). For the 153 pts who had at least two set of AutoAbs at different times, 76% of the time there was concordance between the two sets of autoantibodies (both Pos 59%, both Ng 17%) compared with 24% who experienced seroconversion: 18% went from AutoAb Pos to Ng; 6% converted from Ng to Pos.
Conclusions: Similar to prior studies, ~15% of individuals diagnosed as T1D are AutoAb negative. With the exception of gender and age at diagnosis, there were no differences between AutoAb Ng versus. Pos pts among the pt characteristics assessed. Further examination of characteristics of pts with true AutoAb negative profiles may help in further characterizing the heterogeneous nature of T1D.

P/215/FRI

Comparison between autoantibodies presence, HbA1c and C-peptide levels according to age and sex in a Brazilian type 1 diabetes mellitus pediatric population

C.G.B. Passone, L.S. Oliveira, T.D. Manna & R.D. Savoldelli
Instituto da Criança – HCFMUSP, Pediatric Endocrinology, São Paulo, Brazil

Objective: To evaluate the prevalence of type 1 diabetes mellitus (DM) related autoantibodies and laboratory parameters of disease severity at clinical onset in a pediatric population according to age and sex.
Methods: We analyzed 112 patients, enrolled in a Brazilian pediatric tertiary center, diagnosed with type 1 DM since 2005, subdivided according to sex (72 female and 60 male) and age at diagnosis (39 patients under 5 years old and 73 older than 5 years). Autoantibodies against insulin (IAA), glutamic acid decarboxylase (GADA) and tyrosine phosphatase IA2 (IA2A), C-peptide and HbA1c levels were measured at diagnosis and compared between groups, independently. Statistical analysis was performed with Mann–Whitney and chi-Square tests when appropriated and P < 0.05 was considered significant.
Results: Younger patients had lower C-peptide levels than older ones (median 0.0 vs. 0.4, respectively; P = 0.02 – undetectable levels are considered 0.0). There was no significant difference between age and levels of HbA1c (P = 0.09), GADA titers (median = 672 vs. 170 U/mL, P = 0.085), IA2A titers (median = 665 vs. 1549 U/mL, P = 0.064) in < 5year and ≥ 5year groups, respectively, neither in the positivity of GADA (n = 27/39 vs. n = 46/73, P = 0.51), IA2A (n = 18/36 vs. n =46/69, P = 0.09) or IAA (n = 24/38 vs. n = 41/71, P = 0.58). We found a significant association between female gender and positive IA2A (P = 0.014), but no association with others antibodies or C-peptide levels.
Conclusion: In this Brazilian population there was no correlation between the autoantibodies presence and titers and the age at diagnosis, despite the lower C-peptide levels in the younger age-group. Female gender was associated with higher IA2A titers in this pediatric population. Studies are controversial about relationships between young age and presence of autoantibodies in type 1 DM.

P/216/FRI

Autoimmune thyroiditis and metabolic control in young adults with type 1 diabetes mellitus

A. Madej[1], K. Walczak[2], I. Korzeniewska-Dyl[2], E. Czerniawska[1], D. Moczulski[2] & A. Szadkowska[1]
[1]*Department of Pediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz, Lodz, Poland,* [2]*Department of Internal Diseases and Nephrodiabetology, Medical University of Lodz, Lodz, Poland*

Autoimmune thyroiditis (AIT) is one of the most frequent diseases coexisting with type 1 diabetes mellitus. Screening for AIT is performed in T1DM children every 1–2 years. In adults such monitoring is rather rare.
Aim: The aim of the study was to estimate the prevalence of thyroid autoantibodies (Ab) in young T1DM patients and the influence of thyroid function on metabolic control of diabetes.
Methods: A total of 149 patients (62 women, 87 men) at the age 18–40 years (mean 25.5 ± 4.4 years) with duration of diabetes ranged 2–28 years (mean 13.6 ± 5.8 years) with the onset of diabetes at the age < 18 years were included in the study. All of them were treated with intensive insulin therapy. In all patients free triiodothyronine, free thyroxine, thyroid-stimulating hormone, anti-thyroid peroxidase antibody, anti-thyroglobulin antibody and HbA1c were measured.
Results: A total of 50 patients (33.6%) had minimum one type of thyroid autoantibodies. The presence of one type of thyroid Ab was found in 16.8% patients, two types of thyroid Ab was noted in 16.8%. In women the prevalence of thyroid Ab was higher than in men (51.6% vs. 20.7%; P = 0.004). 27 patients with thyroid Ab and five individuals without them had positive history of AIT. In 23 patients AIT was newly recognized. In five patients hypothyroidism and in 20 subclinical hypothyroidism was found. In one patients without Ab hyperthyroidism was recognized. The patients with Ab had longer duration of diabetes than patients without them (15.3 vs.12.8 years, P = 0.01). There was no differences in HbA1c in patients with and without thyroid Ab (7.12 vs. 7.41, P = 0.17) and between patients with hypothyroidism and normal level of thyroid hormones (7.31 vs. 7.34%; P = 0.89).
Conclusion: In one third of T1DM adults patients the presence of thyroid autoantibodies was observed. This disturbance was more frequent in females than in males. There was no difference in metabolic control in patients with and without thyroid autoantibodies or with hypothyroidism.

P/217/FRI

Complex analysis of processes in immunocompetent cells and their relevance to T1D development

L. Petruzelkova[1], R. Blatny[2], J. Vcelakova[1], Z. Sumnik[1], S. Kolouskova[1] & K. Stechova[1]
[1]*2nd Medical Faculty of Charles University and University Hospital Motol, Paediatric Department, Prague, Czech Republic,* [2]*Central European Biosystems, Prague, Czech Republic*

Objectives: We addressed the question if there are differences in gene expression profile of peripheral blood mononuclear cells

among T1D patients, their first degree relatives, patients with non-autoimmune diabetes and healthy controls. We tried to estimate ''prodiabetogeneic'' gene expression pattern. We were also interested in the effect of diabetes associated autoantigens on immune cells.

Methods: Total RNA from 28 T1D patients, 46 relatives (split according autoantibody status), 10 MODY patients and 27 controls was processed by a high density whole genome expression microarray. We studied a basal gene expression as well as the changes after the exposure to GAD65, IA2 and proinsulin derived peptides. With our results we performed MetaCore pathway analysis in order to estimate their functional aspects.

Results: We observed the most significant differences in basal gene expression between relatives and controls. We found 547 genes which were expressed in a different way in Ab negative relatives group compare to controls ($P < 0.05$). Some of them play an important role in immune responses (TLR2, TLR6, CD19, CD22 etc.). We found significant differences in gene activation of cell processes including non-specific immune responses (TLR signalling, CCR3 signalling in eosinophiles), humoral immune reactions (BCR pathway), costimulation, cytokine responses (CD137, CD40, CD28 signalling) or proinflammatory answer (IL-1 pathway). After autoantigens exposure we observed the activation of Th17 and TGF-β related cell processes which were the most significant in relatives.

Conclusion: For the beginning of autoimmune destructive insulitis the establishment of proinflammatory settings seems to be crucial. It is followed by proTh17 polarisation and dysbalance in cytokine spectrum. Mentioned genes and pathways may serve as promising T1D related biomarkers on genomics or proteomics level.

Acknowledgments: Supported by projects NT/11407-5, P302/10/1679, NPVII2B06019, NPVII2B08066, MZOFNM2005.

P/218/FRI

The influence of vitamin D levels in children of different genetic risk defined by HLA, CTLA-4 and the insulin gen

J. Svensson[1], J. Johannesen[1], H.B. Mortensen[1], A. Linneberg[2], M. Fenger[3], S.U. Thorsen[1] & F. Pociot[4], DSBD

[1]*Paediatric Department, Herlev University Hospital, Herlev, Denmark,* [2]*Research Center for Prevention and Health, Glostrup University Hospital, Glostrup, Denmark,* [3]*Department of Biochemistry, Hvidovre University Hospital, Hvidovre, Denmark,* [4]*Glostrup University Hospital, Glostrup Research, Glostrup, Denmark*

Background and aims: Vitamin D insufficiency has been suspected as a contributing factor to the development of type 1 diabetes. Accelerating factors such as vitamin D insufficiency may be more important in those with low risk genes. We speculated if effect of vitamin D insufficiency could be altered by genetic risk.

Materials and methods: Data is derived from *The Danish Diabetes Registry* (*DIA-REG B&U*) with an attached bio bank. Vitamin D was analyzed using HPLC and divided in very low, low, normal and high using the following cut-points (25, 50, 75 nmol/l). Data was analyzed using logistic regression with patient status as outcome and vitamin D and CYP27B1, HLA, Insulin and CTLA-4 genotype as explanatory variables together with age and gender.

Results: The study included 466 children with diabetes and 466 healthy siblings. A total of 509 were males and 423 were females. We found equal vitamin D levels in patients and siblings. The gene distribution for HLA, insulin and CTLA-4 differed significantly between sibling and patients ($P < 0.001$) as expected; whereas there was no difference for CYP27B1. The genetic risk defined by a combination of HLA, CTLA-4 and the insulin gene revealed 74% and 38% with high risk genes; 19% and 27% with moderate risk and 7% vs. 35% with low risk genes in patients and siblings respectively. Among siblings 11% and patients 9.5% were below 25 nmol/l in vitamin D. The missing association between vitamin D and patient status was unaltered by genetic risk profile and there were no signs of higher proportion of children with vitamin D insufficiency in those with low genetic risk.

Conclusion: We could not confirm a low vitamin D level in newly diagnosed children at onset in comparison with their healthy siblings. Furthermore vitamin D levels in children with a low genetic risk were comparable with those with moderate or high risk genes. Therefore the role of vitamin D at onset of diabetes may be questioned.

P/219/FRI

T1D risk stratification for the first degree relatives of diabetic patients in the Czech paediatric population

L. Petruzelkova, J. Vcelakova, K. Stechova, J. Lebl, M. Vyhnankova & S. Kolouskova

Paediatric Department, 2nd Medical Faculty of Charles University and University Hospital Motol, Prague, Czech Republic

Objectives: The first degree relatives of T1D patients are at increased risk of diabetes development. We searched for the strongest predictors of progression to clinical diabetes within the factors as HLA genotype or type and titer of pancreatic autoantibodies.

Methods: This study is a part of the Czech T1D Prediction Programme where siblings and offspring of T1D patients are HLA genotyped (DQA1, DQB1 by PCR-SSP) and regularly tested for autoantibodies (GADA, IA2A, IAA by RIA). In our study, 152 children positive for at least one Ab and 374 Abs negative children as a control group were enrolled. Median follow up in both groups was 3 years. A total of 36 Ab positive children (23.7%) developed diabetes during their follow-up. The prevalence of GADA and IA2A in Abs positive group was 118 (77.6%) and 77 (50.7%) respectively. A total of 72 children from positive group were examined for IAA as well and 16 of them (22.2%) were IAA positive. 41 Abs positive children underwent ivGTT.

Results: The study confirmed a strong association between T1D development and HLA status ($P < 0.001$; the most risky genotype was DQA1*05-DQB1*0201/DQA1*03-DQB1*0302). Analysis of Ab positive group showed significant association among T1D risk and Ab type (GADA $P < 0.021$, IAA $P < 0.006$; IA2A n.s) and Ab titer (IA2A $P < 0.001$, GADA $P < 0.002$, IAA $P < 0.012$) and the total number of Abs ($P < 0.001$). We observed that prolonged Ab positivity leads to the slow decrease in FPIR but no association between HLA status or detailed Abs characteristics and the duration of Ab positivity or the duration to the pathological findings in ivGTT was observed.

Conclusion: We are able to define children at risk of diabetes progression by estimation of HLA genotype and detailed Abs monitoring. On the other hand, the estimation of the time period to T1D manifestation is very difficult because the duration of β-cells destruction is highly variable and without any association with investigated risk factors.

Acknowledgments: Supported by project MZOFNM2005.

Poster Session I: Monogenic Diabetes Forms and their Treatment

P/220/WED

Neonatal diabetes mellitus; experience in BIRDEM

F. Mohsin[1], K. Azad[1], S. Akhter[1], B. Zabeen[1], J. Nahar[1], T. Begum[1], N. Nahar[1], Z. Hassan[2], D. Mackay[3], S. Ellard[4] & A.T. Hattersley[4]
[1]*Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Paediatrics, Dhaka, Bangladesh,* [2]*Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Physiology and Molecular Biology, Dhaka, Bangladesh,* [3]*Division of Human Genetics, University of Southampton, Salisbury, United Kingdom,* [4]*Institute of Biomedical and Clinical Science, Peninsula Medical School, Exeter, United Kingdom*

Objectives: Neonatal diabetes mellitus (NDM) is diagnosed within first 6 months of life and can be either transient (TNDM) or permanent (PNDM). The study was undertaken to determine clinical phenotype and genetics in patients with NDM diagnosed during 2001–2009 in BIRDEM.
Methods: Seven patients with NDM were evaluated. Genetic testing was performed by sequence analysis of the *KCNJ11, ABCC8, EIF2AK3* and *INS* genes or by methylation analysis of the 6q24 locus associated with TNDM.
Results: Two patients had TNDM. A female baby, birth weight (BW) 1.7 kg, presented at 3 days of age with hyperglycaemia. Paternal uniparental isodisomy of chromosome 6 was detected. A male baby, BW 2.7 kg, presented with weight loss at 17 days. He had a homozygous mutation c.-331C>A in the *INS* gene promoter. Remission occurred at 10 months and 80 days of age respectively. Five children had PNDM. One female baby, BW 2.6 kg, presented at 14 days with DKA. A novel heterozygous de novo *INS* mutation, S101C was detected. Two patients had homozygous *E1F2AK3* mutation confirming the diagnosis of Wolcott–Rallison Syndrome;one female baby, BW 2.2 kg presented at 80 days with polyurea. Another male baby, BW 2 kg presented at 70 days with convulsion. Two patients have been successfully switched over to oral Glibenclamide. A female baby, BW 2.2 kg, was diagnosed at 8 days incidentally. She was heterozygous for *KCNJ11* mutation, R201H and was switched to Glibenclamide at 1 year of age. HbA1c reduced from7.9% to 6.2% after 3 months. A male baby, BW 2 kg, presented with polyurea at 64 days. He was homozygous for a novel *ABCC8* mutation, V215A and was switched to Glibenclamide at 6 months. HbA1c changed from 5.4% to 5.7% after 3 months with marked reduction in hypoglycaemia.
Conclusion: Genetic diagnosis was possible in all seven patients. Molecular genetic analysis is useful for prediction of outcome, mode of treatment and genetic counselling.

P/221/WED

Diabetes in infancy: clinical and laboratory perspectives and glycemic control

I.M. Ghali, M.H. Hafez, M.M. Hassan & H.M. Mehawed
Pediatric Department, Diabetes Endocrine Metabolic Pediatric Unit, Cairo University, Cairo, Egypt

Background: Diabetes mellitus is rare during the first 2 years of life. Type1A diabetes is probably the most prevalent subtype. Diabetes in the first 6 months of life is unlikely to be a classic type 1 diabetes, but rather is 'Monogenic diabetes of infancy'. Monogenic diabetes results from the inheritance of a mutation (s) in a single gene. It may be dominantly or recessively inherited or may be a *de novo* mutation.
Objective: Characterizing clinical and biochemical features of children diagnosed with diabetes mellitus < 2 years.
Methodology: Retrospective study for 45 patients with onset of diabetes before 6 months in 20 patients and from 6–24 months in 25 patients. Medical records of these children were reviewed, Abdominal U/s & CT scan, genetic testing (was performed in five out of 20 patients) were done for patients with the onset before 6 months and HLA for DQB1 (20 patients), AGAD65, ICA& IA2 antibodies (18 patients), TORCH screening for CMV & rubella (18 patients) for patients from 6–24 months they were treated with basal/bolus regimen and CSII in six patients.
Results: Patients < 6 months presentation was mainly DKA, irritability, LBW, vomiting and diarrhea. More than 50% was of the permanent type. The glycemic control, blood glucose excursions, HbA1c and hypoglycemia were better in patients on basal regimen only compared by basal/bolus regimen. For patients from 6–24 months: the presentation was mainly DKA (85%), disturbed conscious level (65%), acute infection (53%) and polyuria and polydipsia (40%). Predisposing alleles DQB1 0201,0202, 0302,0303 were found in 83%, protective alleles DQB1 0301,0602 in 3%, both was found in 5%. Prevalence of CMV infection was (20%) & rubella was (5%) at diagnosis. CSII was a very useful tool for young patients with diabetes when used intelligently.
Conclusion: Type 1 diabetes before the second year of age is due to an interaction between genetic and environmental factors. Basal insulin and CSII give more satisfactory and safe control.

P/222/WED

Prevalent mutations in the 125th amino acid of the HNF4A gene causing HNF4A-MODY: founder effect or mutation hot-spot?

P. Dusatkova, S. Pruhova, J. Lebl & O. Cinek
Department of Pediatrics, Second Faculty of Medicine, Charles University in Prague, University Hospital Motol, Prague, Czech Republic

Objectives: No evidence of the ancestral origin or of a mutation hot-spot in the *HNF4A* gene among families with HNF4A-MODY has been reported, to our best knowledge. However, from a national-based register of families with genetically confirmed MODY, we have identified 10 apparently unrelated families with mutations in the 125th amino acid in the *HNF4A* gene: R125Q was carried in seven families, R125P in two, and R125W in one family. The aim of our study was to investigate whether this mutation clustering reflected a common origin of the respective mutations or a mutation hot-spot.
Methods: We genotyped 31 mutation carriers and their 34 healthy relatives from the 10 families, as well as 94 population controls using 12 single nucleotide polymorphism markers that cover a 10 Mb region around the *HNF4A* gene and that are not in mutual linkage disequilibrium in the general population (Pearson's $r^2 \leq 0.08$ for all pairs). Haplotypes were inferred using the Haploview and Phase software.
Results: We observed no definable haplotype around any of the mutations: R125Q (Pearson's $r^2 \leq 0.04$ for the mutation and any of the markers), R125P (Pearson's $r^2 \leq 0.01$), R125P/Q/W (Pearson's $r^2 \leq 0.03$). This implies that the mutations originated by an independent events.
Conclusions: The prevalent occurrence of the mutations in the 125th amino acid of the *HNF4A* gene could be likely attributed to a mutation hot-spot, as the amino acid arginine (R) is coded by CGG nucleotides which form a common position for substitutions due to the deamination of methylcytosines at CpG dinucleotides. In support of the results, the literature

suggests that the mutations in the 125th amino acid arginine lead to impaired function of HNF4A due to dimerization failure of the transcription factor, and thus HNF4A-MODY phenotype could have decreased the reproduction fitness of the mutation carriers in the past.

P/223/WED

Rabson Mendenhall syndrome in a six year old boy: a case report

R.D. Savoldelli[1], M.G. Carballo[1], T. Della Manna[1], M.A.G. Fortes[2], M.L. Corrêa-Giannella[2], D. Damiani[1]

[1]*Instituto da Criança – HCFMUSP, Pediatric Endocrinology Unit, São Paulo, Brazil,* [2]*São Paulo University, LIM-25, São Paulo, Brazil*

Rabson mendehall syndrome (RMS) is a rare autosomal recessive disorder caused by mutation in the insulin receptor (INSR) gene. It is characterized by dental anomalies, thick and hyperpigmented skin, hirsutism, macrogenitossomia and severe insulin resistance (IR) that may evolve to diabetes mellitus (DM). The RMS represents an intermediate form among syndromes related to mutations in the INSR gene as the leprechaunism and type A and B IR syndromes.

Objective: To report the clinical and laboratorial characteristics of a patient with RMS.

Patient and methods: A 6-year-old boy born in Bahia, Brazil, from unrelated parents developed hyperpigmentation in areas of skin folds since his first year of life; one first degree cousin with similar physical features was also reported. Examination showed cervical, axillary, inguinal and peri-umbilical acanthosis nigricans; hypertrichosis and dental abnormalities; penis of 5.0 cm in length. Laboratorial work-up and molecular analysis were performed.

Results: Glucose and fasting insulin: 70 mg/dl and 178.6 mcU/ml. Oral GTT showed a peak insulin and glucose of 2287.2 mcU/ml and 138 mg/dl, respectively. HbA1c: 5.8%. Molecular investigation demonstrated a homozygous mutation in exon 19 of INSR gene, codon 1135, GCG (alanine) to GTG (valine). Parents were heterozygous. The patient has not developed DM yet, only few episodes of postprandial hyperglycemia (220–234 mg/dl) and prolonged fasting hypoglycemia (minimum 43 mg/dl). There are descriptions of the same mutation changing the alanine codon (GCG) by glutamic acid (GAG) providing insulin resistance. It is known that alanine at codon 1135 is highly conserved in species and valine is one of the amino acids designated as not to be tolerated in this position.

Conclusion: A RMS patient is described with an identified mutation in codon 1135, GCG (alanine) to GTG (valine) in exon 19 of the INSR gene, presentig a tipical phenotype, severe IR but not DM until 6 years of age.

P/224/WED

The identification of KNCJ11, ABCC8 and INS gene mutations in patients with Infancy-onset diabetes mellitus: results of 2-year investigation

Y. Tihonovich[1], N. Zubkova[1], E. Petraikina[2], O. Stotikova[3], I. Volkov[3] & A. Tiulpakov[1]

[1]*Department of Inherited Endocrine Disorders, National Endocrinology Research Centre, Moscow, Russian Federation,* [2]*Children Endocrinology Department, Moscow Clinical Hospital, Moscow, Russian Federation,* [3]*Children Endocrinology Department, Russian Clinical Hospital, Moscow, Russian Federation*

Introduction: The aim of our study was to analyze the prevalence of KCNJ11, ABCC8 and INS genes mutations in Russian patients diagnosed with diabetes mellitus (DM) in the first year of life.

Materials and methods: KCNJ11, ABCC8 and INS genes were sequenced in 38 patients. The 27 children presented with DM before 6 months of life (median age: 2.4 month), and in 11 cases DM was diagnosed between 6 and 11 months (median age: 8.2 month).

Results: In 10 out of 27 patients (37%) diagnosed before the age of 6 months seven different KCNJ11 mutations were found: V69M, V59M, R201C, R201H (four cases), L164P, C42R and V231_Q235delVPLHQ. Two different ABCC8 mutations (D209E, D212G) were found in two patients (7.4%) in the same group. Two KCNJ11 mutations V69M and V231_Q235delVPLHQ) and 1 ABCC8 mutation were novel. Nine patients carrying KCNJ11 mutations had permanent neonatal DM (PNDM). Patients with V59M and V69M mutations also had severe developmental delay (iDEND-syndrome). Patients with ABCC8 mutations (D209E, D212G) and one child with KCNJ11 mutation (V231_Q235delVPLHQ) had transient DM (TNDM). After genetic analysis seven patients with K_{ATP} channel mutations (R201H-2 cases, R201C, C42R, V59M, V231_Q235delVPLHQ, D209E, D212G) have been successfully transferred from insulin to glybenclamide.

In 11 subjects diagnosed with DM at the age of 6–11 months we found one mutation in KCNJ11 gene (D323Y) and 1 mutation in INS gene (L30R). Both mutations were novel. Patient with INS gene mutation had insulin-dependent PNDM presented at 7 months of age. Patient with KCNJ11 mutation was diagnosed at the age 8 months, and after genetic analysis was successfully transferred from insulin to glybenclamide. His family history revealed mild DM in several relatives on paternal side.

Conclusion: We recommend sequencing of KCNJ11, ABCC8 and INS genes in all children with DM diagnosed in the first year of life

P/225/WED

Is primary hypothyroidism a new feature of Wolcott-Rallison syndrome?

A. Spehar Uroic[1], V. Kotori[2], N. Rojnic Putarek[1], S. Ellard[3], E. Young[3], J. Radanovic[1], V. Kusec[4] & M. Dumic[1]

[1]*Department of Pediatrics, University Hospital Centre Zagreb, Zagreb, Croatia,* [2]*Pediatric Clinic Prishtina, Prishtina, Serbia,* [3]*Peninsula Medical School, Exter, United Kingdom,* [4]*Department of Laboratory Diagnostics, University Hospital Centre Zagreb, Zagreb, Croatia*

Introduction: Wolcott–Rallison syndrome (WRS) caused by mutations in EIF2AK3 encoding PERK enzyme is the most common cause of permanent neonatal diabetes mellitus (PNDM) in consanguineous families and isolated populations. It also includes skeletal abnormalities, liver and renal dysfunction and other inconsistently presented features that, however, did not involve primary hypothyroidism.

We present Albanian girl from Kosovo with WRS and primary hypothyroidism.

Case report: A Girl was born to healthy, unrelated parents and was diagnosed with PNDM at the age of 10 days. Since 5 months old, she had greasy stools. At the age of 2 years primary hypothyroidism was diagnosed: TSH 19 mU/L (ref: 0.3–3.8), low normal T3 and T4, negative thyroid antibodies, hypoplastic thyroid gland. L-thyroxine was prescribed, but she was not compliant.

She was admitted to our Clinic at the age of 7 years. Severe growth retardation, microcephaly, spondyloepiphyseal dysplasia, hypoplastic pancreas, exocrine pancreatic insufficiency, elevated liver enzymes, anemia and subclinical hypothyroidism (TSH 8.7 mU/L) were present. Homozygous nonsense mutation of EIF2AK3 gene (R902X) was found. Parents are heterozygous for the same mutation.

Her younger brother was diagnosed with PNDM at 2 weeks of age and died in acute hepatic insufficiency at the age of 7 months. Mutation analysis was not performed, but obviously he also had WRS.

Conclusion: Since another Albanian girl from Kosovo with WRS and the same genotype was recently reported (1), there are three patients with WRS described so far coming from Kosovo. Since they are not related, same genotype could be due to founder effect.

Primary non-autoimmune hypothyroidism was already described in two patients with WRS (1, 2), but it was consider coincidental. Third WRS patient with the same disorder might suggest that primary hypothyroidism could also be phenotypic reflection of mutation of pleiotropic gene EIF2AK3.

References: 1. Rubio-Cabezas, 2009
2. de Wit, 2006

P/226/WED

Two novel insulin receptor gene mutations: a case of severe insulin resistance syndrome

F. Meschi[1], R. Bonfanti[1], M. Viscardi[1], A. Rigamonti[1], G. Frontino[1], R. Battaglino[1], V. Favalli[1], C. Bonura[1], V. Grasso[2], F. Barbetti[3,4] & G. Chiumello[1]

[1]*Department of Pediatrics, San Raffaele Scientific Institute, Milano, Italy,* [2]*Department of Laboratory Medicine, University of Tor Vergata, Rome, Italy,* [3]*Department of Internal Medicine, University of Tor Vergata, Milano, Italy,* [4]*Department of Internal Medicine, Bambino Gesù Children's Hospital IRCCS, Rome, Italy*

Case report: The male patient was born with a birth weight of 2.225 g at 39 weeks of gestation, as first child to non-consanguineous parents. Adaptation to extrauterine life and routine blood tests were normal, including blood glucose (BG). The newborn was discharged. On the 16th day of life the patient was brought to the emergency department due to hyporeactivity and poor appetite. Physical examination showed some characteristics of insulin resistance syndrome: protruding abdomen, elfin facial appearance, hypertelorism, saddle nose, broad lips, acanthosis nigricans, hypertrichosis. Some features were compatible with the patients african origins. Glycosuria and hyperglycemia (621 mg/dl) with normal acid-base homeostasis were found. Triglycerides were 181 mg/dl. Type 1 diabetes autoantibodies were negative. C-peptide and insulin levels were 42.3 ng/ml and 3,234.4 mIU/l respectively. I.v. insulin was started at 0.01 U/Kg/h and progressively increased to 0.25 U/Kg/h. Fasting BG and post-meal BG oscillated between 100–200, and 200–300 mg/dl, respectively. A single episode of hypoglycemia (42 mg/dl), responsive to glucagon, was observed after several hours of fasting. Insulin pump therapy at doses up to 10 U/Kg/day did not elicit any improvement in glucose control. Genetic screening of *INSR* gene revealed two heterozygous mutations: the splice-site mutation IVS5+2T > C, which likely disrupts the function of one allele, and mutation R41W, which may have two possible effects: a reduced insulin binding to the receptor, or a defective insulin receptor transport to the cell membrane. On the 34th day of life insulin therapy was substituted with metformin at a dose of 25 mg b.i.d. with improvement in BG control (mean BG 150 mg/dl, SD 62 mg/dl). The patient, now 3 months old, thrives well. In conclusion, results of molecular screening supported the choice of the insulin-sensitizer metformin for therapy. Follow up is needed to establish the durability of this therapy in our patient.

P/227/WED

New mutations in Wolfram syndrome

C. Aloi, A. Salina, L. Pasquali, F. Lugani, K. Perri, R. Tallone, G.M. Ghiggeri, G. d'Annunzio & R. Lorini

IRCCS G. Gaslini Institute, Genoa, Italy

Background: Wolfram syndrome (WS) is an autosomal recessive neurodegenerative disorder characterized by diabetes insipidus, diabetes mellitus, optic atrophy, and deafness identified by the acronym ''DIDMOAD''. The WS gene, *WFS1,* encodes a transmembrane protein called Wolframin which recent evidence suggests may serve as a novel endoplasmic reticulum calcium channel in pancreatic β-cells and neurons. WS is a rare disease, with an estimated prevalence of 1/550,000 children, with a carrier frequency of 1/354.

Objective: The aim was to determine the genotype of WS patients in order to establish a genotype/phenotype correlation.

Population and methods: We clinically evaluated nine young patients from nine unrelated families (six males, three females). Basic criteria for WS clinical diagnosis were coexistence of insulin-treated diabetes mellitus and optic atrophy occurring before 15 years of age. Genetic analysis for *WFS1* was performed by direct sequencing.

Results: Molecular sequencing revealed five heterozygous compound and three homozygous mutations. All of them were located in exon 8, except one in exon 4. In one proband only an heterozygous mutation (A684V) was detected. Two new variants c.2663 C > A and c.1381 A > C were detected.

Conclusions: Our study increases the spectrum of *WFS1* mutations with two novel variants. The male patient carrying the compound mutation [c.1060_1062delTTC]+[c.2663 C > A] showed the most severe phenotype: diabetes mellitus, optic atrophy (visual acuity 5/10), deafness with deep auditory bilaterally 8000 Hz, diabetes insipidus associated to reduced volume of posterior pituitary and pons. He suddenly died at the age of 13 years. While the other patient carrying the compound mutation [c.409_424dup16]+[c.1381 A > C] showed a less severe phenotype (DM, OA).

P/228/WED

Clinical application of best practice guidelines for genetic diagnosis of MODY2

A. Salina, C. Aloi, L. Pasquali, A. Mascagni, M. Cassanello, R. Tallone, F. Lugani, R. Lorini & G. d'Annunzio

IRCCS G. Gaslini, Pediatric Clinic, Genoa, Italy

Background: In Caucasian population maturity-onset diabetes of the young (MODY) is estimated to be less than 5% in patients with type 2 diabetes. Clinical guidelines for the molecular diagnosis of MODY have been recently published, *GCK* should be molecularly analyzed in non obese children and young adults with persistent fasting hyperglycaemia, HbA1c level just above the upper limit of normal, small 2h-glucose increment after oral glucose tolerance test (OGTT). Moreover presence of family history of mild fasting hyperglycaemia is not presented as an essential prerequisite.

Objective: The aim was to evaluate the clinical guidelines for the molecular diagnosis of MODY considering family history of diabetes as essential pre-requisite.

Population and methods: A total of 39 Italian probands, (21 males and 18 females) with mean age 11.9 ± 4.5 years evaluated during the last 2 years for incidental hyperglycaemia. In all cases there was absence of obesity or insulin resistance phenotype. All were negative for auto-antibodies. The impaired fasting glucose, was persistent and stable over a period of months or years. Family history of diabetes was considered as essential prerequisite to select probands to be molecularly screened for *GCK* mutations.

Genetic *GCK* sequencing was performed by direct sequencing in all the probands satisfying all diagnostic criteria.
Results: The molecular investigation confirmed *GCK* mutations in the familiar pedigree in 31/39 probands (79.4%).
Conclusion: Application of the strict criterion to the Italian population lead to the identification of *GCK* molecular defects in 79.4% of the probands. These data are higher than previously reported in South European population. Family history of diabetes should be considered as essential prerequisite for a correct and early MODY2 genetic diagnosis. This could help to identify several *GCK* mutations in children and young adults that have to receive the genetic diagnosis necessary for optimal treatment.

P/229/WED

Neonatal diabetes due to KCNJ11 mutation (V59M); can early therapy with sulfonyl urea prevent mental impairment?

M. Kocova
University Childreńs Hospital, Skopje, Macedonia, the Former Yugoslav Republic of

Introduction: Neonatal diabetes is usually caused by gene mutations. The approach and therapy depends on the type of gene mutation. Kir 6.2 mutations can cause permanent or transient neonatal diabetes. V59M variant is associated with developmental delay and neurological impairment.
Objective: To present a boy with neonatal diabetes and V59M KCNJ11 mutation early treated with sulphonylurea followed up for 4 years.
Case report: A 50-day-old boy baby presented with severe hyperglycemia, (76 mmol/l) diabetic ketoacidosis (pH 7.01, BE-26.5 mmol/l), accompanied with hypernatremia (164 mEq/l), hypokalemia 3.6 mEq/l, and one attack of seizures. HbA1c was 12.3%. Continuous insulin infusion with rapid acting insulin improved the ketoacidosis. Intensive insulin therapy with 4 daily doses of insulin failed to provide metabolic control during the post-ketotic phase, therefore, the boy was put on insulin pump. The condition of the baby improved immediately, he started gaining weight and the HbA1c measured 6 weeks after initiation of pump therapy decreased to 8.7%. Molecular analysis confirmed V59M mutation, in the KCNJ11 gene. At the age of 4 months, insulin was gradually replaced with sulphonylurea tapered to 0.8 mg/kg divided in two doses daily. Three months later the HbA1c was 5.7% with a stable glycaemia, and C-peptide values normalized to 1.7 ng/ml. Patient was followed at 6 months intervals for 4 years. The average HbA1c during this period was 6.1%. The height, weight and all other findings were normal. Developmental milestones (walking, talking, toilet training etc) were reached on time. The psychological testing confirmed normal development.
Conclusion: Molecular diagnosis should be performed in neonatal diabetes. Patients with KCNJ11 mutation respond well to a therapy with sulphonylurea. Although the V59M mutation is usually associated with developmental delay, our patient did not have any developmental impairment, probably due to early therapy.

P/230/WED

Mixed meal test combined with repaglinide – a useful tool to assess ß-cell function and to determine oral therapy options in patients with diabetes other than type 1

D. Simm, H.-J. Veeze & H.-J. Aanstoot
Diabeter (National Center of Diabetes in Children and Young Adults), Diabetology, Rotterdam, Netherlands

Objectives: The correct diagnosis of diabetes is not always evident, especially in young patients. In this age group monogenic diabetes forms and type 2 diabetes are often initially misdiagnosed as type 1 diabetes. For patients with uncertain diagnosis we aimed to develop a test to assess ß-cell function and determine the option of oral medication.
Methods: A total of 18 patients (8–54 years), seven of them with unclear diagnosis, one Kir6.2, MODY1 (n = 2), MODY2 (n = 3), MODY3 (n = 4), MODY5 (n = 1) and one healthy control person underwent after an overnight fasting period a mixed meal test (MMT) with Boost® (6 ml/kg, max.: 360 ml) combined with repaglinide 1 mg, a short acting insulin secretagogue. Glucose and C-peptide were determined before and 30, 60, 90 120, 150 and 180 minutes after meal intake. Incremental areas under the C-peptide curve ((I)AUC) were calculated using the trapezoidal rule.
Results: Sixteen individuals including the control person showed C-peptide release (average max. release 2.2 nmol/l at 90 and 120 minutes, (I)AUC 3.15 nmol/l x h) which led to a blood glucose decline after an average maximum of 10.3 mmol/l at 60 minute. Among the responders were five of the patients with unclear diagnosis of diabetes and all patients with proven monogenic diabetes except the one with MODY5. Of the seven with unclear diagnosis two had to be classified as idiopathic type 1 (1B) diabetes, one by lack of C-peptide secretion, the other by low C-peptide secretion ((I)AUC 0.45 nmol/l x h) and absence of glucose decline after 60 minutes. Another patient could be classified as type 2 diabetes (C-peptide (I)AUC 11.0 nmol/l x h). Based on these test results five of the seven patients with unclear diagnosis switched from insulin to oral medication.
Conclusion: We identified individuals with repaglinide responsive ß-cell function. The combination of MMT with repaglinide turned out to be a useful tool in the assessment of diabetes with unclear aetiology and allows to switch patients to adequate oral therapy.

P/231/WED

Characterization of sleep in KATP-related monogenic neonatal diabetes mellitus (NDM): a pilot study

K.H. Dillard[1], K. Spruyt[2], N. Devine[1], D. Gozal[2], L. Kheirandish-Gozal[2] & S.A.W. Greeley[1]
[1]*University of Chicago, Adult and Pediatric Endocrinology, Chicago, United States,* [2]*University of Chicago, Pediatric Sleep Medicine, Chicago, United States*

Objectives: NDM is commonly due to activating mutations in *KCNJ11*, encoding the kir6.2 subunit of the KATP channel. 20% also exhibit a range of neurodevelopmental disability, with the V59M mutation associated with moderate global developmental delay and R201H with seemingly normal development. Anecdotal reports of sleep disruption led us to hypothesize that abnormal sleep may be related to brain expression of mutated KATP channels. Our aim is thus to gather pilot data on sleep in individuals with KATP-related NDM and healthy sibling controls.

Methods: Subjects were recruited through the US NDM Registry. Each subject wore an Actiwatch to record time spent in movement or inactivity for at least 7 days and completed sleep surveys: infant sleep questionnaire (ISQ; 0–4 years), children's sleep habits questionnaire (CSHQ; 0–12 years) and Pittsburgh sleep quality index (PSQI).
Results: Eight so far completed the study: three with V59 mutations (2 V59M, 1 V59A), three with R201 mutations (2 R201H, 1 R201C) and two non-diabetic siblings. The NDM group displayed a greater number of night time disruptions and worse global sleep scores on PSQI and CSHQ. Each sleep characteristic on CSHQ showed a trend of difference between cases and controls, including sleep duration, sleep anxiety and night time awakenings but no concerns regarding sleep disordered breathing. Actiwatch activity profiles supported the suggestion of increased night time activity.
Conclusions: Although statistical analysis was limited by the small sample size, preliminary analysis is thus far consistent with apparent sleep disruption in those with KATP mutations. Notably, those with less severe R201 mutations showed a similar trend as those with more severe V59 mutations. Continued recruitment will allow demonstration of any conclusive differences. Further characterization of particular patterns of abnormal sleep will allow for possible intervention that could improve developmental progression, behavioral problems, or glucose control.

P/232/WED

Developmental outcome in KCNJ11 neonatal diabetes mellitus (NDM): can disability be prevented by early sulfonylurea treatment?

R. Shah[1], B. Kragie[1], S.A. Greeley[2] & M. Msall[1]
[1]*University of Chicago, Developmental Behavioral Pediatrics, Chicago, United States,* [2]*University of Chicago, Adult and Pediatric Endocrinology, Chicago, United States*

Objectives: Activating mutations in KATP genes cause NDM that may be associated with a spectrum of neurodevelopmental disability, with the V59M mutation in *KCNJ11* being a common cause of the intermediate DEND syndrome, involving moderate developmental delay. The degree of disability may depend on various factors and has been suggested to improve with sulfonylurea (SU) therapy; however, longitudinal data utilizing validated instruments are lacking. Our aim is thus to characterize the degree of neurodevelopmental impairment in SU-treated DEND patients and elucidate factors upon which it may depend.
Methods: Children aged 24–204 months with the V59M (or V59A) mutation were identified through the US NDM registry. Subjects completed screening surveys of development, including the ages and stages questionnaire (ASQ), and were assessed in person using the Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI).
Results: Three of four children who completed the ASQ had fine motor concerns. The one who had significantly better scores than the others had been treated with SU within days of diagnosis soon after birth. All nine children undergoing VMI had scaled scores and percentiles that were significantly lower than expected for their chronologic age. The three children with scores closest to normal had begun SU treatment at the earliest ages.
Conclusions: Neurodevelopmental disability in DEND patients includes fine motor problems, in addition to variable motor and speech delay, that may be ameliorated by early treatment. Although the patients treated with SU at the youngest ages exhibit a better outcome, these are also the youngest in the cohort, and the number of cases is very small. Data on greater numbers of patients tracking long-term outcome will be essential. Our report on a significant number of rare patients exhibiting impaired visual-motor integration corresponds to recent data in mice implicating a role for expression of mutated channels in the cerebellum.

P/233/WED

Development of a common core dataset for rare diabetes syndromes registry: the EURO-WABB registry for Wolfram, Alström and Bardet-Biedl syndromes

T. Barrett[1], P. Beales[2], A. Farmer[3], N. Jaffre[4], R. Paisey[5], K. Parkinson[6], S. Ayme[7], M. Lopez de Heredia[8], J. Rohayem[9], S. McCafferty[10], P. Maffei[11], W. Mlynarski[12], V. Nunes[13], V. Paquis[14], R. Sinnott[10], V. Tillmann[15] & L. Tranebjaerg[16]
[1]*School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, United Kingdom,* [2]*London University, University College London, London, United Kingdom,* [3]*Birmingham Children's Hospital, Wellcome Trust Clinical Research Facility, Birmingham, United Kingdom,* [4]*French Wolfram Association, Paris, France,* [5]*Torbay District General Hospital, Medicine, Torbay, United Kingdom,* [6]*Alstrom Syndrome UK, Torbay, United Kingdom,* [7]*INSERM, Paris, France,* [8]*CIBERER, Barcelona, Spain,* [9]*Technische Universitat, Dresden, Germany,* [10]*University of Glasgow, eSciences Centre, Glasgow, United Kingdom,* [11]*Università degli Studi di Padova, Padova, Italy,* [12]*Medical University of Lodz, Lodz, Poland,* [13]*Fundació Institut Investigació Biomèdica de Bellvitge, Barcelona, Spain,* [14]*Centre National de la Recherche Scientifique, Nice, France,* [15]*University of Tartu, Tartu, Estonia,* [16]*Institute of Cellular and Molecular Medicine, Wilhelm Johannsen Center of Functional Genomics, Copenhagen, Denmark*

Rare diabetes syndromes affecting less than 1:100,000 children are under-recognised; delayed diagnosis is common; treatable complications may not be identified; and it is challenging to recruit sufficient patients to clinical trials. We aimed to develop a common core dataset for notifying children with Wolfram, Alström, Bardet-Biedl, Wolcott-Rallison, Thiamin-responsive megaloblastic anaemia deafness and diabetes, and other rare diabetes syndromes, to an international registry. We convened two meetings of international researchers in rare diabetes syndromes (French Wolfram syndrome association 2010; EURO-WABB meeting 2011); we reviewed the case records of patients attending the national specialist commissioned Alström and Bardet-Biedl services during 2010 (UK); and published clinical descriptions of rare diabetes syndromes to April 2010. We developed a consensus core and extended dataset. The core dataset includes 50 data fields of which nine relate to referring physician and consent data; 18 define the clinical and molecular genetic features and differentiate between syndromes; and 23 relate to age of onset of symptoms, optional free text and tissue storage records. The extended dataset comprises over 100 fields of detailed phenotyping information. The core dataset can be completed in 20 minutes.
Agreement on a common core dataset for very rare diabetes syndromes is essential in order to compare data between national registries, link registries and identify subgroups of patients that may be eligible for clinical trials or to prioritise genes for mutation searches. We have developed a common core dataset for European Union states that can be shared between national rare disease registries as they are developed; and will allow linkage with other international disease registries. The core dataset can be found at: www.euro-wabb.org.

Poster Session II: New Insulins and Pharmacologic Agents

P/234/FRI

The Preschool study: hypoglycemia assessed by continuous glucose monitoring in 125 children under age 6 with type 1 diabetes treated with multiple daily insulin injections

T. Danne[1], A. Philotheou[2], D. Goldman[3], T. Guo[3], L. Ping[3] & P. Johnston[3]
[1]*Kinderkrankenhaus auf der Bult, Hannover, Germany,* [2]*UCT Private Academic Hospital, Capetown, South Africa,* [3]*Sanofi-Aventis, Bridgewater, United States*

Objectives: Young children with type 1 diabetes mellitus (T1DM) are at high risk for hypoglycemia. The Preschool study evaluated hypoglycemia, and glycemic control and variability, with multiple daily injection (MDI) therapy in young children using continuous glucose monitoring (CGM).
Methods: Preschool was a 24-week, randomized, multinational study among young children treated with glargine (n = 61) given once a day in the morning versus NPH insulin (n = 64) given once or twice a day, with bolus lispro insulin provided in both groups. Primary endpoint was rate of ''all hypoglycemia'', a composite of symptomatic hypoglycemia, SMBG < 70mg/dl (3.9 mmol/l), and low (glucose < 70 mg/dl) CGM. Secondary endpoints included: change in A1C and% of CGM glucoses 70–180 mg/dl (3.9–10.0 mmol/l).
Results: At baseline, the mean values for patients' age was 4.2 (1–6) years, diabetes duration 2.1 (1.0–5.3) years, and A1C 8.1 (6.0–12.0)%. The initial average dose of basal insulin (mean ± SD) was 0.36 ± 0.18 U/kg. Overall, mean change from baseline in A1C was 0.018% and mean percentage of CGM glucose in the target range ≥ 70 and ≤ 180 g/dl (3.9–10.0 mmol/l) was 39.9 ± 11.6%. The mean overall rate of ''all hypoglycemia'' was 180.5 ± 110.5 episodes/pt-year, and of symptomatic hypoglycemia, 29.4 ± 43.1 episodes/pt-year.
Conclusions: The study shows high rates of symptomatic and asymptomatic hypoglycemia in these young children with T1D on MDI therapy. Ongoing analyses will compare the effect of insulin glargine vs. NPH on hypoglycemia and on glycemic control and variability, and will assess the contributions of multiple factors affecting these outcomes.

P/235/FRI

Antidiabetic effects of Trigonella foenum graecum and sodium orthovanadate on antioxidant enzymes, membrane bound ATPases and glucose transporter expression in muscle, liver and brain in female diabetic rats

P. Kumar, R.K. Kale & N.Z. Baquer
Lab #215, JNU, School of Life Sciences, Jawaharlal Nehru University, New Delhi, India

Objectives: Oxidative stress in diabetic tissues is accompanied by high level of free radicals and the simultaneously declined antioxidant enzymes status leading to cell membrane damage. In the present study, the effect of sodium orthovanadate (SOV) and *Trigonella foenum graecum* seed powder administration has been studied on blood glucose and insulin levels, membrane bound ATPases (Na^+K^+ATPase , Ca^{2+}ATPase) , antioxidant enzymes (superoxide dismutase, glutathione S-transferases), DNA degradation, lipid peroxidation, and distribution of glucose transporter in liver, muscle and brain tissues of the alloxan induced diabetic rats and to see whether the treatment with SOV and *Trigonella* is capable of reversing these effects.
Methods: Diabetes was induced by administration of alloxan monohydrate (15 mg/100 g body weight) and female rats were treated with 2 IU insulin, 0.6 mg/ml SOV, 5% *Trigonella* in the diet and a combination of 0.2 mg/ml SOV with 5% *Trigonella* separately for 21 days.
Results: Diabetic rats showed hyperglycemia with almost four fold high blood glucose levels. Hyperglycemia increases lipid peroxidation and DNA degradation, causing decreased activities of membrane bound ATPases , antioxidant enzymes and glucose transporter expression with diabetes in the rat tissue. Rats treated with combined dose of vanadate and *Trigonella* had glucose levels comparable to controls, similar results were obtained with the activities of antioxidant enzymes, membrane bound ATPases, DNA degradation, lipid peroxidation and glucose transporter in diabetic rats.
Conclusion: Our results showed that lower doses of vanadate (0.2 mg/ml) could be used in combination with *Trigonella* to effectively counter diabetic alterations without any toxic side effects.

P/236/FRI

Low doses of vanadate and Trigonella synergistically regulate monoamine oxidase activity, lipofuscin, membrane fluidity and GLUT4 translocation in alloxan-diabetic rats

P. Kumar, R.K. Kale & N.Z. Baquer
Lab #215, School of Life Sciences, Jawaharlal Nehru University, New Delhi, India

Objectives: Oral administration of vanadate to diabetic animals have been shown to stabilize the glucose homeostasis and restore altered metabolic pathways. The present study explored the prospect of using low doses of vanadate with *Trigonella foenum graecum,* seed powder (TSP), another antidiabetic agent, and to evaluate their antidiabetic effect in diabetic rats. The effect of these antidiabetic compounds was examined on general physiological parameters, monoamine oxidase activity, calcium homeostasis, membrane fluidity and distribution of lipofuscin accumulation in liver, brain and heart tissues. Expression of glucose transporter (GLUT4) protein was also examined by immunoblotting method in experimental rat heart after three weeks of diabetes induction.
Methods: Diabetes was induced by administration of alloxan monohydrate (15 mg/100g body weight) and rats were treated with 2 IU insulin, 0.6 mg/ml SOV, 5% *Trigonella* in the diet and a combination of 0.2 mg/ml SOV with 5% *Trigonella* separately for 21 days.
Results: Diabetic rats showed high blood glucose levels. Activity of monoamine oxidase increased in diabetic brain, liver and heart. Diabetic rats exhibited an increased level of calcium with lipofuscin accumulations and decreased membrane fluidity. GLUT4 distribution was also significantly lowered in heart of alloxan diabetic rats. Treatment of diabetic rats with insulin, TSP, vanadate and a combined therapy of lower dose of vanadate with TSP revived normoglycemia and restored the altered level of monoamine oxidase, calcium homeostasis , lipofuscin and membrane fluidity and also induced the redistribution of GLUT4 transporter. TSP treatment alone is partially effective in restoring the above diabetes-induced alterations.
Conclusion: Combined therapy of vanadate and TSP was the most effective in normalization of altered metabolic parameters and GLUT4 distribution without any harmful side effect.

P/237/FRI

Treatment with insulin Glargin or Detemir during 24 months from onset in children and adolescents with T1DM

J. Åman & L.G. Holmgren
Department of Pediatrics, Örebro University Hospital, Örebro, Sweden

Aim: In this observational clinical study the aim was to compare the long-acting basal insulins Glargin and Detemir in newly diagnosed T1DM.
Methods: All children 5–16 years of age with recent onset T1DM were treated with Glargin once daily or Detemir twice daily in a randomized order during 2005–2008. In all, 73 children (33 girls) with a mean age of 10.5 years were included. After initial iv insulin infusion for at least 24 hours, a subcutaneous basal analog was initiated and combined with 3–5 pre-meal injections of a fast-acting insulin analog. In 37 and 36 children, Glargin and Detemir were used, respectively. All but eight children was followed during 24 months. HbA1c (mono-S; reference value < 5.3%), weight, dose of insulin, DKA and severe hypoglycaemia was registered at each visit.
Results: The two groups were quite comparable at onset. Initial HbA1c declined rapidly with equal values (5.7%) in both groups at 6 months with 31% and 25% of children with HbA1c values below the upper normal reference limit (n.s). A similar gradual increase of HbA1c occurred in both groups with mean values at 24 months (7.2 vs. 7.0%) and 34% vs. 30% of children with HbA1c within the target (< 6.5%) for Levemir and Glargin, respectively, n.s. The weight gain 3–24 months was similar in both groups. The total daily insulin dose was 0.3 U/kg higher and the basal daily dose was 0.2 U/kg higher in children treated with Detemir compared to Glargin(both $P < 0.0001$). The frequency of severe hypoglycaemia was 6 vs. 7.5/100 patient years in the groups (n.s) and none of the children had an episode of DKA.
Conclusion: This clinical observational study for 24 months displayed no difference in glycemic control, weight gain, hypoglycaemia or DKA in children with recent onset T1DM treated with insulin Glargin or Detemir from onset. Target for HbA1c was reached by 30% of children after 24 months. The need for basal insulin was significantly increased by 50% in children treated with Detemir.

P/238/FRI

Usefulness of biphasic insulin aspart 70 as meal-time insulin to control 3 hours or greater postprandial blood glucose levels after a protein- and fat-rich meal

T. Urakami, R. Kuwabara, M. Habu, K. Komiya, A. Yoshida, J. Suzuki, S. Takahashi & H. Mugishima
Nihon University School of Medicine, Pediatrics, Tokyo, Japan

Objective: To evaluate the efficacy of biphasic insulin aspart 70 (BIAsp70), which is formulated with a 7:3 ratio of rapid-acting insulin analogue (Ra) and intermediate-acting fraction, as mealtime insulin to reduce the subsequent increase of blood glucose (BG) after a protein- and fat-rich meal.
Methods: Subjects consisted of 25 children with T1DM treated with basal-bolus regimens. All the subjects used single daily injections of long-acting insulin analogs as basal insulin. They were divided into two groups based on the type of mealtime insulin used, i.e. 20 children using Ra (group Ra) and five using BIAsp70 (group BIAsp70). The calculation of the mealtime insulin dose was based on the amount of carbohydrates (carbohydrate counting) of both groups' meals. Thus, the insulin dose in group BIAsp70 accounted for an increase in BG 1.4 fold that of group Ra. BG profiles before and 1, 2, 3 and 6 hours after taking a Japanese-style meal (protein 25 g, fat 11 g) and a protein- and fat-rich meal (hamburger with curry and rice; protein 28 g, fat 19 g) were measured and the rising rates (postprandial to preprandial BG concentrations; Δ%) were compared between the two groups.
Results: Serial changes of Δ% 1, 2, 3 and 6 hours after Japanese-style meals in group Ra were 14 ± 68, 15 ± 77, 10 ± 84 and -8 ± 59%, and those in group BIAsp70 were -8 ± 17, 62 ± 92, -11 ± 31 and -30 ± 36%. 3 and 6 hours postprandial BG levels were lower in group BIAsp70. Moreover, the serial changes of Δ% after protein- and fat-rich meals in group Ra were 97 ± 186, 63 ± 169, 49 ± 193 and 34 ± 193%, and those in group BIAsp70 were 69 ± 169, 43 ±95, 40 ± 100 and -24±30%. A 6-hours postprandial BG levels significantly decreased in group BIAsp70. Frequencies of hypoglycemia (BG ≤ 70 mg/dl and BG ≤ 40 mg/dl) were not different between the two groups after both meals.
Conclusions: BIAsp70 as mealtime insulin seems to be superior to Ra to control 3 hours or greater postprandial BG levels in children with T1DM, especially after a protein- and fat-rich meal.

P/239/FRI

Metabolic control of once versus twice-daily administration of insulin Detemir in basal-bolus therapy, treat-to-target study, for children and adolescents with type 1 diabetes mellitus

R. Nimri, S. Demol, Y. Lebenthal & M. Phillip
Schneider Children's Medical Center, Endocrinology and Diabetes, Petah Tikva, Israel

Objective: To assess the efficacy and safety of insulin Detemir therapy (once/twice daily) using a treat-to-target titration protocol in children and adolescents with type 1 diabetes mellitus (T1DM).
Research design and method: This prospective, open label study enrolled 50 patients with T1DM aged 6–18 years and HbA1C > 7.7%. Eligible patients were assigned to receive insulin Detemir once daily before breakfast and pre-meal insulin Aspart for 16–20 weeks. Detemir dose titration was based on fasting blood glucose levels. The active titration phase was 4–8 weeks after which if target range was achieved patients continued on once daily Detemir; if up-titiration could not be done due to hypoglycemia they were switched to twice daily Detemir.
Results: A total of 37 patients completed the study (At baseline: mean age 12.7 ± 3 years; HbA1c 8.8 ± 0.8%; diabetes duration 4.2 ± 3 years). 19(51%) remained on once daily Detemir and 18(49%) were switched to twice daily Detemir. The differences between the once and twice daily Detemir groups were age (13.8 ± 3.2 vs. 11.5 ± 2.3 years, $P = 0.01$, respectively) and pubertal stage which showed more patients in active puberty (Tanner 2–3) in the twice daily group (50% vs. 11%, $P = 0.003$). HbA1c decreased in both groups, (-0.66%, $P = 0.02$ and -0.77%, $P = 0.004$) with no significant difference between groups. Nocturnal hypoglycemic events/week reduced in both groups but was only significant for the once daily group (10.9–2.7, $P < 0.05$ vs. 8.7–5.8, n.s); with no change in frequency of severe hypoglycemic episodes between groups. No significant differences were found between and within groups for body mass index SDS, insulin requirement, glucose variability or treatment satisfaction.
Conclusion: Since there was no proven advantage of twice daily over once daily Detemir, commencing all children on once daily Detemir would be reasonable but it is necessary to remain aware that younger children and those during active puberty are more likely to require twice daily therapy.

P/240/FRI

Children randomized to long acting insulin glargine or determir from diagnosis of type 1 diabetes mellitus have lower HbA1C after one year as compared to those randomized to NPH insulin

P. Bang[1], J. Salemyr[2], K. Ekström[2], M.-A. Pulkkinen[2], C. Carlsson-Skwirut[2] & E. Örtqvist[2]

[1]*Department of Clinical and Experimental Medicine, Division of Pediatrics, Linköping University, Linköping, Sweden,* [2]*Department of Womens and Childrens Health, Karolinska Instiutet, Stockholm, Sweden*

Objective: To study if long acting insulin analogs improve HbA1c in children with Type 1 Diabetes Mellitus, which have been reported in retrospective but so far not in prospective controlled studies.

Subjects and methods: In the present prospective controlled trial, 120 patients (7–17 years of age) were randomized at diagnosis of Type 1 Diabetes Mellitus (T1DM) to receive NPH, Glargine or Determir (1:1:1) as basal insulin combined with insulin Aspart in a meal insulin therapy (MIT) regimen. Patient randomization was stratified for pubertal status and sex. 28 patients met exclusion criteria (incl. Celiac disease in eight patients) or requested to discontinue the study.

Results: After one year of treatment the median (25th–75th percentiles) HbA1C in patients with long acting insulin analogs Glargine or Detemir was 52.1 (47–57) mmol/mol, significantly lower than 56.3 (49–67) mmol/mol in the NPH group ($P = 0.041$). There was no difference in the median (range) age (10.7 (8.9–13.7) vs. 11.5 (9.6–13.8) years; $P = 0.576$) or the sex distribution (22 F/42 M vs. 9 F/19 M; $P = 0.738$). Pre-pubertal children randomized to long acting or NPH insulin did not obtain different median HbA1c after one year (53.1 (51–57) vs 55.2 (51–61) mmol/mol; $P = 0.566$) while children that had entered puberty at diagnosis demonstrated significantly better metabolic control when receiving long acting insulin analogs Glargine or Detemir (50.0 (45–57) vs. 59.9 (49–70) mmol/mol; $P = 0.028$).

Conclusion: This is the first randomized controlled study demonstrating improved HbA1c by treatment with long acting insulin analogs. Overall, the effect is explained by HbA1c improvements in pubertal patients. We also assessed glucose variability by CGM, meal stimulated C-peptide and components of the GH-IGF-system to evaluate how this positive effect of long acting insulin analogs are mediated. These results should impact on the clinical practice and choice of basal insulin from diagnosis of pediatric T1DM.

P/241/FRI

Clinical experience with prandial biphasic insulin aspart 30/70 three-times daily (TID) in paediatric patients with type 1 diabetes (T1D): results from a single-centre audit

N.K. Thalange[1], H. Langford-Wood[1], V. Datta[1] & P. Stella[2]

[1]*Jenny Lind Children's Department, Norfolk & Norwich University Hospital, Norwich, United Kingdom,* [2]*Novo Nordisk Ltd, Crawley, United Kingdom*

Aims: Data on the use of biphasic insulin aspart 30/70 (BIAsp 30) in paediatric T1D are limited, partially due to its off-label use in paediatric patients. Thus, a single-centre audit provides useful information.

Methods: This was a retrospective audit of 113 paediatric patients with T1D from a single UK centre, treated with prandial BIAsp 30 TID as a step towards escalating treatment to a basal-bolus regimen.

Results: The mean age of patients at baseline was 11.8 years (range 2–19 years). Mean daily BIAsp 30 doses were split between breakfast (B): 8.1 U, lunch (L): 7.7 U and dinner (D): 7.9 U. At 3, 6 and 12 months, 86, 60 and 35 patients, respectively, remained on BIAsp 30. Baseline HbA1c was 10.9 ± 2.0% and fell to 7.7 ± 1.2%, 7.5 ± 1.1% and 8.3 ± 1.4% at 3, 6 and 12 months, respectively. Mean BIAsp 30 dose was marginally increased by 12 months versus baseline (B: 9.7 U, L: 9.2 U and D: 9.9 U). Three hypoglycaemic episodes were possibly severe. In total, hypoglycaemic episodes affected 14.7%, 5.6% and 12.5% of patients at 3, 6 and 12 months, respectively. During the 12 months of follow-up, three patients were hospitalised due to hypoglycaemia and another two patients due to diabetic ketoacidosis.

Summary: Prandial BIAsp 30 TID appears safe and effective in paediatric patients with T1D and permits planned transition to basal-bolus insulin. It may lend itself to ambulatory management of newly diagnosed patients. For those patients unwilling to progress to basal-bolus insulin, it was an effective treatment for up to 3 years after diagnosis.

Poster Session I: Pumps and Sensors

P/242/WED

Does initiation of insulin pump therapy during the first year after diabetes onset have a better impact on long-term metabolic control than initiating pump therapy at a later stage?

S. Shalitin[1,2], T. Lahav-Rite[2], Y. Lebenthal[1,2], L. de Vries[1,2] & M. Phillip[1,2]
[1]*The Jesse Z and Lea Shafer Institute of Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider, Petach Tikva, Israel,* [2]*Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Objectives: To determine if the initiation of continuous subcutaneous insulin infusion (CSII) during the first year after diagnosis of type 1 diabetes (T1D) results in better metabolic control over time than later initiation.

Patients and methods: An observational cohort study conducted in a tertiary pediatric medical center. The sample included 488 patients with T1D (273 females) aged 2.6–39 years (mean 19.9 ± 7.65) who started CSII in 1998–2009 and used it for at least one year. Their medical charts were reviewed for background, disease-related, and treatment-related variables. Study end-points were HbA1c levels, rates of severe hypoglycemia and diabetic ketoacidosis (DKA) events during CSII use. Findings were compared between patients who started CSII during the first year after diagnosis and patients who started later. Good metabolic control was defined by the target HbA1c, according to ISPAD.

Results: At pump initiation, patients who started CSII early were significantly younger than those who started later (10.7 ± 5.7 vs. 16.4 ± 7.0 years, $P < 0.001$), and they monitored blood glucose levels more frequently (5.4 ± 1.8 vs. 3.9 ± 1.5 times/day, $P < 0.001$). The durations of diabetes and of CSII therapy were significantly shorter in the early-initiation group (diabetes duration: 4.3 ± 2.1 vs. 11.9 ± 6.4 years $P < 0.001$, CSII therapy duration 3.6 ± 2.1 vs. 4.7 ± 2.5 years $P < 0.001$).

There were no significant between-group differences in patient sex or ethnicity, indications for initiating pump therapy, mean HbA1c level, attainment of target HbA1c, rate of severe hypoglycemia or DKA events after pump initiation.

Conclusions: Although the use of CSII has increased dramatically during the last decade, especially in younger patients, its initiation at an early disease stage does not have an additive benefit to later initiation on long-term metabolic control. Therefore, the timing to initiate CSII therapy should be tailored to the individual patient by the diabetes-care team.

P/243/WED

Long term follow-up in children and adolescents with type 1 diabetes using insulin pump therapy: a retrospective multicentre, multinational study (Input(log) Study)

C. Mameli[1], A. Scaramuzza[1], J. Ho[2], R. Cardona-Hernandez[3], L. Suarez-Ortega[3] & G.V. Zuccotti[1]
[1]*Luigi Sacco Hospital, University of Milano, Pediatrics, Milano, Italy,* [2]*Faculty of Medicine, University of Calgary, Pediatrics, Calgary, Canada,* [3]*Sant Joan de Déu Hospital, Endocrinology and Diabetes, Barcelona, Spain*

Objectives: We evaluated the long-term glycaemic control in children with type 1 diabetes (T1DM), using insulin pump therapy (CSII) for at least 4 years in three countries: Italy, Canada and Spain.

Methods: Each Centre reviewed charts of patients with T1DM, using CSII. Inclusion criteria were: age 4–20 years., T1DM > 4 years. and CSII therapy ≥ 4 years. Data collected included gender, age, T1DM duration, date of CSII initiation, BMI, HbA1c, insulin requirement (IR), DKA and severe hypoglycaemic episodes (SH) at baseline and every 6 months during follow-up.

Results: We present the data of 101 patients (61 M), aged 4–20 years. (mean: 14.6 ± 3.8years.), with T1DM from 9.7 ± 3.3 years., using CSII from 5.6 ± 1.7 years. (range 4–11 years.). HbA1c data are shown in the table (significance among groups has been evaluated by Kruskall–Wallis test: P = 0.03; *P = 0.003; when evaluated as a whole HbA1c has been evaluated using paired test statistic vs. baseline: §P = 0.005; P=0.05). After CSII initiation HbA1c showed a significant improvement only in the first year; during the follow-up, HbA1c values tended to increase. Evaluating HbA1c according to Countries, a difference has been observed with slightly lower values in Italy than in Canada and Spain. No significant difference has been observed about BMI, IR, SH and DKA episodes from baseline throughout the follow-up.

	Baseline	T +6mo	T +12mo	T +24mo	T +36mo	T +48mo	T +60mo	Last visit
Canada	8.17±1.02	7.78±0.91	8.09±1.24	8.23±1.18°	8.30±1.07°	8.40±1.05*	8.16±0.96	8.51±1.22*
Italy	8.08±0.99	7.73±0.78	7.69±0.96	7.51±0.79°	7.67±0.82°	7.61±0.78*	7.81±0.33	7.83±0.72*
Spain	9.08±1.36	7.95±0.78	8.14±0.51	8.61±0.92°	8.12±0.53°	8.45±0.75*	8.18±0.63	8.51±0.64*
All	8.52±1.25	7.83±0.81§	7.95±0.85§	8.10±1.18	8.07±1.02§	8.24±1.07	8.27±1.09°°	8.33±1.04

[Table - HbA1c values according to Country.]

Conclusion: CSII seems an effective therapy in the long term, although the major benefit in HbA1c is seen in the first year of CSII initiation. In this preliminary study, a difference in HbA1c during long term follow-up was observed among Countries. Further studies will evaluate which factors may be responsible for this observation (i.e., different dietetic habits, lifestyle, etc.).

P/244/WED

An experience of surgical procedures in children with T1D and pump therapy using real-time glycaemia monitoring

E.E. Petryaykina, I.G. Rybkina, E.A. Pronina, V.L. Fomina, I.V. Garyaeva & T.D. Mikchaylova
Moscow Health Care Department, Morozovskaya Children City Clinical Hospital, Endocrinology, Moscow, Russian Federation

Surgical interventions in children with T1D require strict glycaemia control in order to avoid manifestation of DKA or hypoglycemia. It is not always possible to reach optimal glycaemia control beforehand, as the surgical intervention may be urgent. We may secure normal metabolism of the patient and reach target glycaemia level injecting microdoses of insulin with an insulin pump and controlling the outcome with a continuous glucose monitoring system during the surgical intervention.

We carry out the research in order to estimate importance of insulin microdosation and continuous glucose monitoring system use in real time during surgical interventions in children with T1D.

Data were analyzed for 13 children with T1D, medium age of 11 ± 2.7 years, medium duration of the disease 4.2 ± 1.9 years. All of them underwent surgical treatment under general narcosis. Surgery lasted for 1.5–3 hours. During this time, insulin was injected using pumps and glycaemia was controlled via continuous system. Characteristics of acid-base balance of blood were measured before and after the surgery, together with glycaemia and ketonemia levels.

Basal insulin level was adjusted based on pre-surgical glycaemia. Temporary basal level decrease was given in percents. During the surgery time, basal insulin injection rate was 50% lower than normal basal level. Pre-surgical glycaemia lay in the interval of 9.4 ± 2.3 mmol/l, acid-base balance characteristic showed normal values. There were no significant differences between laboratory data estimated during the surgery and after it. Normal basal insulin injection rate was given after the postanesthetic recovery. In 10% of cases a correcting bolus was needed: glycaemia of 10.7 ± 0.9 mmol/l.
Insulin pumps and continuous real-time glucose monitoring systems provide stronger confidence during surgical treatment for T1Dchildren. Keeping glycaemia during the surgery within its target levels decrease probability of T1D complications.

P/245/WED

The importance of using insulin dosage devices in young children with newly-manifested T1D in Moscow region

E. Petryaykina, I.G. Rybkina, E.A. Pronina, V.L. Fomina, I.V. Garyaeva & T.D. Mikchaylova

Moscow Health Care Department, Morozovskaya Children City Clinical Hospital, Pediatric Endocrinology, Moscow, Russian Federation

The incidence of type one diabetes mellitus (T1D) is rising among young children in Moscow Region. Portable insulin dosage devices provide optimal insulin injection rate; they are proven to be helpful in reaching target glycaemia levels. It is never late to start pump therapy, but early switch to pumps is associated with better carbohydrate control.
Our study aimed to compare T1D compensation level in patients treated with CSII and those treated with MDI.
A total of 147 children with T1D were studies in the study. The first group received CSII therapy and consisted of 83 children (medium age 6.4 ± 2.5 years, time since diagnosis 1.7 ± 1.3 years). The second group was on MDI therapy. It consisted of 64 children (7.8 ± 1.2 years, time since diagnosis 1.2 ± 1.1 years). Characteristics included in the study were HbA1C and fatty hepatosis signs as seen by ultra-sound screening, while nephropathy was assessed by albuminuria test results. We used Student T-criterion to treat the data.
Both groups demonstrated decrease in HbA1C. It shows uniformity of groups and high motivation of the patients' families they use to reach target carbohydrate metabolism characteristics. But HbA1C decrease rate differed between groups. The decrease became significant after 3 months of treatment in the CSII therapy group and after 6 months of treatment in MDI groups in the MDI treatment group and hold for the whole study time. After one year of treatment, HbA1C was 7.2 ± 0.09% in the CSII treatment group and 8.0 ± 0.4% ($P < 0.05$ for all cases) in the other. Ultrasound signs of fatty hepatosis were diagnosed in 5.2% of patients in the first group and in 9.2% of patients in the second. All the children in both groups showed neither signs of albuminuria, nor of severe hypoglycemia.
CSII therapy provides better control of the T1D development when started earlier after diagnosis of the disease and decreases the risk of T1D complications, when compared to MDI therapy.

P/246/WED

Telemedicine delivered interpretation and improvement using a standardised protocol, for continuous glucose monitoring with multiple daily injections or pump therapy

L. McKenzie, A. Tasker & S. Greene

University of Dundee, Child Health, Dundee, United Kingdom

Aims: Continuous glucose monitoring (CGM) is used to monitor the outcome of therapy and to direct changes to improve glycaemia in Type 1 diabetes (T1D). In an RCT comparing multiple daily injection therapy (MDI) with pump therapy (CSII) we assessed the impact on glucose variability of analysing patient collected CGM data via telemedicine using a standardised protocol to instruct changes in therapy.
Methods: During 6 months of MDI and CSII subjects (n = 10; age 9–15 years.) performed real time CGM (7 days) 8 weeks after starting therapy and blind CGM (3 days) at end of each randomisation period. CGM data was downloaded to a home PC and stored in a data base (Carelink®). The subject was phoned on day 3/4 and the results reviewed and recommendations made to change therapy according to a standardised protocol. The subject and the health professional viewed the data simultaneously on their own PCs discussing the results by phone. The consultation required the sharing of password/username and each session lasted ~30 minutes. Data from the sensor was extracted and variability compared between MDI with CSII and pre- with post telemedicine analysis by ANOVA.
Results: Analysis of the blood glucose variability (daily mean and SD, mmol/l) showed a significant improvement in switching from MDI to pump therapy ($P < 0.05$) and before and after the telemedicine protocol determined instructions to change management ($P < 0.05$); this was greater on CSII and the improvement was maintained on CSII but not on MDI.
Discussion: In this RCT, comparing MDI with CSII in young people with T1D, the use of a protocol determined instruction algorithm via a simple telemedicine system appears to improve the outcome of real time CGM especially for CSII. This effect is sustained to greater degree on pump therapy, despite the short time that the system is used. Further studies are required to assess the impact of a structured telemedicine approach in more aggressive use of real time CGM.

P/247/WED

Simultaneous vs delayed initiation of Real -Time Continuous Glucose Monitoring (RT-CGM) in children and adolescents with established type 1 diabetes starting insulin pump therapy: a pilot study

M.L. Lawson[1,2], P. Olivier[3], C. Huot[3], C. Richardson[1], M. Nakhla[1] & J. Romain[3]

[1]*Children's Hospial of Eastern Ontario, Pediatrics, Ottawa, Canada,* [2]*University of Ottawa, Pediatrics, Ottawa, Canada,* [3]*CHU Sainte-Justine, Pediatrics, Montreal, Canada*

Background: Uncertainty remains about effectiveness of RT-CGM in children and adolescents with type 1 diabetes (T1D). Success with RT-CGM is directly related to adherence (i.e. willingness to wear and use RT-CGM) which may be related to readiness to make the behaviour changes required for effective use. We hypothesize that readiness for behaviour change is higher at pump initiation than in established pump users and that this will predict future RT-CGM success.
Objective: To establish acceptability and feasibility for a trial randomizing children and adolescents who are starting pump therapy to simultaneous versus delayed RT-CGM initiation and

to obtain a preliminary estimate of the difference in RT-CGM adherence.
Methods: This pilot RCT study was conducted at two pediatric centers. Participants were randomized to start RT-CGM 1–2 weeks before the pump start or to standard pump therapy for 4 months. RT-CGM adherence was tracked weekly via web-based download (CareLink).
Results: Twenty out of forty one eligible children agreed to participate. 5/20 withdrew (one due to difficulties with RT-CGM; four from control group including two post randomization to start simultaneous RT-CGM). 15 subjects completed the study (7M; age 11.8 ± 4.0 years; T1D duration 2.7 ± 2.7 years; mean A1C 8.2 ± 0.8%). Amongst the eight subjects in the simultaneous group, RT-CGM adherence was > 60% for the first 14 weeks, with highest adherence over the first 10 weeks (73.7–89.6%), then decreasing to a nadir of 36.1% at the 18thweek. The seven control group subjects were offered RT-CGM at 4 months including provision of RT-CGM supplies: one declined, five used it < 2 weeks, and one used RT-CGM > 80% of the time for 4 months.
Conclusions: An RCT of simultaneous versus delayed initiation of RT-CGM in children and adolescents with established T1D starting pump therapy is warranted and feasible. Lessons learned from the pilot study have been used to inform development of the full-scale multicentre RCT now underway.

P/248/WED

Glycemic variability in pediatric patients with DM type 1 in Ukraine: a comparison between continuous subcutaneous insulin injection and multiply daily insulin injections

Y. Globa, N. Zelinska & L. Nifontova
[1]*Pediatric Endocrinology Department, Ukrainian Center of Endocrine Surgery, Kyiv, Ukraine*

Objectives: Although HbA1c is the most generally accepted marker for the risk of long-term complications, the adverse effect of glycemic variability is increasingly becoming recognized.
Methods: A total of 41 children 2–17 years old with DM 1 were divided into two groups: treated with MDII (21 pts 8.15 ± 1.96 years old, duration of DM – 2.53 ± 1.23 years) or CSII (20 pts 11.1 ± 1.83 years old, duration of DM – 4,0 ± 1,39 years). In all of them was studied glycemic variability by CGMS Medtronic: baseline and after 18 ± 5.8 months of therapy by MDII; before start of CSII and after 18 ± 5.4 months on this therapy. The baseline HbA1c at group MDII was 8.42 ± 0.86%, vs. 10.04 ± 0.87% at group CSII (P < 0.05). The markers of glycemic variability were: BG (average, minimal, maximum, fasting, post breakfast), number of excursions, duration above high, below low, within limit (3.9–10 mmol/l), HbA1c.
Results: At 18 months CSII group had lower glycemic variability, despite the increase of HbA1c.

Variables	Baseline MDI	After	Before CSII	After
BG,mmol/l: average	9,6±1,2	10,6±1,2	10,8±1,1	9,4±0,9 [1,2]
max	20,2±1,3	19,9±1,5	20,3±1,4	18,4±1,5 [1]
fasting	9,8±1,3	9,5±1,3	11,3±1,3	8,9±1,4 [1]
post meal	11,6±1,5	11,9±1,2	12,5±1,4	10,1±1,5 [1, 2]
Number of excursions	23,9±7,1	18,1±4,5	20,8±4,5	15,3±3,7 [1]
high	18,0±5,1	13,9±2,9	15,3±2,8	11,2±3,1 [1]
low	5,9±2,9	4,2±2,2	5,5±2,6	4,1±1,2
Duration (%) above high	45,4±8,1	52,8±9,8	52,9±11,1	38,4±9,1 [1, 2]
within limits	50,1±7,2	39,8±6,8 [1]	42,4±9,1	56,5±8,9 [1, 2]

[Glycemic variability in pediatric patients]

After 18 months HbA1c increased in both groups: to 9.35% in group MDII (from the previous level on 11.04%) and to 10.27% in group CSII (on 2.39%).
Conclusions: Glycemic variability is better controlled on CSII treatment. The children on MDII kept unfavorable glycemic variability with decreasing of normoglycaemia plateau, higher growth rates HbA1c, compared with children on CSII. Indexes of low BG were similar in both groups.

P/249/WED

To evaluate and compare the outcome of pregnancies in women with type 1 diabetes treated with continuous subcutaneous insulin pump or multiple insulin injections

B. Saboo
Dia Care - A Complete Diabetes Care Center, Diabetes, Ahmedabad, India

The study was aimed to compare the outcome of pregnancies in women with type 1 diabetes treated with continuous subcutaneous insulin infusion pump (CSII) or multiple insulin injections (MDI). Total 14 patients were treated with insulin pump and 20 patients were treated with multiple injections; were mainly investigated for HbA1c, incidence of hypoglycemia, fetal outcome, rates of pregnancy induced hypertension and cesarean section. HbA1c with insulin pump was significantly better from that obtained with multiple injections. Hypoglycemic events were significantly less in CSII group as compared to MDI group. Moreover, severe hypoglycemia was not seen in CSII group, whereas there were numerous episodes of severe hypoglycemia in MDI group, few of them required hospitalization. Rate of early or mid pregnancy abortion was 10% treated with multiple insulin injections, while no abortion was seen in CSII group. Fetal prognosis was also better in pump treated patients, macrosomia was seen in 4 new borns in pump group whereas 12 in MDI group. The occurrence of pregnancy induced hypertension was similar in both groups. The rate of cesarean section was not influenced by therapeutic device, similar in both groups.

P/250/WED

Parental diabetes knowledge: does CSII education provide superior knowledge?

P. Gallagher, V. McDarby, N. McDowell, A. Flinn & D. Cody
Our Lady's Children's Hospital Crumlin, Diabetes and Endocrinology, Dublin, Ireland

Objectives: We hypothesised that parents of children on insulin pump therapy would have a better range of knowledge on their child's diabetes management due to the rigorous education provided pre CSII initiation. To assess parental knowledge we used an adapted version of the validated ADKnowl tool suitable for type 1 diabetes. The 18 item-sets (80 true/false/don't know items) assess knowledge of; diabetes treatment, insulin administration, sick day rules, hypoglycaemia, effects of exercise, diet, complications and glycaemic control.
Methods: The ADKnowl questionnaire was completed by parents of children aged 0–18 years with type 1 diabetes during attendance at our diabetes clinic between February and April 2011. Families remained anonymous. Ethics approval was granted. Results were analysed using SPSS.
Results: A total of 194 questionnaires were analysed with a 97% response rate. This included 54 patients on pump therapy. CSII patients had a mean HbA1c of 7.8% with non-CSII patients 8.5% (P < 0.001). No significant difference was detected between; age, duration of diabetes and age at diagnosis for the two groups. Significant differences (P < 0.05) were elicited in 20 items

between pump (n = 54) and non-pump (n = 140) parents. CSII parents provided more correct responses in each of these items. Better knowledge was evident in the CSII group in the areas of; insulin administration (total 88% correct response rate (CRR) vs. 78%), hypoglycaemia treatment (79% CRR vs. 68%), exercise management (86% CRR vs. 68%) and diet knowledge (80% CRR vs. 69%). The pump groups ''highest HbA1c they would be satisfied with'' was significantly lower ($P < 0.05$) at 7.81% vs. 8.21%.

Conclusion: Our sub-group analysis comparing CSII vs. non-CSII responses has shown significant superior knowledge in some categories in our pump population. This data will be used by our multidisciplinary team as we continue to modify and improve the diabetes education we provide to ensure optimum diabetes care for all our patients.

P/251/WED

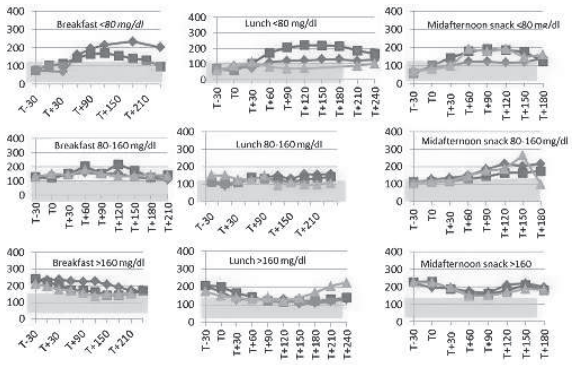
Evaluation of three bolus calculators in children with type 1 diabetes using insulin pump therapy

A. Scaramuzza, L. De Angelis, A. Bosetti, A. Gazzarri, F. Platerote, F. Redaelli, M. Macedoni, S. Mazzantini, O. Marchi, D. Maio, A. De Palma, F. Peio & G.V. Zuccotti
University of Milano – Luigi Sacco Hospital, Pediatrics, Milano, Italy

Objectives: We compared the efficacy of three bolus calculators (BC) (Animas 2020, AccuChek Combo, Paradigm Veo) to safely reduce postprandial hyperglycemia in children with type 1 diabetes (T1D) using insulin pump therapy (CSII).

Methods: We enrolled 22 patients, aged 9–22 years (mean 16.2 ± 4.9 years) with T1D from 1 to 18 years (9.1 ± 4.1 years), BMI 21.9 ± 4.5 kg/m2, using CSII for more than 6 months (insulin requirement 0.86 ± 0.27 U/kg/day, HbA1c 8.3 ± 0.9%). For each patient we studied on three occasions (order of BC used randomly assigned) three different meals (breakfast, lunch and midafternoon snack); their composition was exactly the same in terms of quality and quantity on the 3 days. Insulin bolus, was injected 15 minutes prior meal. Patients checked glycaemia 30 minutes before meal and every 30 minutes for the following 4 hours.

Results: Data is shown in the figure. The performance of the 3 BC was similar and did not show any statistical difference among them ($P = 0.278$ by ANOVA). In case of preprandial hyper or hypoglycemia, Medtronic BC showed the best performance on average when compared with both Animas and Roche bolus calculators ($P = 0.003$ for hypo and $P = 0.041$ for hyper, respectively).



[Glycaemic values (mg/dl) after using 3 BC]

Conclusion: BC seems a good feature to improve CSII performance in children with T1D, without difference among the three different BC tested. However, when in hyperglycemia, it is wise to separate the correction bolus from the meal bolus (to be injected 30 minutes prior the meal, and 15–20 minutes prior the meal bolus).

P/252/WED

Good glucose sensor accuracy and less pain with insertion on the lower back

P. Adolfsson[1], H. Örnhagen[2], K. Cooper[3], R. Gautham[3] & J. Jendle[4,5]
[1]*Department of Pediatrics, Göteborg Pediatric Growth Research Centre, Institute of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden,* [2]*Sportdykarförbundet, Idrottshuset, Farsta, Sweden,* [3]*Medtronic Diabetes, Northridge, United States,* [4]*Faculty of Health and Medicine, Örebro University Hospital, Örebro, Sweden,* [5]*Endocrine and Diabetes Center, Karlstad Hospital, Karlstad, Sweden*

Objective: In children, pain and a limited insertion area can be a hindrance for continuous glucose monitoring (CGM). We evaluated pain and accuracy when ENLITE^{TM} sensors were placed in two different locations: abdomen and the back.

Methods: A total of 48 ENLITE sensors were used in one healthy individual. On day one, 24 ENLITE sensors were inserted in a randomized procedure on the left side of the body, 12 on the abdomen and 12 on the lower back. The procedure was repeated on day 2 with equal number of sensors placed on the right side of the body. Pain was registered using a VAS scale (1–10). Plasma glucose was measured with HemoCue Glucose 201 in parallel to the interstitial glucose values generated by the ENLITE sensor. Comparison was made between paired glucose values.

Results: Insertion of the sensors on the back was regarded less painful than insertion on the abdomen, light pain (mean VAS 1) on the lower back and moderate pain (mean VAS 3) on the lower quadrant of the abdomen. 43/48 (90%) sensors worked, generating 310 (abdomen) and 295 (back) values for comparison. Mean Absolute Relative Difference (MARD) was 10.1% (abdomen) and 10.5% (back), ns ($P > 0.05$). Analysed with the Continuous Glucose Error Grid Analysis (CG-EGA), 100% of the sensor values was found in the A + B (clinical accurate) region.

Conclusion: Insertion of ENLITE sensors on the back was associated with less pain than placement on the abdomen. The accuracy was good and no significant difference was found when placement on abdomen and the back was compared. We conclude that sensors could be inserted on the back as an alternative to the abdomen. In a pediatric population, alternative injection sites like this are important, since the total area of possible injection sites are limited due to size and there is a minimum recommended injection distance for placement of CGM and insulin pump. Placement on the back might also be beneficial in certain cases or activities.

P/253/WED

Which type of dual-wave insulin bolus optimizes postprandial glycemia after different meals in type 1 diabetic adolescents on continuous subcutaneous insulin infusion?

A. Galli-Tsinopoulou, I. Kyrgios, E. Kotanidou & E. Efstratiou
4th Department of Pediatrics, Medical School, Aristotle University of Thessaloniki, Papageorgiou General Hospital, Thessaloniki, Greece

The aim of this study was to evaluate the impact of different types of dual-wave insulin boluses (DWb) on postprandial glycemic profile (PPG) after three given meals, in adolescents with type 1 diabetes mellitus (DM1) on continuous subcutaneous insulin infusion (CSII).

	HFC			HFP-LC			HFP-VLC		
Type of bolus (% ratio)	50/50	55/45	60/40	50/50	45/55	40/60	15/85	10/90	SWb
AVER±SD (mg/dl)	102.±19.3	100.9±18.2	102.9± 19.4	90.2±22.7§	99.6±12.8	98.7± 20.2	106.6±22.2**	115.4±25.5ς	116.7±23.3
AUC±SD (mg/dl.h)	612.3±116.2	605.2±109.6	616.5±116.3	536.7±135.8§	592.9±76.3	587.8±120.8	634.6±32.8**	688.0±152.3ς	695.4±139.8
Hypoglycemias (%)	1.4	1.8	4.1*	22.2§	2.0¶	11.5	2.8	0	0

[Results]

A randomized crossover study investigating the effect of different types of boluses on 6h PPG, measured by a Continuous-Glucose-Monitoring-System (Medtronic), was conducted. Seven DM1 adolescents (11.3–20 years) on CSII (duration: 2.8 ± 0.8 years) were enrolled. All participants consumed three given meals: one high-fat/high-carbohydrate meal (HFC: fat 37%, proteins 12.9%, carbohydrates 50.1%), one high-fat/high-protein/low-carbohydrate meal (HFP-LC: fat 58.8%, proteins 11.7%, carbohydrates 29.5%) and one high-fat/high-protein/very low-carbohydrate (HFP-VLC: fat 65.7%, proteins 14.2%, carbohydrates 20.1%). Meals were served three times on three study days. Each meal was covered with the same individualized insulin dose with different type of DWb each time. The meals were covered: HFC meal with DWbs over 3 hours (50/50%)/(55/45%)/(60/40%); HFP-LC meal with DWbs over 3 hours (50/50%)/(45/55%)/(40/60%); HFP-VLC meal with DWbs over 3 hours (20/80%)/(15/85%)/(10/90%) or a square-wave bolus (SWb) over 3 hours. Paired *t*-test and Mann–Whitney *U*-test were used for statistical analysis.
Both 50/50% and 55/45% DWbs are more preferable than 60/40% in HFC meals, whereas 45/55% predominates to both 50/50% and 40/60% in HFP-LC meals since they are associated to less hypoglycemias. We suggest the coverage of HFP-VLC meals with 15/85% to optimize the PPG; however 10/90% could be used in younger children due to lack of hypoglycemias.

P/254/WED
Efficiency and safety of CSII at onset of diabetes in children

J. Amsellem-Jager[1], C. Hasselmann[2], E. Bonnemaison-Gilbert[2], E. Perrodeau[3], N. Faure[2], I. Mercat[2] & A. Chantepie[2]
[1]*CHRU Tours, Gatien de Clocheville Hospital, Pediatric Specialities Unit, Tours, France,* [2]*CHRU Tours, Gatien de Clocheville Hospital, Tours, France,* [3]*CIC, CHRU Tours, Tours, France*

Background: Continuous subcutaneous insulin infusion (CSII) has been used in diabetic children for many years. Its use at onset of type I diabetes (T1D) has seldom been studied.
Objective and hypotheses: The goal of this study was to compare CSII started at onset of T1D in children to multiple daily injections (MDI), in regards of metabolic control and safety.
Methods: A total of 41 children treated by CSII at onset of diabetes (January 2005–July 2009) were paired with 41 newly diagnosed T1D children treated by MDI. They were paired by age and gender. Data such as HbA1c, BMI, insulin requirement, severe hypoglycaemia and hospitalization due to diabetic ketoacidosis (DKA), were recorded retrospectively over a period of 18 months.
Results: The proportion of children with an HbA1c constantly remaining below the threshold of 7.5% during the entire study was significantly higher in the CSII group (43.3% vs. 8.7%). Insulin doses were lower in the CSII group after a year of treatment (0.6 vs. 0.71 IU/kg/d). No difference was found regarding BMI, severe hypoglycemia and hospitalization.
Conclusions: Our study suggests that CSII started at onset of T1D allows a better metabolic control than MDI, with lower insulin doses. CSII is as safe as MDI regarding severe hypoglycaemia and DKA. Further prospective studies are currently led in our team to compare the quality of life of patients with CSII and with MDI.

P/255/WED
Performance evaluation of a novel blood glucose monitoring system

T. Bailey[1], J.F. Wallace[2], C. Greene[2], S. Pardo[2], J.L. Parkes[2] & H.C. Schachner[2]
[1]*AMCR Institute, Escondido, CA, United States,* [2]*Bayer HealthCare LLC, Diabetes Care, Tarrytown, NY, United States*

Objective: Assess performance of an investigational blood glucose monitoring system (BGMS) that uses a new FAD-GDH enzyme test strip with a proprietary mediator and can communicate with an insulin pump.
Methods: A total of 93 subjects aged 18–74 years with type 1 (75%) or type 2 (25%) diabetes participated. 88% and 45% of subjects were users of insulin or an insulin pump, respectively. HCPs and subjects tested fingerstick samples on the BGMS and a YSI. Results were evaluated based on ISO 15197:2003 guidelines and proposed more stringent accuracy criteria. A questionnaire rated usability of features based on a scale of 0 to 5.
Results: 100% of subject results met current ISO 15197:2003 and ≥ 99.3% met proposed more stringent accuracy criteria (Table 1). Similar results were obtained from HCP testing. Based on questionnaire results, 99% of subjects rated their overall satisfaction as good to excellent; similar ratings were reported for meter features such as ease of using the AutoLog feature (100%), ability to adjust target ranges (96%), lighted test strip port (96%), and ease of accessing (100%) and usefulness (98%) of the TRENDS menu. There were no serious, device-related, or non-anticipated adverse events.

Glucose concentration	Data comparison	Number (%) of results within the ISO 15197:2003 minimum acceptable performance criteria and more stringent criteria			
<75 mg/dL		**±10 mg/dL**	**±12.5 mg/dL**	**±15 mg/dL**	**±20 mg/dL**
	Subject vs YSI (n = 14)	14 (100%)	14 (100%)	14 (100%)*	14 (100%)
≥75 mg/dL		**±10%**	**±12.5%**	**±15%**	**±20%**
	Subject vs YSI (n = 166)	158 (95.2%)	163 (98.2%)	165 (99.4%)	166 (100%)*
<100 mg/dL		**±10 mg/dL**	**±12.5 mg/dL**	**±15 mg/dL**	**±20 mg/dL**
	Subject vs YSI (n = 36)	36 (100%)	36 (100%)	36 (100%)†	36 (100%)
≥100 mg/dL		**±10%**	**±12.5%**	**±15%**	**±20%**
	Subject vs YSI (n = 144)	136 (94.4%)	141 (97.9%)	143 (99.3%)†	144 (100%)

*Current ISO 15197 minimum acceptable performance criterion. †Proposed more stringent criterion (±15 mg/dL or ±15% for samples with glucose concentrations <100 and ≥100 mg/dL, respectively).

[Table 1]

Conclusion: The new BGMS met current and proposed tighter accuracy guidelines in the hands of intended users. Subjects found the meter features useful and easy to use. Accurate and easy to use SMBG technology may be important considerations for patients with diabetes who use insulin.

P/256/WED
Performance of the Enlite subcutaneous glucose sensor in pediatric subjects

F.R. Kaufman[1], J. Shin[1], J.A. Atchison[2], B. Nathan[3], G. Prakasam[4], D. Shulman[5] & J.B. Welsh[1]
[1]*Medtronic Inc., Northridge, United States,* [2]*University of Alabama, Birmingham, United States,* [3]*University of Minnesota, Minneapolis, United States,* [4]*Sutter Medical Center, Sacramento, United States,* [5]*University of South Florida, Tampa, United States*

Objectives: The new Enlite subcutaneous glucose sensor (Medtronic MiniMed, Inc.) is smaller and shorter than its

predecessor, the Sof-Sensor. We examined the Enlite sensor's performance in children.
Methods: Enlite was studied in 83 pediatric subjects (53% male, mean age 12.5 years [range, 7–17], mean A1C 8.2% [range, 5.5–11.5%]) with type 1 diabetes at four investigational centers in the US. Each subject wore an Enlite sensor in the abdomen or buttock; the sensor was attached to a MiniLink transmitter and worn for two 7-day periods. The Guardian REAL-time display device (Medtronic) was used to collect data. Self-monitored blood glucose (SMBG) values were collected four times/day for accuracy determination. Safety and accuracy were analyzed for all 83 subjects and all 187 sensor insertion events.
Results: Eighty subjects completed the study. Device survival based on sensor functionality showed that 117 of 179 successfully-calibrated sensors (65.4%) operated to the end of day 6 (mean functional life, 134.1 hours; median functional life, 164 hours). The Enlite sensor exceeded the prespecified accuracy criteria to the end of day 6. The mean agreement rate (± 20% of SMBG) was 72% (95% CI, 70–74%). Data collected from Enlite sensors worn to the end of day 6 showed that 95.6% of paired SMBG-sensor values were within the A + B zones of the Clarke error grid. The overall mean absolute relative difference (ARD) was 16.3% (median ARD: 11.9%). By comparison, historical mean and median ARD values for the Sof-Sensor were 19.7% and 15.6%. No serious or unanticipated adverse events were reported. Transient redness in the area of the adhesive patch was the most frequently-reported adverse event (51 events, 37 subjects, 187 sensor insertions).
Conclusions: In pediatric subjects, the Enlite sensor was safe and provided accurate results for 6 days (144 hours) when worn on either the abdomen or buttock. The Enlite sensor improves upon the accuracy and durability of the Sof-Sensor.

P/257/WED

Are there benefits in using patch vs. established pump: results of a 12-week user evaluation with the mylife OmniPod® in children, adolescents and adults with type 1 diabetes?

T. Biester[1], N. Datz[1], K. Remus[1], S. Bläsig[1], K. Lange[2], R. Hartmann[1], O. Kordonouri[1] & T. Danne[1]
[1]*Children's Hospital auf der Bult, Diabetes Centre for Children and Adolescents, Hannover, Germany,* [2]*Department for Psychology, Hannover Medical School, Hannover, Germany*

Objective: In type 1 diabetes (T1D), continuous subcutaneous insulin infusion (CSII) is rapidly gaining acceptance as means of intensive insulin therapy. The Omnipod® patch-pump is a tubing-free device consisting of a handheld and a pump that communicate wirelessly. Acceptance, treatment satisfaction and HbA1c were investigated in experienced and well-controlled users of CSII that switched to Omnipod® for 12 weeks.
Methods: A total of 37 patients with T1D (54.1% female; 14 children,10 adolescents,13 adults) entered the study, 27 completed it (discontinuation rate 24.3%). Diabetes Treatment Satisfaction Questionnaires (Bradley score 0 = low, 36 = maximum) with additional pump-related items on a Likert scale (0 = not satisfied to 6 = very satisfied) were answered and compared to a group of 30 matched patients (60% female; 6 children, 14 adolescents, 10 adults). HbA1c at baseline and 12 weeks were evaluated. Mean patient age was 18.9 ± 11.1 years, T1D duration 12.2 ± 10.7 years, CSII duration 4.5 ± 2.9 years, baseline HbA1c 7.8 ± 1.2%.
Results: Treatment satisfaction decreased during Omnipod® use (27.9 ± 4.6 vs. 24.2 ± 8.0; P = 0.040). Better scores were seen for Omnipod® in handling when taking a shower (4 ± 1.5 vs. 5.2 ± 1.2; P = 0.005) and tubing (3.9 ± 1.6 vs. 5 ± 1.1; P = 0.013). HbA1c increased after 12 weeks (8.2 ± 1.4%; P = 0.018). One severe hypoglycemia occurred.1/3 of the evaluated patients wanted to keep the Omnipod®, 1/3 did not and 1/3 was undecided. No significant differences in treatment satisfaction were found between study and control group (28.8 ± 4.4 vs. 29.9 ± 3.6; P = 0.838).
Conclusions: Well-controlled patients on CSII are very satisfied with their treatment. In these patients, patch pump received significant better scores in infusion set handling and in taking a shower than conventional pump. However, a significant increase in the overall HbA1c occurred during Omnipod® use. Future patch-pump studies should also focus on naïve CSII patients.

P/258/WED

Does the fat protein meal increase postprandial glucose level in type 1 diabetic patients on insulin pump - the conclusion of a randomized study

E. Pankowska[1], M. Blazik[1] & L. Groele[2]
[1]*Institute of Mother and Child, Pediatrics, Warsaw, Poland,* [2]*Medical University of Warsaw, Pediatrics, Warsaw, Poland*

Background: Our study examines the hypothesis that in addition to sugar starch-type diet, a fat protein meal elevates postprandial glycemia as well, and it should be included in calculated prandial insulin dose accordingly.
The aim: The impact of the inclusion of fat-protein nutrients in the general algorithm for mealtime insulin dose calculator on 6 hour postprandial glycemia.
Material and method: Of 26 screened Type 1 diabetic patients on insulin pump, were randomly assigned to an experimental Group A and to a control Group B. Group A received dual wave insulin boluses for their pizza dinner, consisting of 45 g/180 kcal of carbohydrates and 400 kcal from fat- protein where the insulin dose was calculated using the algorithm: nCarbUnits × IR + nFat-ProteinUnits x IR/6 hours (standard + extended insulin boluses), for the control Group B on the algorithm: nCarbUnit × IR. The glucose, C-peptide, and glucagon concentrations were evaluated before the meal and at 30, 60, 120, 240, and 360 minutes postprandial.
The results: There were no statistically significant differences involving patients' metabolic control, C-peptide, glucagon secretion, the duration of diabetes, between Group A and B. In Group A the significant glucose increment (Δ-G) occurred at 120–360 minutes, with its maximum at 240 minutes: 60.2 versus 3.0 mg/dl, P = 0.04, respectively. There were no significant differences in glucagon and C-peptide concentrations postprandial.
Conclusions: The mixed meal, effectively elevates postprandial glycemia after 4–6 hours. Dual wave insulin bolus, in which insulin is calculated for both the carbohydrates and fat proteins, is effective in controlling postprandial glycemia.

P/259/WED

17-years old girl with autoimmune polyendocrine syndrom type 2 - how to obtain the best metabolic control of diabetes

D. Witkowski[1], E. Piontek[2], M. Szalecki[2] & R. Janas[3]
[1]*Department of Endocrinology and Diabetology, The Children's Memorial Health Institute, The Institute of Mother and Child, Outdoor Department of Diabetology, Warsaw, Poland,* [2]*Department of Endocrinology and Diabetology, The Children's Memorial Health Institute, Warsaw, Poland,* [3]*Department of Radioimmunology, The Children's Memorial Health Institute, Warsaw, Poland*

The association between Addison's disease (AD) and type 1 diabetes (T1DM) is well recognised. The prevalence of T1DM in

patients with autoimmune polyendocrine syndrome type 2 (APS-2) ranges above 50%.
We report the case of 17 years old girl with AD recognised at age of 11 and AITD who developed T1DM after 6 years. The immunological status has been observed for several years before clinical diabetes onset.
It is well known that glucocorticoid replacement therapy in patients with AD and T1DM may lead to quite often and significant changes in insulin requirement and insulin sensitivity. That is why the multiple pen injection regimen was replaced by CSII after one month since the diabetes onset. There are several options of ''smart'' pumps to participate in improving and maintain good metabolic control in such patients.
Conclusion: In the immunological course of diabetes, there was no increase of autoantibodies against β cell, in particular, anti-IA2 just before clinical manifestation of diabetes
1. The patient with APS require observation for clinical signs of diabetes and glucose monitoring by the determination of HbA1c at least once/twice a year.
2. Type 1 diabetes treatment commencement using personal insulin pump allows to obtain good metabolic control of diabetes in spite of insulin requirements changes consequently steroid replacement therapy.
3. Insulin pump treatment will improve the quality of life in patient with APS type 2.

Date	4.11.2004	6.03.2009	2.12.2010
HbA1c	5.00%	5.40%	9.30%
Anty GAD /U/ml/N: < 0.9	0.56	2.11	1.18
Anty IA2 /U/mL/N: < 0.75	< 0.2	< 0.7	< 0.7
Anty TG-AB/U/mL/N: 30–70	75.9	183	1.48
Anty TPO-AB/U/mL/N: 30–50	277.9	1660	139.17
TSH-R-AB/U/L/N: < 9.0			< 5.0
p-ANA	1:320 (+), 1:640 (+)		
anty-21-H/N: < 1.0		5.33	

[The immunological data]

P/260/WED

The impact of continuous subcutaneous insulin infusion on clinical parameters and complication rates in young people with type 1 diabetes between 2006 and 2010

K. Heels[1], Y. H. Cho[1], A. Chan[1], G. Ambler[1,2], M. Craig[1,2,3] & K. Donaghue[1,2]
[1]*Institute of Endocrinology and Diabetes Childrens Hospital Westmead Australia, Sydney, Australia,* [2]*University of Sydney, Sydney, Australia,* [3]*University of New South Wales, Sydney, Australia*

Objectives: To examine the impact of Continuous Subcutaneous Insulin Infusion (CSII) on clinical parameters and microvascular complications in young people with type 1 diabetes (T1D).
Methods: Complications screening between 2006 and 2010 (n = 1156, age < 20 years), using 7-field fundal photography (retinopathy ≥21 Airlie-House classification), urine albumin:creatinine ratio(ACR) or albumin excretion rate (AER) and peripheral nerve function by thermal/vibration threshold (foot). Insulin therapy was grouped as CSII, multiple daily injections (MDI) or <3injections/day. Baseline groups were compared using Kruskal–Wallis/C^2 tests. Longitudinal analysis, including repeated measures over time, was performed using generalised estimating equations.
Results: At baseline, 20% used CSII, 68% MDI and 12% <3inj/day. CSII children were younger (14.2 years) vs. MDI or <3inj/day (15.6 and 14.9 years) (P < 0.01). Diabetes duration did not differ between groups (6.6 vs. 7.0 vs. 6.6 years) (P = 0.58). Those on CSII had lower total daily dose insulin (TDD)(D = –0.24 U/kg/day; P < 0.01), HbA1c (–0.4%; P < 0.01) and DBP SDS (–0.18; P < 0.01) than those on MDI, higher cholesterol (0.13 mmol/l; P < 0.01) but no significant difference in microvascular complications, severe hypoglycaemic episodes, BMI or SBP SDS in treatment groups during follow up. At the last visit, 26% used CSII with average CSII duration 2.6 years [1.4–3.8].
Conclusions: In the past 5 years, the majority of adolescents screened in our centre were managed by intensive insulin therapy. CSII helped achieve lower HbA1c on a lower TDD than those on MDI, with a trend to a lower risk of overall microvascular complications.

P/261/WED

Insulin pump therapy; what is the effect on metabolic control in different age groups?

D. Goksen, G. Demir, O. Korkmaz & S. Darcan
Ege University Faculty of Medicine, Pediatric Endocrinology, Izmir, Turkey

Aim: To determine the impact o f insulin pump therapy on key parameters of diabetes including metabolic control and nutrition.
Materials and methods: Age, duration of diabetes, metabolic control, nutrition indices and anthropometric data of 59 CSII patients (disease duration >3 years, pump duration >1 year) were collected prospectively before and during pump treatment. The total patient population was divided into four groups based on age at the start of CSII therapy.
Results: 59 children ranging in age from 2.4 to 22 8 years received CSII for an average of 3 years. The total patient population was divided into four groups based on their age at start of CSII therapy: group A; 1–5 years, group B, 5–10 years, group C, 10–15 years, group D, >15 years. Mean HbA1c levels were 8.9% in group A; 7.1% in group B; 7.4% in group C; 7.8% in group D prior to start of CSII. There was a significant and consistent reduction in mean HbA1c levels after12 months of CSII in the first two age groups (to 7.4% and 6.5%) and a non-significant reduction in group C and D4 (to 7.0% and 7.5%).This non-significant reduction was maintained at the end of 2 years in all age groups. Improved diabetes control was achieved with CSII without increasing daily basal insulin doses and serum lipid levels. Only a significant increase in BMI was found in group C from –0.2 to 0.46 kg/m^2.
Conclusions: CSII is an effective alternative to injection therapy for the first year of therapy in every age group. Although a non-significant reduction in metabolic control continues in the second year on metabolic control in the pre-schoolers and pre-adolescents, in the older group it is hard to maintain the same control.

P/262/WED

Patient perceptions of using OmniPod System compared with conventional insulin pumps in young adults with type 1 diabetes

Y. Lebenthal[1], L. Lazar[1,2], H. Benzaquen[1], S. Shalitin[1,2] & M. Phillip[1,2]
[1]*Schneider Children's Medical Center of Israel, National Center for Childhood Diabetes, Petach Tikva, Israel,* [2]*Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*

Objectives: To evaluate treatment satisfaction, comfort and function using the wireless OmniPod™ Insulin Management

System compared with conventional (infusion set) insulin pumps in young adults with type 1 diabetes.
Research design and methods: Twenty nine patients (age 24.0 ± 5.1 years; diabetes duration 12.1 ± 5.7 years; insulin pump duration 6.4 ± 3.1 years; HbA1c >8%) participated in a randomized, two-arm open crossover study comparing two consecutive 12-week periods of continuous subcutaneous insulin infusion (CSII): one period using the OmniPod system and the other, conventional CSII. The main outcome measures were treatment satisfaction (Diabetes Treatment Satisfaction Questionnaire), user evaluation (OmniPod System User Evaluation Questionnaire) and glycated HbA1c levels.
Results: Treatment satisfaction at baseline was high, with a mean 28.6 ± 4.6 and no significant difference between the two randomized groups. Upon completion of the study period 43% "would switch to OmniPod", 36% were "undecided" and 21% "would not switch pumps"; 76% preferred the OmniPod automated cannula insertion system and 56% reported that OmniPod fit better into their lifestyle than conventional CSII; HbA1c levels significantly decreased with both OmniPod and conventional CSII (7.93 ± 0.87% vs. 8.79 ± 0.74% and 8.19 ± 0.87% vs. 8.51 ± 0.54%, respectively, $P < 0.001$ for both groups) after completion of the first treatment arm. The decrease in HbA1c was more marked in the OmniPod group ($P = 0.044$), without additional improvement at end of study in either group.
Conclusions: The OmniPod system was well received by young adults with type 1 diabetes experienced with conventional CSII. Although the significant decrease in HbA1c in the entire cohort may be attributed to the participation in a research study, the more marked improvement of HbA1c in the patients on the OmniPod System indicates that there may be additional benefits.

P/263/WED

Security and efficacy of insulin pump vs. multiple daily injections

C. Hasselmann, E. Bonnemaison, N. Faure, I. Mercat & A. Chantepie[1]
François Rabelais' University Hospital, General Pediatrics Department, Tours, France

Objective: In our experience, a mean HbA1c below 7.5% is more likely to be obtained in children with type-1-diabetes treated with continuous subcutaneous insulin infusion (CSII) rather than multiple daily injections (MDI). Our goal was to compare the metabolic control of children treated with CSII vs. MDI.
Methods: 38 children treated with CSII and 38 children treated by MDI, have been paired on criterion of age, sex and age at diagnosis of diabetes. The following data have been recorded every 3 months, retrospectively: HbA1c (%), BMI (SDS/age), insulin requirements (UI/kg/d), number of severe hypoglycemia (event/patient/year), number of in-patient hospital stays (event/patient/year).
Results: After 3 years' follow-up, HbA1c was significantly lower in the CSII group (7.67% vs. 8.21%, $P = 0.004$). The proportion of patients with an HbA1c below 7.5% was also significantly different (47% in CSII vs. 26% in MDI, $P = 0.025$). There was no significant difference in BMI, insulin requirement, and adverse events (hypoglycemia, hospitalization).
Conclusion: This study suggests that treating type-1-diabetes with CSII in children allows a better metabolic control, even after a long time using this treatment, without increasing adverse events or stoutness, compared with MDI treatment.

P/264/WED

Observational study: continuous glucose monitoring in children under 7 years old

E. Bonnemaison[1], C. Hasselmann[1], K. Dieckmann[2], S. Perdereau[3], C. Marques[4], N. Faure[4], I. Mercat[4], F. Monceaux[3], H. Mouna[2] & C. Roze[3]
[1]*CHU Tours, Unité de Spécialités Pédiatriques, Tours, France,* [2]*Centre Hospitalier de Blois, Pédiatrie, Blois, France,* [3]*Centre Hospitalier Régional d'Orléans, Pédiatrie, Orléans, France,* [4]*François Rabelais' University Hospital, General Pediatrics Department, Tours, France*

Objectives: To evaluate the use and tolerance of long term sensor augmented pump therapy in children aged 7 or less, with type-1-diabetes.
Methods: This is a multicentric prospective study, taking place in 3 hospitals of Région Centre, France, where every child with type-1-diabetes under 7 years old, treated with an insulin pump is offered to use a continuous glucose monitoring system. The following data are recorded every 3 months: HbA1c, insulin requirement (UI/kg/d), number of severe hypoglycemia, number of in-patient hospitalization linked with diabetes, time spent in hypoglycemia, in hyperglycemia, overall duration of sensor use, skin lesions induced by the sensor, number of self glucose monitoring (SGM) performed/day, parents satisfaction. Patients who do not want to wear a sensor will be included in the control group. Since September 2010, 15 children have been included in the sensor group.
Results: Preliminary results show a mean age of 3 years and 6 months (17 months – 6 years 7 months), a mean HbA1c of 7.1% (6.2–8). Mean insulin requirement is 0.7 UI/kg/d. Patients are using the sensor 85.3% of the time. No skin infection has been recorded. Patients perform only 3 SGM/d. There has been no severe hypoglycemia, no hospital stay. The parents are satisfied but the insertion of the sensor is reported as difficult for all of them.
Conclusion: These first results show that sensor augmented pump therapy in toddlers and young children is well tolerated, even though the device insertion remains difficult for parents. There are much less SGM performed and metabolic control is very good, with a mean HbA1c is within internationally recommended target (<7.5%).

P/265/WED

'It's not for me' – patterns of glycaemia in youth who discontinue CSII

M. A. O'Connell[1,2] & F. J. Cameron[1,2]
[1]*The Royal Children's Hospital, Melbourne, Endocrinology & Diabetes, Melbourne, Australia,* [2]*Murdoch Childrens Research Institute, Melbourne, Australia*

Objectives: To compare the characteristics of youth with T1DM who discontinued (D-CSII) with those who continue on CSII (C-CSII).
Methods: Demographic & HbA_{1c} data were recorded on all youth who commenced CSII at our clinic to end of 2010. Data are reported as mean (±SEM) or median(range). Between group comparisons were made using *t*-tests, χ^2 tests and odds ratios.
Results: Data were available on 398/418 youth who commenced CSII. N = 43(10.8%; 27 female) discontinued CSII after a median of 25(2–63) mo. Low adherence to integral tasks & poor glycaemic control were the reasons for discontinuation in n = 34(79%); 17 disliked using CSII. Age & duration of T1DM at CSII start were similar in D-CSII & C-CSII groups. Pre-CSII HbA1c was however higher in the D-CSII group: 8.7% (±0.14) cf 8.3% (±0.05), $P < 0.03$. 25.6% of D-CSII youth showed no improvement in HbA1c with CSII as compared with 6.5% of C-CSII (OR 4.9 [95%CI 2.2–11.1], $P < 0.001$). HbA1c < 7.5% was

attained in 37.2% of D-CSII (cf 74.9% of C-CSII), but sustained to 1 year in only 7%. HbA1c nadir on CSII was higher in D-CSII youth:7.8% cf 7.1%, $p< 10^{-5}$. A subsequent increase of >1% from nadir was also more frequent in D-CSII (90.7% cf 46.5%; OR 11.2[95%CI 3.9–32.1], $P < 0.0001$), occurring early at a median of 12(4–36) mo. Deteriorating control (HbA1c>7.5% & increasing on 2 consecutive readings) was more frequently observed in the first year of CSII in D-CSII youth (51.2% cf 16.6%: OR 4.26[95%CI 2.2–8.2]; $p< 0.001$). Mean 6 monthly HbA1c was significantly higher in D-CSII cf C-CSII at all timepoints to 4 years (all $P < 0.001$). HbA1c at cessation of CSII was 9.6 (±0.2)%. All switched to injected insulin regimens; however HbA1c remains suboptimal at 9.3(±0.2)% 12mo post-CSII.

Conclusions: A small but significant proportion of youth fail to successfully employ CSII. Higher pre-CSII HbA1c and a failure to achieve & maintain good glycaemic control over the first year of CSII were more commonly seen in this subset of our cohort.

Poster Session II: Type 2 Diabetes in Children

P/266/FRI

The relationship between insulin resistance and body mass index in malnourished and obese children

K. Karabag & Z. Orbak
Ataturk Univ, Erzurum, Turkey

The aim of this study is to investigate the relationship between body mass index and fasting insulin and HOMA-IR in malnourished and obese children aged 3–7 years.
76 children participating in our study were defined as underweight, normal weight, overweight and obese using parameter of body mass index. 15 of the children were classified as underweight, 31 of the children were classified as normal weight, 30 of the children were classified as overweight and obese. Composite index was used to determine the socioeconomic level of children. HOMA (homeostasis model assessment) index was used for the diagnosis of insulin resistance. A cut-off HOMA level of 2.5 in children was used to identify an insulin-resistance status. Insulin resistance was found in 20% of underweight children and 26.7% of overweight and obese children whereas it wasn't found in normal weight children. In our study, some of the children with malnutrition was found to have insulin resistance, too.
As a result, the cases of acute malnutrition have the risk of insulin resistance so they should be investigated for insulin resistance like obese children. Malnutrition and obesity must be fought for more healthy life in children.

P/267/FRI

Measuring insulin secretion in youth

M. Henderson[1], J. -P. Baillargeon[2], R. Rabasa-Lhoret[3,4,5], J. -L. Chiasson[4,6] & M. Lambert[7]
[1]*McGill University, Epidemiology, Biostatistics & Occupational Health, Montreal, Canada,* [2]*Université de Sherbrooke, Department of Medicine, Sherbrooke, Canada,* [3]*Université de Montreal, Department of Nutrition, Montreal, Canada,* [4]*Centre Hospitalier de l'Université de Montreal, Diabetes Research Center, Montreal, Canada,* [5]*Institut de Recherches Cliniques de Montréal, Montreal, Canada,* [6]*Université de Montréal, Department of Medicine, Montreal, Canada,* [7]*Université de Montréal, Department of Pediatrics, Montreal, Canada*

Objective: Simple estimates of insulin secretion that are feasible for large epidemiologic studies have been proposed in adults, but have been little evaluated in youth. Our objective was to examine in children the correlation between OGTT derived and fasting based indices of insulin secretion against the acute insulin response to glucose (AIRg), a validated index of insulin secretion based on the frequently sampled intravenous glucose tolerance test (FSIVGTT).
Methods: Twenty children (mean (SD) age: 9(2) years) were studied: 9 boys and 11 girls. Their mean (SD) BMI z-score was 1.5 (0.8). All participants had normal fasting and 2-hour post-load glucose. Each child underwent an insulin modified minimal model FSIVGTT (reference method), and a 3-hour OGTT. AIRg was computed from the FSIVGTT using the MINMOD software. OGTT derived measures included the Δinsulin $_{t0–30\ minutes}$ ÷Δglucose $_{t0–30\ minutes}$, known as the insulinogenic index (IGI), and the ratio of the area under the curve (AUC) for insulin to the AUC glucose ($AUC_{0–120}$ Ins/$AUC_{0–120}$ Glc). HOMA%beta and HOMA2%beta were computed from fasting insulin and glucose. Correlations were established using Spearman's rank correlations.
Results: The IGI was highly correlated to the AIRg (r = 0.80). HOMA%beta (original formula) was modestly correlated to AIRg (r = 0.62), as was HOMA2%beta (computer-based) [r = 0.65]. $AUC_{0–120}$ Ins/$AUC_{0–120}$ Glc was poorly correlated with AIRg (r = 0.42).
Conclusions: Our results suggest that IGI derived from the OGTT is a robust estimate of first phase insulin secretion in children. HOMA2%beta and HOMA%beta represent an acceptable compromise, however, given the limited performance at lower physiologic ranges of insulin and glucose of the original HOMA method, HOMA2%beta may be preferable in youth, as it allows for the use of a broader spectrum of insulin and glucose values that are physiologic in this age group.

P/268/FRI

Serum C reactive protein, but not IL-6, is strongly associated with obesity in pre-pubescent Latino children

D. Dixon[1], H. Meng[2], R. Goldberg[3], N. Schneiderman[4] & A. Delamater[5]
[1]*Stony Brook Children's Hospital, Pediatrics, Port Jefferson Station, United States,* [2]*Stony Book University Medical Center, Preventive Medicine, Stony Brook, United States,* [3]*University of Miami School of Medicine, Medicine, Miami, United States,* [4]*University of Miami, Behavioral Medicine Research Center, Miami, United States,* [5]*University of Miami School of Medicine, Pediatrics, Miami, United States*

The recently noted increased occurrence of Type 2 Diabetes Mellitus (T2DM) in children has been linked to obesity and insulin resistance. Serum C-reactive protein (CRP) and Interleukin 6 (IL-6) have been determined as increased in adults who later developed diabetes and cardiovascular disease. We examined whether CRP and IL-6 are similarly associated with BMI/obesity and insulin resistance in school-aged Latino children. One hundred twelve (112) Latino children aged 5–10 years recruited from elementary schools, of whom 43.8% were found to be obese (BMI ≥ 95th percentile) and 51.8% had a family history of T2DM. With one exception, all had normal glucose tolerance. Assessment of insulin sensitivity was performed by the homeostasis model assessment (HOMA-IR), serum CRP levels were measured using high sensitivity nephelometric methodology (Dade-Behring) in 73 children, and IL-6 levels were assessed with ELISA in 104 children. CRP levels were higher in obese than in non-obese children (.20 ± .03 vs. .03 ± .03 mg/l; F (1.71) = 45.38, P < .000). Moreover, CRP levels were significantly higher in obese children with versus without a family history for T2DM (.24 ± .04 vs. .11 ± .04 mg/l; F (1.28) = 5.16, P < .03). CRP was positively correlated with both HOMA-IR (P < 0.04) and with BMI (P < 0.001) in separate regression analyses after controlling for age, gender and fasting glucose. When analyzed together with BMI, HOMA-IR lost its association with CRP. In contrast, IL-6 levels were non-detectable in 103/104 children, and were thus not entered into any of the statistical analyses. Therefore, as in adults, CRP is elevated in obese school-aged Latino children in proportion to their body weight, with a weaker relationship with a surrogate measure of insulin resistance, HOMA-IR. While CRP may represent an early indicator of the increased risk for diabetes and atherosclerosis, IL-6 may not be a reliable marker of inflammation or disease processes in obese Latino children.

P/269/FRI

Youth with type 2 diabetes (T2D) exposed to maternal diabetes (DM) in utero have a lower HDL concentration

J. R. Law[1], R. B. D'Agostino, Jr[2], J. S. Andrews[2], D. J. Pettitt[3], D. Dabelea[4], T. L. Crume[4], L. M. Dolan[5], A. Badaru[6], J. M. Lawrence[3] & E. J. Mayer-Davis[7]

[1]*University of North Carolina at Chapel Hill, Pediatrics Dept, Pediatric Endocrinology Division, Chapel Hill, United States,* [2]*Wake Forest University, Winston-Salem, United States,* [3]*Kaiser Permanente Southern California, Pasadena, United States,* [4]*University of Colorado, Denver, Denver, United States,* [5]*Cincinnati Children's Hospital, Cincinnati, United States,* [6]*Seattle Children's Research Institute, Seattle, United States,* [7]*University of North Carolina at Chapel Hill, School of Public Health, Dept. of Nutrition, Chapel Hill, United States*

Objectives: Determine if exposure to maternal diabetes in utero is associated with hemoglobin A1c (HbA1c) or cardiovascular disease (CVD) risk factors [systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG)] in youth with T2D.

Methods: Participants (N = 280) were youth in the SEARCH For Diabetes In Youth study with T2D duration >3 months. Exclusion criteria: glucocorticoid use; non-diabetes related renal disease or CVD; and unknown maternal DM status during pregnancy. Exposure was self-reported. ANCOVA was used to examine the association between exposure and HbA1c, SBP, DBP, TC, LDL, HDL, and logTG(transformed due to large SD) adjusting for age at diagnosis, gender, race, study center, body mass index(BMI) z-score, diabetes duration, and waist circumference (WC).

Results: Both groups had similar BMI z-score, diabetes duration, gender, and race. The exposed group were younger at diagnosis and had smaller WC (P < 0.05 for both) (See Table). Adjusted HDL was significantly (P = 0.03) different between groups, 36.9 mg/dl (exposed) vs. 40.9 mg/dl(unexposed). Adjusted logTG approached statistical significance (P = .06), logTG = 5.2(exposed) vs. 5.0 (unexposed). Other outcomes were not statistically different after adjustment.

Characteristic	Exposed to Maternal DM, Percentage or Mean (SD unadjusted variables, SE adjusted variables) N=35	Unexposed to Maternal DM, Percentage or Mean(SD unadjusted variables, SE adjusted variables) N=245	p-value
Age at diagnosis (years)	12.0 (2.4)	13.8 (2.3)	<.0001
Time since diagnosis (months)	20.6 (17.1)	25.7 (22.7)	.12
Gender: Male, Female Male Female	37.1, 62.9	39.2, 60.8	.82
Race/Ethnicity: White, Nonwhite	20.0, 80.0	22.5, 77.6	.74
BMI z-score	2.0 (.6)	2.1 (.7)	.68
Waist Circumference (cm)	103.6 (18.0)	111.4 (25.4)	.03
HbA1c*	7.9 (.4)	7.5 (.2)	.29
Lipid Profile (mg/dL): TC*, LDL*, HDL*, logTG*	180.8 (7.9), 104.2 (6.2), 36.9 (1.8), 5.2 (.1)	182.6 (3.6), 106.8 (2.8), 40.9 (.8), 5.0 (.1)	.83, .67, .03, .06
Blood Pressure (mmHg): SBP*, DBP* *Adjusted for age at diagnosis, time since diagnosis, gender, race, BMI z-score, and WC	119.3 (2.1), 73.8 (1.9)	118.0 (1.0), 71.9 (.9)	.56, .31

[Characteristics By Exposure To Maternal DM inUtero]

Conclusions: Exposure to diabetes in utero is associated with lower HDL concentrations in youth with T2D, thereby increasing their risk of developing CVD.

P/270/FRI

Health status and behavioral functioning of minority youth with type 2 diabetes participating in a family behavioral intervention

A. M. Patino-Fernandez[1], A. Delamater[1], A. Carrillo[2] & J. Sanchez[2]

[1]*University of Miami Miller School of Medicine, Pediatrics/Clinical Psychology, Miami, United States,* [2]*University of Miami Miller School of Medicine, Pediatrics/Endocrinology, Miami, United States*

This study examined health status and behavioral functioning of youth with type 2 diabetes (T2D).Twenty-six youth (*M* age = 14 years; 62% female) from low-income minority (Black, Hispanic) families were recruited from a medical center and completed standardized questionnaires. All but one was overweight. Half had high (>90th%ile) SBP, 32% had high LDL, 32% had high triglycerides, and 44% had low HDL (<10th%ile). Most (93%) mothers were overweight, and family history was positive for T2D (73%), heart disease (40%), hypertension (60%), and high cholesterol (44%). Self-reported regimen adherence showed inadequate levels (≤50% of the time) for checking BG (50%), taking medications (23%), following meal plan (46%), and exercising (23%). Parent-report revealed inadequate levels for glucose checking (39%), taking medications (23%), following meal plans (58%), and exercising (54%).21% of youth reported clinical levels of depressive symptoms and 13% reported at-risk levels. Similar reports of anxiety and interpersonal problems were also made; 63% of youth did not talk with their friends about their diabetes. Analyses revealed *z*BMI (*M* = 2.2) and HbA1c (*M* = 7.8%) were unrelated to parent and youth-reported adherence and psychosocial variables. Higher levels of youth-reported regimen adherence were associated with positive family support (r = .51, P = .01), and better physical quality of life (QOL; r = .42, P = .03) and social functioning QOL (r = .46, P = .02). Youth reported QOL was also related to depression (r = –.78, P < .01), anxiety (r = –.88, P < .01) and positive family support (r = .45, P = .02). These findings indicate:

(1) many youth already have health complications;
(2) regimen adherence is inadequate;
(3) supportive family behaviors and improved QOL are related to better adherence; and
(4) many youth report depression, which is related to poorer QOL.

Family-based interventions to decrease depressive symptoms, improve adherence, and increase family support may benefit this patient population.

P/271/FRI

White UK children are older, more obese and more insulin resistant than non-white UK children at diagnosis of type 2 diabetes: baseline results of the UK national type 2 diabetes cohort

T. Barrett[1], A. Barnett[2], D. Dunger[3], J. Shield[4] & J. Wales[5]

[1]*University of Birmingham, School of Clinical and Experimental Medicine, Birmingham, United Kingdom,* [2]*University of Birmingham, Birmingham, United Kingdom,* [3]*University of Cambridge, Paediatrics, Cambridge, United Kingdom,* [4]*Bristol University, Paediatrics, Bristol, United Kingdom,* [5]*Sheffield University, Sheffield, United Kingdom*

Type 2 diabetes has increased in UK children since the first reports in 2000, but the increase has been slower than expected. We have recruited a UK-wide patient cohort; here we report the baseline characteristics of the first 100 children recruited.

We wrote to all UK paediatricians caring for children with diabetes with the inclusion criteria of physician diagnosis of T2DM; body mass index (BMI) above 85th centile for age and sex; and other diagnoses such as monogenic diabetes excluded.

Clinical data was collected prospectively on case report forms, collated centrally into a national database. Blood was taken for type 1 diabetes antibody status.

Out of 250 affected children notified to us nationally, we have consented 100 to date. Ten proved antibody positive so were excluded. Of the remainder, the M:F ratio was 1:2.5 and 50% were non-white UK origin (mainly from the South Asian subcontinent). Females had a younger mean age at diagnosis (F 11.9 years (SD1.6) vs. M 15.8 years (SD1.1); $P < 0.001$); and were less obese (F mean BMI-*z* score 2.76 (SD 0.69) vs. M BMI-*z* 3.24 (SD 0.88); $P < 0.02$. There was a trend for non-white children to have a younger mean age at diagnosis (mean 12.5 years (SD 2.3) vs. 13.2 years (SD 2.2); $p = 0.07$); and were less obese than white UK children (mean BMI-Z score 2.68 (SD 0.85) vs. 3.10 (SD 0.71); $P < 0.01$). For all the groups, children had fasting or post-prandial C-peptide measurements within (50%) or above (50%) the cut points for normal range.

White UK children are older at diagnosis of type 2 diabetes than non-White UK children, are more obese, and probably tolerate a higher level of insulin resistance before developing type 2 diabetes than non-white UK children. Almost all children have normal or raised C-peptide levels soon after diagnosis of diabetes. This raises the possibility of therapeutic intervention to preserve pancreatic beta cell function early in the disease process.

Poster Session I: Diabetes Project in Developing Countries

P/272/WED

Egyptian uprising against diabetes and its complications

N. S. Elbarbary & M. H. Elsamahy
Ain Shams University, Department of Pediatrics, Cairo, Egypt

Egypt is listed number ten among countries estimated to have the highest number of people with diabetes in 2030. We started to face the challenges of diabetes by preparing a multidisciplinary clinical education program bringing together physicians, dietitians, child psychiatrists, and nurse educators in our teaching hospital. The program was funded by Sanofi-aventis and a total of 45 patients were enrolled. Inclusion criteria included: children ≤16 years, poor socioeconomic condition and glycemic control. The program focused on basic information about diabetes, providing patients with insulin, pens, blood glucose (BG) meters and log books. Patients were taught insulin injection techniques and testing BG regularly. Follow up investigations for patients as HbA1c, microalbumin in urine, lipid profile and fundus examination were made. Registered dietitians were assigned to demonstrate to patients how to follow Nutrition Practice Guidelines. While waiting for their turn at the clinic, patients were afforded the opportunity to watch animated teaching films on DVD players. Further, child psychiatrists meet patients on regular basis to detect the level of psychological burden of diabetes. Diabetes camps for kids and their families aim at providing educational as well as recreational opportunities, devoting special time for patients to do art competition and practice physical exercises. The program significantly improved 6-month clinical outcomes, including a reduction in A1C, an increased likelihood of attaining a target A1C of <7%, and a one-third reduction in emergency department visits. The success of the project constituted an important motive to turn our energies to train teams of health-care professionals from other Egyptian districts, known for their remoteness from the capital and lack of resources, to take up the task of educating patients in their respective locales. In other words we attempt to help patients to help themselves.

P/273/WED

Challenges of managing T1DM against the tide of alternative medicine

M. S. Limbe
Aga Khan University, Nairobi, Paediatrics, Nairobi, Kenya

Case discussion: This is a case report of a 16-year-old girl diagnosed with type 1 diabetes mellitus 4 years ago, whose mother is a homiopathist. The girl only attends hospital in diabetes crisis and has had several admissions for Diabetes ketoacidosis. She gets stabilized each time and her insulin doses adjusted, at discharge the family promises to definitely come regularly for follow-up, but never follows through.

P/274/WED

Characteristics of children presenting with newly diagnosed type 1 diabetes

Y. Reddy[1], Y. Ganie[2] & K. Pillay[3]
[1]*Nelson R. Mandela Medical School, University of Kwa Zulu Natal (UKZN), Department of Paediatrics and Child Health, Durban, South Africa,* [2]*Inkosi Albert Luthuli Central Hospital, Division of Paediatric Endocrinology, Durban, South Africa,* [3]*Westville Hospital, Center for Paediatric Endocrinology and Diabetes, Durban, South Africa*

Background: The clinical presentation of type 1 diabetes in children can be acute or insidious and symptoms may be subtle and frequently misinterpreted. Presentation with Diabetic Ketoacidosis (DKA) may be associated with significant morbidity and mortality in the paediatric population. This study set out to determine the characteristics of those children presenting with DKA at diagnosis to the paediatric endocrine service at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, South Africa and to determine the frequency of missed diagnoses in the month prior to diagnosis.
Methods: A retrospective study was done at IALCH. The study sample included all children presenting with an initial diagnosis of type 1 diabetes diagnosed from January 2008 to June 2010. Children presenting with DKA were compared to those who presented without DKA.
Results: During the period under review, 63 children presented with type 1 diabetes. 44 of 63 patients (60%) presented with diabetic ketoacidosis at diagnosis. The median duration of symptoms preceding diagnosis in the DKA group was 2 weeks versus 4 weeks in the non-DKA group (P = 0.002). There was no significant difference between the groups when compared for ethnicity, gender, age at presentation. 27 of the 42 patients (64%) who presented to health care facilities in the month preceding diagnosis were misdiagnosed.
Conclusion: Patients who present in DKA have a shorter duration of symptoms than the non-DKA group. Ethnicity has no effect on characteristics at presentation. There is an unacceptable rate of missed diagnoses of type 1 diabetes in both the private and public sector in Durban, South Africa.

P/275/WED

Challenges of investigating, diagnosing and treating an endocrine patient in a resource limited country

K. C. Muze & E.S. Majaliwa
Muhimbili National Hospital, Pediatric and Child Health, Dar es Salaam, Tanzania

Background: The management of type 1 diabetes mellitus (T1DM) dramatically changed over the past 30 years, in particular new insulin strategies improved the ability to achieve near normal glycaemia. However this is still difficult in developing countries, where even the mean of reaching a correct diagnosis is difficult.
Case report: We report a case of a 17 years old child who was referred to us from a peripheral clinic with Poor growth, Delayed puberty, and poor blood sugar control. Diagnosis of Type 1 DM was made at the age of nine years. Was born at term, birth weight 2.5 kg. On examination the height was below the 3rd centile. He had a moon shaped face, striae, buffallo hump, trunk obesity, and was normotensive (110/80 mmHg). Morning and midnight Cortisol levels were normal. Bone age 8 years and 10 months. Brain Computed tomography showed features of brain atrophy, Abdominal Uss normal.We are still working on

multiple diagnosis: Is it Cushing Syndrome causing poor controlled Diabetes, or Growth Hormone deficiency, or Anterior pituitary hormones deficiency or just a Mauriac Syndrome?

Discussion and conclusion: No diagnosis has been confirmed to date, most of the investigation were not done due to lack of facilities or high costs. This implies that it is very difficult to have a final diagnosis and manage endocrine patients fully.

P/276/WED

Diabetes still an issue among the children and adolecents in the West Nile region-Ugnada

A. Joyo[1,2,3]

[1]*Arua Diabetes Association, Medical, Kampala, Uganda,* [2]*Arua Diabetes Association, Medical, Arua, Uganda,* [3]*Arua Diabetes Association, Medical, Arua Municipal Council, Uganda*

Introductions: The age used to be one of the risk factors, considered in elderly people, the older you grow the more you become prone to Diabetes, but this seems to be changing, from the way, it used to be, it is more else all the age groups are affected , as result Diabetes spread across the age groups, though age bract of 35 years above is still leading but this is because the other age bracts have been neglected by the world at the beginning, this was reflected in the 12 Diabetes Clinics in the West Nile region-Uganda.

Method: In a data analysis in 12 Diabetes Clinics we have found at least a child has been diagnose with Diabetes The question is how many are still there dying undiagnosed? Or been treated as Malaria as first line treatment, Uganda being a tropical region? And how many have missed the opportunity to be diagnosed at early stages of life due to lack of diagnostic equipment? We have come out with 156 Adolescents and children live of this population of west Nile Region-Uganda, where are the rest of children in the population of 2,626,729? Lost in the world? To trace them time.

Results: The support from WDF/Nodisk to one of the Diabetes Clinics will help to improve and boost diagnosis of more type1 Diabetes Children and adolescents through the free insulin, glucometers and stripes supply they get from Diabetes Clinic, however, this cannot meet all the demand of Children with Diabetes in the region because it is only in one Diabetes Clinic, and taking the challenge of transport cost to travel to come and access the services, Many Children and Adolescents still lack the opportunity to access the services in west Nile Region.

Conclusion: We should look at decentralizing the services to all the Diabetes Clinics to be accessible and available to all the Children and Adolescents living with Diabetes in the region for a better quality of life. Stakeholders like the government of Uganda and its partners should begin to look at Diabetes in children and adolescent.

P/277/WED

Where do we go from here in diabetes care in sub Saharan Africa

E. S. Majaliwa[1], K. C. Muze[2], E. Licoco[3], D. McLarty[4] & K. Ramaiya[5]

[1]*Muhimbili National Hospital, Dar es Salaam, Tanzania* [2]*Muhimbili National Hospital, Paediatric and Child Health, Dar es Salaam, Tanzania* [3]*Muhimbili National Hospital, Internal Medicine, Dar es Salaam, Tanzania* [4]*Tanzania Diabetes Asssociation, Dar es Salaam, Tanzania* [5]*Hindumandal Hospital, Dar es Salaam, Tanzania*

Background: The children clinic for diabetes in Muhimbili National Hospital (MNH) started in 2005 with 30 children. There have been an improvement of care and many children get their insulin free and strips for measuring of blood glucose is free under the sponsorship of the IDF. Many of children of all ages attend the clinic regularly however there is less family support. The team which is available currently consists of 2 pediatric endocrinologists and Diabetes nurse educators.

Methods: We reviewed clinical records of 150 paedaitrics/adolescents attending Muhimbili National Hospital diabetes clinic. Parents/guardians were interviewed.

Results: For the past 6 months out of 107 patients who had complete data, 36 (33.6%) patients were admitted. The main reason for admission being DKA (76.3%); very few 10.5% were admitted due to severe hypoglycemia And very few were admitted for other reasons like malaria and Pneumonia. Out of these 72.2% of the patients were admitted less than three times, the rest 27.8% were admitted at least three times in the last 6 months. The mean, min, max and standard deviation days of admission were 11.4, 1, 56, and 12 respectively. These children have been missing classes: 62.5% of children, missed school for less than 10 days and 16% missed school for more than 1 month.

Conclusion: Despite free insulin, there are other social factors hindering diabetes care in resource limited countries. Therefore there is a need to have diabetes teams who have at least one social worker to provide psychosocial support to these children as well as family support.

P/278/WED

Growth and nutritional status of Indonesian type 1 diabetes mellitus children based on insulin regimen

F. Soesanti[1], R. Purbasari[2], B. Tridjaja[1], J.R. Batubara[1] & A. Pulungan[1]

[1]*Universitas Indonesia, Cipto Mangunkusumo Hospital, Pediatric Endocrinology Division, Jakarta, Indonesia,* [2]*Indonesian Pediatric Endocrinology Chapter, Jakarta, Indonesia*

Objectives: To compare the growth and nutritional status of Indonesian T1DM children based on insulin regimen and A1c level. Also, to explore any other factors that might contribute to the growth and nutritional status.

Methods: Retrospective national survey was conducted in Indonesian T1DM children during April 2009–February 2011. Data was collected through phone interview. Subjects with complete anthropometric data at diagnosis and registration date were included. Furthermore, subjects with duration of illness <6 months was excluded. Insulin regimen was classified as conventional or intensive therapy, while A1c level was classified as optimal (<7.5%), suboptimal (7.5–9%), and high risk (>9%). Nutritional status was defined based on BMI persentile.

Results: Of 589 registered T1DM children in Indonesia only 41 (15 boys, 26 girls) subjects meet the criteria. Mean length of follow up was 2.45 years. Decreased growth was observed in 20 (48.8%) subjects, while increased & stable growth observed in 10 (24.4%) and 11 (26.8%) subject, respectively. Thirty (73.2%) subjects had normal BMI; while overweight and obesity was observed in 4 and 2 subjects, respectively. No difference of growth and nutritional status observed between intensive or conventional therapy ($P = 0.71$; $P = 0.90$, respectively), but 41.5% of subjects with conventional therapy had decreased growth. Girls had higher proportion of decreased growth compared to boys. The growth and nutritional status also not different based on A1c level ($P = 0.13$; $P = 0.16$, respectively). Other factors such as duration of illness, frequency of DKA, parents' educational level, and health funding resources also not associated with growth rate and nutritional status.

Conclusions: In contrast with other studies, this study found no difference effect in the growth and nutritional status of Indonesian T1DM children based on insulin regimen.

P/279/WED

Novel gene mutation p.G208A and IVS3+2T>C in Chinese child with recurrent pancreatitis

M. Zhang[1], X. Chen[1], L. Cao[2], Z. Zhao[1], S. Shen[1], Y. Yang[2] & F. Luo[1]
[1]*Children's Hospital of Fudan University, Department of Endocrinology and Metabolism, Shanghai, China,* [2]*Children's Hospital of Fudan University, Pediatric Institute, Shanghai, China*

Context: Recurrent pancreatitis is uncommon in child, which can cause diabetes. Testing for genes, implicated with chronic Pancreatitis, should be considered in any patient with acute recurrent pancreatitis with or without a positive family history.
Objective: To analyze cationic trypsinogen gene (PRSS1) and serine protease inhibitor Kazal type 1 gene (SPINK1) gene variation in a Chinese boy with recurrent pancreatitis without family history.
Methods: All exons and the promoter region of the SPINK1 and PRSS1 gene were amplified by polymerase chain reaction, and analyzed using direct sequencing.
Main outcome measures: Sequences of each exon and nearby intron of the SPINK1 gene and PRSS1genes of the family members were compared with the gene bank genomic sequences.
Results: DNA sequence analysis of the entire coding regions and surrounding uncoding regions disclosed a novel heterozygous G/C mutation at nucleotide 569 in exon 5 of the PRSS1 gene and a novel heterozygous IVS3+2T>C mutation in the affected child.
Conclusion: p.G208A and IVS3+2T>C are novel gene mutations that contributes to recurrent pancreatitis in this Chinese child.

P/280/WED

Diabetes care in Sub Saharan Africa: where do we go from here?

E. S. Majaliwa[1], K. C. Muze[2], D. McLarty[3], E. Licoco[2], K. Ramaiya[4]
[1]*Muhimbili National Hospital, Paediatric and Child Health, Dar es Salaam, Tanzania*[2]*Muhimbili National Hospital, Dar es Salaam, Tanzania*[3]*Tanzania Diabetes Asssociation, Dar es Salaam, Tanzania*[4]*Hindumandal Hospital, Dar es Salaam, Tanzania*

Background: The children clinic for diabetes in Muhimbili National Hospital (MNH) started in 2005 with 30 children. There have been an improvement of care and many children get their insulin free and strips for measuring of blood glucose is free under the sponsorship of the IDF. Many of children of all ages attend the clinic regularly however there is less family support. The team which is available currently consists of 2 pediatric endocrinologists and Diabetes nurse educators.
Methods: We reviewed clinical records of 150 paedaitrics/adolescents attending Muhimbili National Hospital diabetes clinic. Parents/guardians were interviewed.
Results: For the past 6 months out of 107 patients who had complete data, 36(33.6%) patients were admitted. The main reason for admission being DKA (76.3%); very few 10.5% were admitted due to severe hypoglycemia And very few were admitted for other reasons like malaria and Pneumonia. Out of these 72.2% of the patients were admitted less than three times, the rest 27.8% were admitted at least three times in the last 6 months. The mean, min, max and standard deviation days of admission were 11.4, 1, 56, and 12 respectively. These children have been missing classes: 62.5% of children, missed school for less than 10 days and 16% missed school for more than 1 month.
Conclusion: Despite free insulin, there are other social factors hindering diabetes care in resource limited countries. Therefore there is a need to have diabetes teams who have at least one social worker to provide psychosocial support to these children as well as family support.

P/281/WED

Changing diabetes in children programme – a comprehensive healthcare to children with diabetes in Bangladesh

B. Zabeen[1], B. Benarjee[1], S. Tayyeb[2], A. Baki[2], J. Nahar[2], F. Mohsin[2], S. Akhter[2], T. Begum[2], N. Nahar[2], K. Azad[1] & A. K. A. Khan[1]
[1]*Diabetic Association of Bangladesh (BADAS), Changing Diabetes in Children Programme, Dhaka, Bangladesh,* [2]*Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Paediatrics, Dhaka, Bangladesh*

Introduction: Diabetes care in Bangladesh is primarily organized by Diabetic Association of Bangladesh (BADAS) through its 80 health care facilities all over the country. Changing Diabetes in Children Programme (CDIC) is an initiative of BADAS in joint collaboration with WDF and Novo Nordisk to establish comprehensive healthcare to children and adolescents with diabetes in Bangladesh. The overall goal of the project is to improve the access to diabetes care for children with diabetes and help them to live better lives.The objectives are-
(1) to establish a central paediatric diabetes clinic in BIRDEM Hospital in Dhaka and two peripheral diabetes clinics in two districts of Bangladesh,
(2) to train doctors and educators in management of diabetes in children,
(3) to develop a training manual for the Health care professionals,
(4) to develop an education programme for children and their families considering the special needs of the children in native language,
(5) to provide free comprehensive care including medical consultations, education, insulin with syringes, HbA1c with other investigations, Glucometer with strips to all children with diabetes,
(6) to organize Diabetes camp once every year,
(7) to establish a national registry of children with diabetes,
(8) to create awareness about diabetes in the community.
A total of 629 children and adolescents are enrolled in CDIC, since June, 2010. Female are predominant with female to male ratio of 1.2:1. Mean age at the onset of diabetes was 11.2 ± 3.9 years and Mean age during registration was 13.3 ± 3.48 years. Eighty seven percent had type 1 and others had fibrocalculous pancreatic diabetes, type 2 and other specific types. Mean HbA1c was 10.5 ± 5.0 during registration in this programme.
Conclusion: The long-term aspiration of this programme is to improve the lives of the children with diabetes and also find ways of integrating components into usual ways of health care delivery in a developing country like Bangladesh.

P/282/WED

Challenges of diabetes management in Nigerian children

J. Elusiyan & O. Odunlade
Obafemi Awolowo University, Paediatrics and Child Health, Ile-Ife, Nigeria

Diabetes Mellitus is the commonest endocrine disease seen in children world-wide. It has hitherto not been found to be common in Nigerian children. There however has been an increase from one patient in 2006 to eight as at December 2010 at the paediatric endocrine clinic of the Obafemi Awolowo University, Ile-Ife, South-west, Nigeria. This is partly due to an increase awareness and publicity of the clinic in the region. It is however not sure if this is a true increase in incidence of the disease in the region or due to the increase awareness.

The eight patients consist of 5 boys and 3 girls with age range between 11 and 14 years. One of the patients died and one was lost to follow-up. The remaining six are regular with follow-up and doing well. All but one are on regular twice daily premix 70/30 Insulin. One that can afford it is on mid evening soluble insulin. Only two have access to regular blood glucose monitoring and one of these two is able to afford HbA1c.
Major challenges include inability to be flexible with insulin type and administration and blood glucose monitoring mainly due to cost. At present no other form of support for patient with Diabetes other than family. Dietary control is also posing a little challenge. All but one of the parents is very enthusiastic and well motivated to comply with treatment. Advocacy to government and NGO to support the plight of these children is currently underway and hopefully will be available soon.

P/283/WED

Unconventional ulcers therapy

E. Ngwa[1] & J.N. Menang[2]
[1]*DIPROLOCC, Administration, Buea, Cameroon,* [2]*Cameroon Laboratory & Medicine Foundation Health Centre, Pediatric Diabetes, Tiko, Cameroon*

Background: Managing diabetes complications especially ulcers are with great challenges for resource restraint nations. At CALMEF Health Centre Cameroon, due to financial cost, illiteracy, cultural beliefs and family influences, unorthodox practices always accompany management of diabetes ulcers. This is more often without the health personneĺs knowledge. It is also oftenly carried in combination with Western approach.
Methods: Investigating the unorthodox practices that many patients belief is of benefit, such as prayers and application of pure water provided by the priest. The commonest is Holy water from a local church that miraculously heal calcaneal and other chronic foot ulcers. Most of the ulcers persisted for years and a good number refused amputations as they were not yielding to available dressing change with either hydrogel, alginates, fomalin and others.
Results: Though the mechanism of action or the healing process of the prayers and Holy water cannot be scientifically explained, a good number of our clients have greatly benefited from the therapy. 78 clients with chronic heel, foot or leg ulcers among our diabetes clinic clients were put to the asessment from July 2009–April 2011 assessment. Issues taken into consideration were proper counselling and consent. About 78% in the unorthodox group recovered in 1–2 months unlike a smaller 22% in the routine care.
Conclusions: No conclusion yet, but in the days ahead when the studies are expected to complete, a thorough analysis is expected to bring a conclusion. There may be no scientific proof of the unorthodox approach but since most clients benefit from it, can that be subsituted for the orthodox to safe limbs? make clients happy and hopeful? A close study is also underway with the priest and the clients.

P/284/WED

Religion, faith and the empowerment process: stories of Iranian people with diabetes

S. Abdoli[1], T. Ashktorab[2], F. Ahmadi[3], S. Parvizy[4] & D. Trisha[5]
[1]*Isfahan University of Medical Sciences, Isfahan, Iran* [2]*Shahid Beheshti University of Medical Sciences, Tehran, Iran* [3]*Tarbiat Modarres University, Tehran* [4]*Tehran University of Medical Sciences, Tehran, Iran* [5]*Deakin University and Barwon Health, Geelong, Australia*

Objectives: This study aims to determine the barriers to and facilitators of empowerment in Iranian people with diabetes.
Methods: A qualitative exploratory study was conducted using in-depth interviews to collect the data from 11 women and women in 2007. Themes were identified using constant comparative analysis method.
Results: Common barriers to empowerment were similar to other chronic diseases: prolonged stress, negative view about diabetes, ineffective health-care systems, poverty and illiteracy. Diabetes education, fear of diabetes' complications, self-efficacy and hope for a better future emerged as being crucial to empowerment. Facilitators specific to Iranians were: the power of religion and faith, the concept of the doctor as holy man, accepting diabetes as God's will, caring for the body because it was God's gift and support from families especially daughters.
Conclusion: Empowerment was strongly influenced by cultural and religious beliefs in Iran and the power of faith emerged as an important facilitator of diabetes empowerment. The findings will help health professionals understand how Iranian people with diabetes view life and the factors that facilitate empowerment.

P/285/WED

Change in quality of life by multiple education program in type 1 diabetic patients

B. Saboo
Dia Care – A Complete Diabetes Care Center, Diabetes, Ahmedabad, India

The aim of study was to recurrently follow quality of life in type 1 diabetes patients after multiple educations and counseling. Ninety-six patients of the age group of between 10 and 25 were initially examined in 2004 and Eighty eight patients of them were re-examined in 2006 after multiple counseling with diabetologist and trained diabetes educator at dia care, Ahmedabad, Gujarat, India. Quality of life was defined as perceived well being and life satisfaction, globally as well as within key domains and functions. Various status and retrospective change ratings were repeatedly performed by patients and significant others. For nine patients quality of life was fairly stable between 2004 and 2006. Further 79 patients had shown very significant and consistent improvement in their quality of life. Delivery of the insulin injection, self monitoring of blood glucose, management of illness, hypoglycemia, hyperglycemia and further topics related to type 1 diabetes were part of education. The study underscores the benefit to other parts of the country that quality of life of type 1 diabetic patients can be improved by continuous and multiple educations.

P/286/WED

Role of eating attitudes and health locus of control on health anxiety of diabetic patients

N. Chaube[1], D. R. N. Siddiqui[1], A. Dixit[2], S. Pattanayak[3], I. Feroz[1] & F. Khanam[1,4]
[1]*Aligarh Muslim University, Psychology, Aligarh, India,* [2]*University College of Medical Sciences, Physiology, Delhi, India,* [3]*Vidya Sagar Institute of Mental Health and Neuro Scinces, Psychiatry, New Delhi, India,* [4]*G.B. Pant Hospital, Neurology, New Delhi, India*

Objective: The objective of the study was to investigate the impact of eating attitudes and health locus of control on health anxiety patterns of type-2 diabetics.
Methods: The sample comprised of 136 diabetic patients, 68 literate patients and 68 illiterate patients between the age range of 31 years to76 years. Of the 136 respondents there were 56 males and 80 females. The average income of the illiterates was rupees 6000 per month whereas it was found to be rupees 15,000 in case of literates. The sample was asked to complete the Eating

Attitude Test, the Health Locus of Control Scale and Health Anxiety Inventory.
Results: Illiterates were found to be significantly higher on bulimia ($t = 4.86$; $P < .01$) and health anxiety ($t = 3.31$; $P < .001$) but they scored significantly lower on internal health locus of control ($t = 4.25$; $P < .01$).
Conclusions: It shows that eating attitudes and health locus of control affect the health anxiety of diabetics.

P/287/WED

Why is blood sugar not controlled?

R. Shukla[1], D. Yagnik[2] & S. Shukla[3]
[1]*Regency Hospital, Endocrinology, Kanpur, India,* [2]*Yagnik Diabetes Care Centre, Medicine, Kanpur, India,* [3]*Regency Hospital, Opthelmology, Kanpur, India*

Aim: In spite of good awareness, blood sugar levels are not controlled among majority of patients. Survey was conducted to find if there were unknown reasons.
Introduction: Managing type1 diabetes is a big problem in India as there is no financial and social support system. Support groups play role in survival of similar patients but control is still the dream.
Material and methods: The survey was done in a regular awareness program organized by a non-government organization (Society for Prevention and Awareness of Diabetes). Total participants were 30, M: F (13/17), age group 8–30 years. They were asked to write in short ''Why your blood sugar is not controlled''. Their comments were as follows-
(1) bad diet habits;
(2) no exercise;
(3) Irregular blood sugar checkups;
(4) No fixed timing for insulin injection;
(5) Not feel like eating so skip insulin;
(6) Due to frequent illnesses (infections);
(7) Stress (work, blood sugar control, future and financial support);
(8) Not able to afford monitoring;
(9) Insulin is not working appropriately;
(10) Frequent irritation (Anger);
(11) Not able to give time due to studies/job pressure.
Conclusion: Stress, financial supports along with unable to control the drive for desired food emerged as important reasons for poor control.

P/288/WED

Impaired glucose tolerance test in β thalassemia major

J. M. Hussein, Z. W. Al-Maaroof, W. H. Al-Dujaily
Babylon Medical College, Pediatrics, Hilla/Babil, Iraq

Background: β thalassemia major is a hereditary disorder of hemoglobin synthesis associated with ineffective erythropoiesis and rapid red cell destruction resulting in severe anemia. Impaired glucose metabolism is one of the above consequences in the pancreatic beta cells.
Objectives: To report the relationship and risk factors of impaired glucose tolerance test in patients with β thalassemia major in Hilla, Iraq.
Patients and method: Ninety-seven patients with β thalassemia major were enrolled in this study, which was done in Babylon Thalassemic center, Hilla, Iraq, between January and June 2009. There were 56 males (57.73%) and 41 females (42.26%). The mean age at the time of enrolment was 9.36 ± 3.75 years. The demographic characteristics of patients with ß-thalassemic major included the age, gender, height, body weight, age at the first blood transfusion, age at the start of iron-chelation therapy, compliance with iron-chelation therapy, previous splenectomy and family history of diabetes. Estimation of serum ferritin concentration, existence of hepatitis B surface antigen, and hepatitis C antibody were done. All 97 patients underwent oral glucose tolerance test (OGTT). Blood samples for glucose were drawn at 0 and 120 minutes.
Results: Impaired glucose tolerance test (IGT) was found in 5 patients (5.15%), and 92 patients (94.84%) had normal glucose tolerance test. Comparing the patients with normal glucose tolerance test to those with impaired glucose tolerance test, significant differences were found in the serum ferritin concentration.
Conclusion: Physicians caring for patients with thalassemia major should be particularly alert to the possibility of diabetes. Serum ferritin concentration, a marker for hepatic iron concentration, was found to be a risk factor in this study.

P/289/WED

Epidemiological aspects and management of type 1 diabetes in a general pediatric ward of Tlemcen-Algeria

B. A. Ahmed Salih
University Tlemcen, Pediatrics, Tlemcen, Algeria

Introduction: The incidence of type 1 diabetes is increasing markedly in worldwide and particularly in developing countries is diabetes mellitus, despite a very strict lifestyle and several daily insulin injections, some of them fail to balance their diabetes adequately, what justifies the study of new therapeutic approaches but also developed various detections.
Materials and methods: Retrospective epidemiological study on a period of 3 years from 01/01/2008 to 31/12/2010 in children with diabetes hospitalized in the Pediatric Hospital "mother-child"-Tlemcen-Algeria and followed in specialized consultation.
Results: 142 diabetic children between 1 and 15 years are affected by our work
Sex ratio: male/female = 1.27, Mean age 6.5 years of discovery.
Circumstances of discovery: 74% ketoacidosis, weight and size:10.5%: Underweight, 86.5%: normal body mass index, 3%: degré1 obesity according to WHO and the International Obesity Task Force 1998, Only 30% were on an adequate diet.
Diagram 1: 40% patients, a mixture prepared from a rapid and intermediate insulin or insulin analogue with a similar rapid means: one injection in the morning and evening.
Diagram 2: 19% patients, Diagram 1 + a similar rapid injection at noon.
Diagram 3: 83%patients ,4 injections with three injections at times like fast food + a similar injection of basal at night or day, Complications: hypoglicimique accident in 43%, Retinopathy 2.3%, nephropathies 0.7%, Associated disease: autoimmune thyroiditis: 6.2%, celiac disease in 1.4%, Half of our patients had a regular monitoring, Glycemic control based on glycosylated hb: Diagram 1: 9.05%, Diagram-2: 8.55%, Diagram-3: 9.43%.
Conclusion: Diabetes mellitus is a chronic, difficult to take charge correctly, you should never impose to little diabetic and his parents but rather adapt to their lifestyle, the important thing is to keep their confidence and personalize taking charge.

P/290/WED

Comprehensive approach towards paediatric diabetes management: NGO initiatives in developing country India

S. Pramod
Health Alert Organization of India [NGO], Community Medicine, Dhule, India

Issues: In developing nations diagnosis of diabetes brings mental-trauma/depression in family. Focused treatment for

pediatric age-group is unavailable in developing-countries. Inadequately trained physicians/Nurses in pediatric-diabetes. Qualitative collaborative relationship between these makes diabetics life bearable. Our NGO-project highlights significance of relationship between nurses and diabetic-children in community clinic setup of rural India. Retrospective analysis shows – counselling improves QOL & attitudes.
Aims: To describe care issues in diabetic-children's. Observe/ modify nature of relationship between nurse and child. To evolve comprehensive treatment plan for patients and families.
Methods: A retrospective analysis of data base from 9 rural health-clinics. Specialized therapy/support to pediatric-age-group not available at any centre. Total 134 children's [4–13 years] diagnosed with diabetes. 32 had additional endocrine/ metabolic problems. Nursing/medical care plan analyzed. No specialized trained personal in rural/tribal India. Opinion/ needs from patient's families collected on feedback questionnaire. Trained 10 nurses & 2 physicians for handling pediatric cases [4 weeks training].
Results: Out of 134, 47 discontinued Rx due to improper counseling/guidance. 3 died. Patient/family's feedback highlights: Better access to newer drugs-delivery-systems, psychosocial support, follow-up-plan. Nurses/physician be sensitized in pediatric care-issues. Main issues of concern: [1] illness, coping with feelings. [2] Initial impact of diagnosis and search for solution? Expectations for future life & its quality? [3] Concerns of cost of RX [4] Availability of proper follow-up centers.
Conclusion: Multifaceted Relationship between physician/nurse and Diabetics childrens is crucial. This relationship provides better continuity of treatment. We show concerns/difficulties while working in Asian set-up to international experts/seniors at ISPAD-2011-congress.

P/291/WED

Non-governmental organizations [NGO's] & diabetes – advocacy project in resource-poor nations

S. Pramod
Health Alert Organization of India [NGO], Community Medicine, Dhule, India

Background: Comprehensive Diabetes support services available only in few city hospitals. NGO's play key role in psychosocial-support/Counseling/rehabilitation in remote towns of India. To formulate policy for trained personals for better, cost-effective Diabetes-support services.
Methods: We mobilized training resources from local primary Health-centers. Training in Counseling & diabetes care imparted to nurses. Team consisted of 2 social workers, 4 nurses & one physician. Local traditional faith-healers & community leaders involved for more effective diabetes awareness/education programs. Aims for physical-comfort, improve patient relationship. We prepared patient/family for long term diabetes care. Discomfort/anxiety decreases overall treatment efficacy. 51 Patients enrolled during community out-reach-programs. Data collected on feedback-questionnaire. Most difficult tasks are discussing cost of long-term therapy & non-availability of newer insulin preparations in rural/tribal areas.
Results: Diabetes Counseling/ support services must be made more accessible in rural-areas. Our NGO's approach is also very cost-effective. Due to non-availability of trained-personal in rural areas this approach crucial in resource poor nations. We noted 86% responded favorably to counseling/nursing care programs, 79% showed willingness to motivate fellow patients to facilitate supportive-care-program. 17 patients themselves became regular active facilitators in our NGO's Diabetes-care workshops. Our Holistic approach helped overcome hopelessness/fear depression. NGO's need to improve access to drugs by collaboration with national diabetes societies.
Conclusion: In no extra cost our NGO's performed good job of Counseling/rehabilitation. Restricted resource-limitations did not permit us to take study large-sample-size, but we can collaborate with other NGO's at ISPAD-congress for larger effort. Our approach most suitable to resource-poor-settings.

P/292/WED

Insulin resistance: Policy plan to address burning issue by NGO from rural India

S. Pramod
Health Alert Organization of India [NGO], Community Medicine, Dhule, India

Issues: Newer anti-diabetic therapies out of reach of >84% populations of Asia. Pharmaceuticals do not provide price discounts in resource-constrained-countries. But rising incidence of Insulin resistance is neglected issue in resource-poor nations. We formed a liaison study group of 4 clinics to analyse this issue & make policy paper. Resource poor nations have little technical expertise/manpower to study Insulin resistance.
Description: In developing countries long term cost economics of diabetes treatment in rural/tribal India leads to poor-therapeutic-compliance. National/international programs do not offer discounted drugs, or diagnostics/technical assistance in diabetes-care. Insulin resistance must be evaluated & corrective steps to minimise it. Health-care NGO's are pivotal to facilitate development of sound/sustainable diabetes care programs.
Results/observations: There is need to provide technical/research skills from Industrialised-nations researchers to filter it to lesser privileged from developing nations like India. Forums are needed to implement/expand this suggestion/policy. Most of conferences address issues of cost/availability/ADR's BUT issues of drug-resistance & its implications are neglected.
Recommendations: Development of tolls to tackle insulin resistance is in infantile stage in developing nations. Promoting dialogue between public institutions/NGO's & western researchers will accelerate policy implementation, increases resource & access to technical expertise on diabetes care. We need to break north-south barriers for better Diabetes research. Patient advocates at ISPAD-2011 need to collaborate in future research-projects on this issue. We NGO-representatives from developing-nations need exposure to research from European/USA. This is indeed possible by my participation at Miami meeting. Do we all fail in addressing issues of Resistance at majority of Diabetes conferences?

P/293/WED

Waist diameter as predictor of risk of diabetes

M. D. C. Caballero Gonzales & C.C. Verduguez Guzman
Centro de Educacion e Informacion Vivir con Diabetes, Cercado, Cochabamba, Bolivia

Vivir con Diabetes Center is an institution dedicated to the care, education and prevention of diabetes, due to changes in lifestyle reaching states of pre-diabetes or metabolic syndrome, which invariably lead to an increased prevalence cases of diabetes. The basis of the pre-diabetes is obesity and abdominal obesity especially central obesity, which can be objectified by measuring the abdominal waist (AW).
Given the new recommendations on the criteria for the diagnosis of metabolic syndrome, our option is the detection of pre-diabetes in youth from 18 years through the election of new

values of fasting glucose and waist Index as a predictor of diabetes risk.
Objectives: Evaluate the presence of abdominal adiposity, as measured by the waist diameter as a predictor of metabolic disorders in a population of university students aged between 18 and 20 years.
Sample: 150 university students (man y woman from 18 to 20 years).
Method: (1) Prospective study·Instrument for data collection and psychosocial characteristics, sociodemographic and lifestyle for young people to identify with high probability of developing diabetes.
(2) Identification of potential risk factors for each couple: LDL and HDL cholesterol, hypertension, type 2 diabetes, smoking and obesity, BMI.
(3) Acting to reduce the risk level of youth.
Strategy: (1) Goals for glycemic control in pre-diabetes (impaired fasting glucose).
(2) Personal history of diabetes.
(3) Changes in lifestyle.
Conclusions: The most important step for people with pre-diabetes is management-intensive lifestyle, because the benefits in glycemic and cardiovascular risk. An appropriate lifestyle prevents or delays the onset of diabetes as well as micro-and macro-vascular disease. It is also proposed to add the control of blood pressure and lipid control of blood glucose, as in diabetes.

P/294/WED

Childhood diabetes project in Sudan

I. M. Omer
University of Khartoum, Pediatrics and Child Health, Khartoum, Sudan

Sudan is a large African country with different ethnic groups, a lot of conflicts and low income. It is still underdeveloped.
Childhood diabetes is spreading very quicly all over the country with limited resources.
Sudanese Childhood Diabetes Association, a charity group, as part of its many objectives, decided to help Sudanese diabetic children in many ways, hence The Sudan Childhood Diabetes Programme, in collaboration with the WDF.
Justifications: (1) Increasing number of diabetic children.
(2) Doctors & Dieticians are not trained in the management of diabetes.
(3) Lack of diabetic educators.
(4) Lack of specialied diabetic clinics & management guidelines.
Objectives: (1) Training of doctors, dieticians & diabetic educators from different states of Sudan.
(2) Opening of 25 diabetic clinics in different states of Sudan.
(3) Providing the clinics with management protocols & educational materials.
Methodology: 2-year programme: May 2009–May2011
Place: Jabir abualiz diabetic center, In Khartoum.
Program: Training course for doctors.
Training course for dieticians.
Training course for educators.
Each course held once/year. 6 day course; 8:00 am–16:00 pm
Candidates selected from different states of Sudan.
Results: Training of 91 pediatricians.
Training of 87 dieticians.
Training of 87 educators.
18 equiped diabetic clinics were opened & 7 in the process.
Conclusion: Awareness was raised among other medical personnel as some of the trained doctors started to hold seminars & workshops at their localities.
Reduction in the cost of diabetes care to the families as the services came to their states.
Childhood Diabetes Ass. has a branch in every state with diabetes clinic.