

# POSTER PRESENTATIONS

## Diabetes Care, Education, Psychosocial Issues – Psychological and Psychosomatic Aspects

P/WED/01

### Psychological and psychosomatic approach in adolescents with juvenile diabetes

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**Objectives:** Aim of this study was to evaluate the psychological restructure in T1DM patients following the appearance of the disease. The presence of a chronic disease during the period of adolescence creates many questions about the person's mental status and structure, particularly about how this structure evolves when living with the disease.

**Methods:** The research sample consisted of 104 adolescents with T1DM and 146 healthy adolescents, who accepted voluntarily to participate. This project was started in November 2003 until September 2006, in which participating adolescents were between the ages of 11 and 21. Testing included the T.A.T. (Thematic Apperception Test), self image questionnaire for adolescents S.I.Q.A., and a structured clinic interview.

**Conclusion:** T1DM appeared during childhood in a large portion of the adolescents (43.3%). The adolescents whose diabetes appeared in childhood, seemed more able to control and more adjusted to T1DM, with much more self-confidence as compared with adolescents whose diabetes appeared in infancy or in adolescence. The overvalue that gives the adolescent to the appearance of his diabetes, leads to mental and physical disorganization, consists of negative emotions, unconscious representations and defense mechanisms, that eventually lead to psychic and mental re-organization.

P/WED/02

### Is art therapy a supportive intervention for adolescents with type 1 diabetes?

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**Objectives:** Art Therapy is a psychotherapeutic intervention, where the making of images and creative processes play a central role in enhancing an individual's ability to better understand and communicate their problems. It has been a recognised profession in the UK since 1982 and has been predominantly used and evaluated in the field of mental health. To date, however, Art Therapy has rarely been used as an intervention for adolescents with diabetes. We explored the feasibility of offering an Art Therapy course to a group of young people with diabetes.

**Structure and Setting:** A group format used the therapist's time most efficiently and facilitated the potentially strong and, in many cases, crucial peer support. Prior to the planning of an investigation into the merits of Art Therapy for this particular patient group we collected preliminary data in this feasibility study. We recruited seven young people (ages 11 to 17 years) who currently are patients of the Tayside Children's and Adolescent Diabetes Service. They were invited to a non-healthcare venue on a weekly basis for 10 (1 hour duration) Art Therapy sessions. Detailed notes of the sessions were kept following each session and an attendance record maintained. All participants were invited to complete a short questionnaire at the start and end of the programme consisting of brief well being and

illness perception questions. The project is ongoing and will be due for completion in June 2007. The results will be analysed using case based reports and graphical presentations.

**Conclusion:** This innovative project aims to evaluate the feasibility of providing Art Therapy as a method of engaging a group of young people who may be struggling to cope with the rigours of managing their diabetes. The results of this project will give us invaluable information on which to base a fully powered intervention study.

P/WED/03

### Diabetes camp for those with poor metabolic control; evaluation of Hemoglobin A1c, self-confidence, locus of control and amount of physical exercise

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**Introduction:** Distinct design and organization is decisive for the outcome of a diabetes camp.

**Objectives:** To evaluate the effect of a diabetes camp where specifically individual with poor metabolic control were invited. The aim was put on each individual involving evaluation and thereafter a definite aim in each case.

**Methods:** Ten adolescents (S) (15–17 years) with 7.4 (2.7–13.4) years duration of diabetes and with poor metabolic control; Hemoglobin A1c: 9.0 (8.3–10.0, DCCT standard), volunteered to participate in this controlled study. The control group (C) was matched according to age (15–16 years), duration: 6.5 (1.5–10.3) and Hemoglobin A1c: 8.8 (7.3–9.4). An adventure camp was organized where each activity symbolized different elements of teamwork, and these were discussed during the camp. Primary focus was set on individual evaluation and aims. Hemoglobin A1c was controlled three and six months before, respectively after. Questionnaires regarding self-confidence, locus of control and amount of physical activity were filled in before and six months after. Acute complications; severe HG and DKA were registered. An evaluation of SMBG was done with a plasma glucose monitor, Ultrasmart (Lifescan Johnson & Johnson) before, during and after the camp. Wilcoxon Signed Ranks Test was used for statistical analysis.

**Result:** Hemoglobin A1c after six months was improved in S; 9.0–8.2, as well as C; 8.8–8.0,  $p = 0.001$ . There was no statistically difference between the two groups, median improvement however greater in S. Self-confidence was significantly improved in S but not in C, whereas locus of control was not improved in S but significantly improved in C. There was no difference regarding the amount of physical exercise or the pattern or frequency of SMBG.

**Conclusion:** In this study of individuals with poor metabolic control we show that attendance during a structured diabetes camp could result in improved Hemoglobin A1c and Self-confidence. Aim and organization of a camp seems to be decisive.

P/WED/04

### Behavioural problems in type 1 diabetics in India

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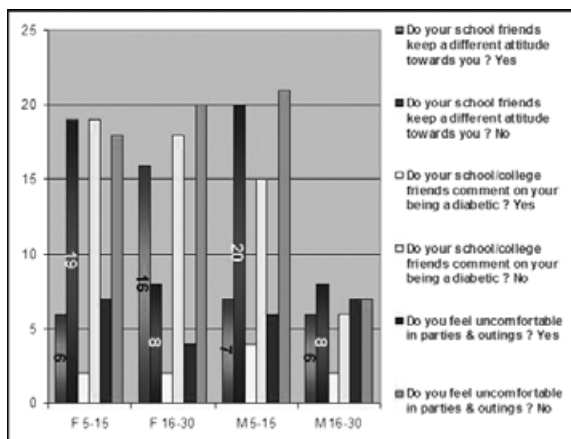
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**Method:** People with type 1 diabetes were surveyed in 'National Type 1 Diabetic Meet 2007' this was the first meet in India involving the people with type 1 diabetes across the country. Total participants -320, Surveyed-25 female (aged-5–15yrs), 24 females (16–30years) 27 males (5–15 years), 14males (16–30 years) survey done on the basis of questionnaire.

Questions asked were

1. Do your school friends keep different attitude towards you?
2. Do you feel comfortable in social gatherings?
3. Do people express pity after knowing your diabetes?
4. Who hurt you most?
5. Do people become more caring after knowing your diabetes?
6. Do you think that you should tell about your diabetes to whomever you meet?
7. To whom should you tell about your diabetes?
8. Is it easy to follow advised diet schedule?

**Results:** Most of the people express pity after knowing the diabetes in early age. Majority of type 1 diabetic are not comfortable in social gatherings. Significant no of type 1 diabetics feel that they should not tell about their diabetes. An acquaintance hurts most of the age groups special relatives. The common finding that to disclose about their diabetes is only to very close relatives or friends. Younger age group find more difficulty in following prescribed diet schedule however older age group is comfortably sticking to diet schedule.



**Conclusions:** Diabetes should be revealed only to the close friends and relatives. Most of type 1 friends are uncomfortable in social gatherings so they need more frequent counselling.

P/WED/05

### Self-injurious and suicidal behavior in Slovenian adolescents with type 1 diabetes

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**Objective:** To investigate the occurrence of self-injurious, behavior suicidal ideation and attempted suicide in a representative sample of Slovenian adolescents with type 1 diabetes.

**Methods:** All Slovenian adolescents with type 1 diabetes aged from 14 to 19 years were invited to participate (185 subjects). Subjects received a specially designed self-report questionnaire including lifetime and previous month prevalence of suicidal ideation, lifetime suicide attempts, perceived probability of future suicide, as well as lifetime prevalence, method and purpose of self-injurious behavior. Results were compared to a previously concluded survey with the same questionnaires in healthy subjects.

**Results:** 126 patients (68%) returned the questionnaires. 37 patients reported occasional, seven repeated and one patient reported frequent suicidal ideation. Nine patients reported attempting suicide once and two patients twice in their lives. Nine patients considered lifetime suicide as probable. 16 patients reported ever engaging in self-injurious behavior, of them seven cutting with a sharp object, three overdosing with insulin and six using other methods.

**Conclusion:** Suicidal behavior in Slovenian adolescents with type 1 diabetes appears to be less frequent as compared to a control group of healthy, age-matched high school students. Even though Slovenia has one of the highest suicide rates in the world, the prevalence of suicidal behavior in our adolescent diabetic population is comparable to the reports from other countries. Some additional adolescents with T1D at risk for such behavior may be among the non-responders. Screening and prevention remain very important.

P/WED/06

### Cognitive and emotional disorders in children with diabetes mellitus

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There are few and controversial data examining the cognitive and emotional disorders in children with diabetes mellitus (DM).

**Objectives:** To determine rate of cognitive and emotional disorders in children with DM and to study correlation between these disorders and metabolic characteristics of disease.

**Methods:** Cognitive and emotional processes were studied in 100 children with DM by using the data of a survey and psychological tests. Statistic analysis: ANOVA, Spearman's correlation (rs).

**Results:** Diabetic children had the cognitive and emotional disorders: cognitive disturbances in 74%, of them 54, 59, 21 and 30% had diminished thinking, sense and mechanical memory, and attention, respectively. A half of the children were found to have emotional disorders such as anxiety, 32% - depression and 25% - aggression. A behavioral deviation was diagnosed in 33% diabetic children. There was the negative correlation between the level of thinking, memory and attention ( $r = -0.73$ ,  $r = -0.9$ ,  $r = -0.41$ ,  $p < 0.01$ ) and the positive correlation the level of the anxiety, depression and aggression ( $r = 0.73$ ,  $r = 0.65$ ,  $r = 0.54$ ,  $p < 0.05$ ) and Hemoglobin A1c, %. Impairments of cognitive and emotional sphere were encountered in decompensated more frequently than in compensated and subcompensated DM ( $p < 0.01$  and  $0.05$ ). Outworked program of the rehabilitation including the music therapy, color therapy, fairytale telling and the course of the treatment of the nootropics (3 months). The program of the rehabilitation showed significant positive changes in cognitive and emotional sphere in 47 (69%) diabetic children ( $p < 0.01$ ).

**Conclusions:** Diabetic children had cognitive (diminished thinking, memory and attention) and emotional (behavioral deviations, higher levels of the anxiety, depression and aggression) disorders. The rehabilitation including nootropics, music therapy, color therapy, and fairytale telling is effective in 69% of children with a diabetes mellitus.

P/WED/07

### Gender differences in compliance and psychosocial factors among adolescents with insulin dependent diabetes mellitus

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**Background:** It has become increasingly obvious that psychosocial well-being is important for young diabetics and their families.

**Objective:** To explore relationships between psychosocial factors, compliance and metabolic control in adolescents with diabetes mellitus.

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**Methods:** Adolescents with DM (n = 46, age 11–17 years, 25 girls) completed measures of compliance, mother's supportive versus non-supportive behaviour in relation to daily diabetes routines, family sharing of diabetes responsibilities, general family functioning, and QOL. Metabolic control was assessed by patient's latest Hemoglobin A1c value.

**Result:** Mean Hemoglobin A1c was 8.45 (0.97). A near-significant association was found between Hemoglobin A1c and compliance (r = 0.30, p = 0.051). No associations between Hemoglobin A1c and the psychosocial factors were found. Correlations between compliance and psychosocial factors are shown in the table below.

	Boys	Girls
Mother's diabetes specific non-supportive behaviour	-0.54*	-0.54*
Mother's diabetes specific supportive behaviour	-0.45*	0.37
Family sharing of diabetes responsibilities	-0.31	-0.61**
General family functioning	-0.27	-0.61**
Impact diabetes	0.13	-0.45*
Worries diabetes	0.05	-0.29
Life satisfaction	0.01	-0.71**

**Conclusion:** Validity of the compliance measure was supported. In both genders, lack of maternal support was associated with poor compliance. General family functioning and way of sharing diabetes responsibilities were more important predictors for girls, and maternal supportive behaviour predicted poor compliance only for boys, suggesting that boys and girls with DM react differently to parental involvement both regarding DM and in general. The difference between boys and girls regarding the association between compliance and quality of life perhaps reflects that boys evaluate self-care as less important than girls. The findings underline the importance of a family and gender perspective in diabetes care.

### P/WED/08

#### Prevalence and persistence of disturbed eating behavior and eating disorders in girls with type 1 diabetes mellitus

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**Objective:** To describe the prevalence and persistence of disturbed eating behavior (EB) and subthreshold/full syndrome eating disorders (ED) in girls with type 1 diabetes over a 5 year study period.

**Research design and methods:** Participants were 9–13 years of age at study inception. Participants completed a structured diagnostic interview for ED at up to five assessment points over 5 years. Body mass index and hemoglobin A1c were also assessed.

**Results:** Of 126 original study participants, multiple assessments were procured for 116 participants. At time 5, 49.0% had current disturbed EB, and 13.3% of girls met criteria for a current ED. Both point prevalence and cumulative prevalence of disturbed EB and ED increased with higher age. Disturbed EB was highly persistent from early to later stages of the study, and was associated with significantly higher body mass index, but not consistently with worse metabolic control. Rates of overweight and obesity were high in this sample (34.7% and 10.2% respectively).

**Conclusions:** Disturbed EB is common and persistent in pre-teen and teen-age girls with type 1 diabetes, suggesting that these disturbances are neither transient nor benign. Further research into effective screening and active intervention is needed in this high-risk group.

### P/WED/09

#### 'Chronic Sorrow' in parents of children with type 1 diabetes

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**Objectives:** Assessment of emotional strain ('chronic sorrow') in parents of children suffering from type-1 diabetes.

**Methods:** In a cross-sectional study 69 parents of children with type 1 diabetes (37 mothers, 32 fathers; aged 28–65 years, = 41,1, s = 6,5; duration of child's illness 0–10 Jahre, = 46,8 months, s = 29,9 months) were investigated by a clinical questionnaire in order to assess their experience of 'chronic sorrow', quality of life as well as clinical and demographical parameters. Comparison groups were parents of children suffering from juvenile idiopathic arthritis (n = 161) and haemophilia (n = 47).

**Results:** Parents of children with type 1 diabetes often experience sadness, because of their child's illness (53,5%) and express pronounced worries, particularly so with regard to the future of their children in general (43,4%). A significant relationship was found between the extent of 'chronic sorrow' and the severity of the child's restrictions in daily life (subjective evaluation, r = 0.39; p ≤ .01). As could be expected, pronounced illness worries go along with severely diminished quality of life in parents (r = -0.42; p ≤ .001). Compared with parents of children with juvenile idiopathic arthritis, parents of children suffering from type 1 diabetes experience 'chronic sorrow' to a lesser extent, compared with parents of children with haemophilia to a greater extent (F = 33.98; p ≤ 0.001).

**Conclusion:** Medical and psychosocial care should be more responsive to the experience of 'chronic sorrow' in parents of children with type 1 diabetes.

### P/WED/10

#### Evaluating the problem of marriage in type 1 diabetics in India

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**Aim:** To highlight main hurdles in marriage of a type 1 diabetic in Indian scenario. Find out the solutions at social level.

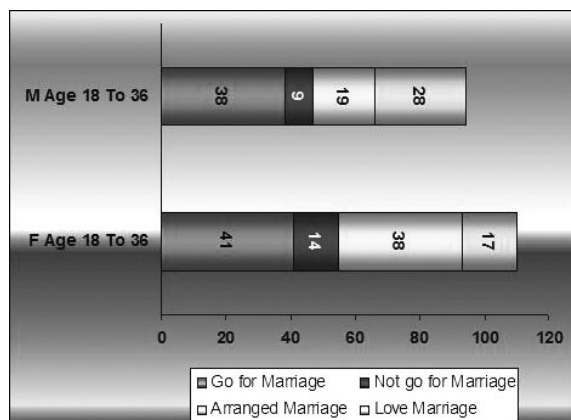
**Method:** India is a big country with many types of society and religions distributed across the country. We collected data from delegates (people with type 1 diabetes) during the session 'marriage and diabetes' in first ever workshop on type 1 diabetes at National Type 1 Diabetic Meet 2007 at Kanpur, a city in Northern India. The study done on the basis of questionnaire to the people with type 1 diabetes. Although the sample size is very small but reflects the real image of problems. The open discussion was there in between patients, parents, socialist and endocrinologist for the problems and their best possible socially accepted solution.

Total participants in the workshop were 320 type 1 diabetics out of them 180 female and 140 male of all age group, and the above 18 years of age male-47/ female-55. The questions are

1. Do you think you should go for the marriage?
2. Do you feel that marriage is problem?
3. What kind of marriage you believe? Arranged / love marriage
4. People who creates maximum problem regarding your marriage?
5. Do you feel benefited by this workshop?

**Results:** Even 25% of diabetic females feel that they should not marry; this percentage is only 20% with males. The problems are more with the females in getting married rather than males. About 70% female opted for arranged marriage against them only 40% male opted for that. Maximum problem during marriage is created

by the parents or relatives. Even after great discussion only 75% were in favour of that they were benefited with the workshop. [Marriage and Diabetes]



**Conclusion:** Maximum problems are with females due to social circumstances. Awareness of type 1 diabetes and their problems is very less in the society therefore nobody wants to marry a 'sick lady'.

## Diabetes Care, Education, Psychosocial Issues – Education

P/WED/11

### Diabetes mellitus type 1: problems of training of children

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Training of children with T1DM is essential for good metabolic control. The problems of training are associated with mental features, particularly in puberty.

**Objectives:** To study the mental features in children with T1DM to evaluate the efficiency of training.

**Methods:** 40 children with aged 10–15 years were investigated. Psychologic status was evaluated by tests of Aisenk (introvert, extravert, neurotism, lying), Leonard-Shmishek (person's accentuation), Belov (temperament), projective pictures. The efficiency of training was evaluated by test of knowledge diabetes, Hemoglobin A1c, incidence of ketosis.

**Result:** Most of children have got a good knowledge, but don't use it. This fact determines a compensation level and depends on psychologic features of children. High levels of aggression, uneasiness and high index of lying were revealed. These features mean the condition of mental stress, and make it difficult to provide self-control.

**Conclusion:** Features of psychologic status in children with type 1 diabetes are necessary to allow for make a special program of training. Methods of psychologic correction should be included.

P/WED/12

### Implementation of a teaching program for diabetes in schools

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**Objective:** To design an education program for nurses within the Kids Outreach Liaison Service (KOLS) at The Children's Hospital at Westmead (CHW), to teach diabetes management in schools.

**Background:** With an increase in intensive management in paediatric diabetes, schools are now playing an important role in managing glycaemic control in children with type 1 diabetes (1). Schools have an obligation to maintain a duty of care for children with diabetes. It is therefore essential that staffs are trained by appropriate health professionals in diabetes management principles in order for students with diabetes to maintain safe glycaemic control at school (2). Diabetes Australia-NSW (DA NSW), the consumer organisation, has limited ability to offer school visits to all NSW. Alternative options to school visits from CHW allied health staff therefore had to be developed in order to sustain demand to teach diabetes within schools.

**Method:** A half day education program was given by a Diabetes Educator, Dietitian and Social Worker to 7 KOLS Registered Nurses who cover community outreach of Western Sydney. Sessions provided staff with knowledge to teach schools basic diabetes management principles: pathophysiology, blood glucose monitoring, injection techniques, hypoglycaemia management, nutrition and social work perspectives. The education program then uses a 'buddy' system for the first two school visits, to observe and then educate/evaluate.

**Results:** To date 7 KOLS staff has been trained within the program. Five of seven staff has completed a 'buddy' school visit with an educator. It is hoped that within 3 months all KOLS staff will have completed the evaluation phase.

**Conclusions:** At 3 months initial feedback has shown KOLS staff enjoy school diabetes education, families have also provided positive feedback. Evaluation is however continuing.

**References:** (1) Diabetes Australia-NSW, 2007 (2) ADA 2005, Diabetes Care.

P/WED/13

### Managing diabetes in children: 'from prescription to empowerment: a comprehensive approach'

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**Objectives:** The overall objective of this study was to evaluate and gather evidence on current perception of populace about role of physical activity (exercise and sports) and lifestyle in the management of a diabetic child and to gauge the effectiveness of intervention provided by the health care professionals to educate the children with diabetes and their carer.

**Methods:** A single blinded epidemiological need assessment has been carried out for a period of three months beginning January 2007 to March 2007. Semi structured qualitative questionnaires (n = 100) were sent to all the children with diabetes under clinical care of local hospital.

**Result:** A significant number responded to the questionnaires (54%); majority of them were active and involved in adequate physical activities/week; also they were aware that having diabetes do not confine their physical activity and entail a little risk. Majority perceived only hypoglycaemia as a risk. 32% encountered some difficulty during exercise and didn't experience any inequality towards them. 72% were satisfied with existing service and support given by the treating professionals but further analysis identified that only 50% of respondents appeared to have requisite knowledge to modify their health status through appropriate interventions during exercise management of diabetes.

**Conclusion:** The study concluded with the convincing evidence that majority of the populace are aware that regular physical activity has a positive role in lifestyle of a diabetic. However there has been insufficient practical knowledge amongst the children and their

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carers emphasising the need for appropriate facilitation of information delivered in this group. Authors can recommend an inclusive approach between clinicians, other support providers and public health through a strong local action plan of managing diabetes in the community (3rd & 5th standards of National Service Framework and NICE guidelines UK).

P/WED/14

### To balance decision-making competence and parent involvement in empowerment education in teenagers with diabetes

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**Objectives:** A previous study that assessed an empowerment programme for teenagers with diabetes showed no effects on metabolic control or empowerment outcomes. In pre/post measures teen-agers > 14 years of age significantly increased their Hemoglobin A1c, and the whole group their readiness for changes. To balance the teen-agers' decision-making competence with parent involvement seems to be important when planning empowerment programmes for teenagers. The aim was to achieve a deeper understanding of teen-agers view on decision-making competence and parent involvement.

**Methods:** The study is a descriptive, qualitative interview study. Thirty one out of 32 teenagers (19 girls, 13 boys, mean age = 14.2) attending an empowerment programme was interviewed after completing the programme. The interviews were transcribed, and analyzed with qualitative content analysis.

**Result:** Decision-making competence: We found four categories that influence decision-making competence. Cognitive maturity: Make abstractions and priorities, understand consequences. Personal qualities: Self-strength, flexibility, intuition and having courage. Experience: Own experiences or experiences from others. Social network can be both promoting and hindering. Parent involvement: We defined three categories of parent involvement: Constructive involvement: Creating safety and teamwork. Parents being there when needed, having trust, sharing responsibility, listening and coaching. Active destructive involvement: Misbelieves, blaming and making too hard demands. Passive destructive involvement: Lack of understanding and engagement, need of control and conflicts.

**Conclusion:** We have elucidated factors that seem to be important when planning empowerment group education programmes for teenagers with diabetes. To facilitate parent involvement the results can be used in discussing efficient coping strategies with teenagers and parents.

P/WED/15

### Training programs for obese children with metabolic syndrome

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Metabolic syndrome (MS) (abdominal fat, insulin resistance and/or high blood sugar, high blood pressure, high triglyceride levels in blood, et cetera) makes obese children unusually prone to type 2 diabetes mellitus and cardiovascular disease. The treatment of patients with MS must include pharmacotherapy and motivating training programs (TP) different from age.

**Aim:** To create different TP for obese children with MS 5–7 years old, 8–12 years old and teen-agers.

**Patients and methods:** 56 obese children with MS (BMI > 95<sup>th</sup>) 5–12 years old were investigated ( $11,9 \pm 1,5$ —mean age). Insulin resistance was diagnosed according to HOMA. BMI, WC, Fat Mass (FM% by BIA) was measured. Patients of group 1 (n = 29) had pharmacotherapy (metformin 500 – 1500 mg in day) after TP, patients of group 2 (n = 27) had pharmacotherapy without TP. All measurements were repeated after 6 months of treatment.

**Result:** Was to create different TP for children with MS 5–7 years old, 8–12 years old and teen-agers. TP includes questionnaires, group training (5–7 kids), fairy-tale therapy, music therapy, consultation of dietologist and psychologist. TP help kids to make healthful choices in physical activity and nutrition motivated them. Significant decrease of BMI ( $26,5 \pm 3,9$  kg/m<sup>2</sup>,  $22 \pm 4,3$  kg/m<sup>2</sup>, p < 0,05) parallel to decrease of FM% ( $34,87 \pm 7,24\%$ ,  $30,75 \pm 7,29\%$ , p < 0,05), HOMA ( $5,6 \pm 0,8$ ,  $3,1 \pm 0,7$ , p < 0,05) were revealed in patients of group 1. Biochemical indexes normalized in 9 (31%) kids. No significant changes in BMI, FM, and HOMA were registered in group 2. Biochemical indexes normalized in 4 (14,8%) kids with pharmacotherapy only.

**Conclusion:** Training of obese children with MS is essential for effective treatment of MS: weight decrease, and good metabolic control.

P/WED/16

### Patients and parents' diabetes mellitus type I knowledge degree and its correlation with haemoglobin A1C value

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Diabetes mellitus type 1, is a chronic disease in which the active participation of patients (pt) together with their families (fl) is an important step towards a good metabolic balance and risk decrease of its future complications. In our paediatric endocrinology unit (PEU), at the diagnosis, all pt and fl start a training program regarding theoretical and practical diabetes aspects.

**Aims:** Evaluation the degree of knowledge of diabetic pt and their parents (pr) concerning their disease, and to correlate these results with the haemoglobin A1c (HgA1c) value.

**Material and methods:** The PEU elaborated an inquiry with 14 questions about the peculiarity of this chronic disease, which was distributed randomly during a month period. The HgA1c value at the time of the inquiry and three months later were evaluated.

**Result:** Fifty pt answered the inquiry, 56% male, mean age 14 years (6–20). Mean HgA1c value at the time of the inquiry was 8,9% (6–14). Three months later 56% of pt improved their HgA1c value. Eighty eight percent of the 25 pt with HgA1c 6–8% answered correctly to more than 60% of the questions. Seventy five percent of the four pt with HgA1c 12–14%, answered incorrectly to more than 60% of the questions. Right answers percent from pt and from pr, in questions related to/with: variability of the glycaemia values (63%pt/58%pr); different types of insulin (35%pt/34%pr); exercise (81%pt/86%pr); diet (88%pt/91%pr); sites of insulin administration (68%pt/77%pr); capillary glycaemia puncture (59%pt/64%pr); infections (20%pt/22%pr).

**Conclusion:** This inquiry allowed the evaluation of diabetic pt and their pr knowledge degree about this disease. There were registered many doubts and some mistakes, which emphasized the need for crescent motivation and involvement of pt and their fl in the treatment, that is the best goal to prevent the acute and long-term complications. HgA1c value can be an indirect measure to evaluate the knowledge degree.

P/WED/17

### Diabetes self-care: the perspectives and experiences of children and adolescents

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**Introduction:** Poor compliance with diabetic treatment can lead to serious complications. Although studies have examined issues relating to compliance, children's understanding of their disease and perceptions around self-care are often not addressed. The purpose of this presentation is to discuss findings related to how youth understand their diabetes as well as the processes that elicit, sustain and inhibit self-care from their perspectives.

**Methods:** A sample of 60 participants between 5–18 years of age who had been diagnosed with type 1 diabetes for at least one year were recruited from the Sick Kids outpatient clinic. Basic demographic data as well as individual interviews comprised the data collection. Interviews were audio taped and transcribed. Data were coded using well-established coding methods.

**Results:** Participants believed that children should take gradual responsibility in caring for their diabetes. A range of challenges and benefits were associated with having diabetes, and suggestions for how to elicit participation from youth were also addressed. For example, adolescents discussed the significance of being recognized for their knowledge of diabetes while also addressing certain approaches by parents which can inhibit self-care initiatives.

**Conclusions:** The findings reinforce the significance of accessing the views of youth with diabetes in order that health care providers and parents can adequately foster self-care initiatives. Future implications for clinical practice will be explored.

P/WED/18

### Effectiveness of educational intervention with Snakes and Ladders board game in children with type 1 diabetes

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**Objectives:** To determine the effect of an educational intervention, using a Snakes and Ladders board game, in children aged 6–16 years with type 1 diabetes.

**Method:** This was a prospective, non-pharmacological interventional case-control unicentre study. A Snakes and Ladders game, modified to increase diabetes knowledge, with positive behavioural messages at the foot of each ladder, and negative messages at each snake mouth, was distributed to 40 children (study group). Children (and parents) were encouraged to play the game at home. A simple bilingual questionnaire was filled in at this visit, and HbA1c monitoring done. Data was collected regarding frequency of glucose estimation, urine testing, and concordance with suggested diet/drug therapy. Similar data was obtained at 3 and 6 months follow up. A control group of 20 children did not receive the board game, but had access to routine diabetes counselling, as did the study group. Similar baseline and quarterly data was recorded for the control group.

**Results:** Rural children reported more frequent use of the game than urban children ( $3.25 \pm 1.91/\text{week}$  vs.  $2.16 \pm 2.66/\text{week}$ ). Girls and boys tended to play with similar frequency ( $2.60 \pm 1.86/\text{week}$  vs.  $2.57 \pm 2.65/\text{week}$ ). The study group showed a marked improvement in diabetes knowledge (score increased from  $12.80 \pm 2.34$  to  $16.50 \pm 2.65$ ), blood glucose monitoring ( $1.60 \pm 1.04$  to  $2.30 \pm 1.88/\text{month}$ ), urine sugar testing ( $3.80 \pm 1.87$  to  $5.40 \pm 1.57/\text{month}$ ), and reported concordance

to diet (dietary indiscretions  $2.10 \pm 1.37$  to  $1.05 \pm 0.76/\text{week}$ ) and insulin therapy ( $2.20 \pm 0.92$  missed doses/week to  $1.40 \pm 0.69$ ) at 3 months. Results were statistically significant for all parameters as compared to the control group. The study was prematurely terminated at 3 months in view of the obvious benefits.

**Conclusion:** A simple educational intervention, using a Snakes and Ladders board game, is effective in improving health-related behaviour in children aged 6–16 years, with type 1 diabetes.

P/WED/19

### The usefulness of continuous glucose monitoring as an educational tool for the improvement of glycemic control in children and adolescents with diabetes type 1

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Intensified insulin treatment is the treatment of choice in children and adolescents with diabetes type 1, and HbA1c values  $< 7.2\%$  are considered an ideal target already from the onset of diabetes even in very young children. However, the fear of hypoglycemia is the main limiting factor, why so many parents, despite acknowledging the importance of good glycemic control, are reluctant to adjust the insulin dose sufficiently to obtain near-physiologic blood glucose levels. Continuous glucose monitoring systems (CGMS) provide health care providers with an additional teaching tool in the education of families of diabetic children. Aim of the study was to assess the effectiveness of CGMS in helping diabetic children and their families achieve a better glycemic control.

**Patients and methods:** Thirty-three children and adolescents with diabetes type 1 aged  $12.7 \pm 3.6$  years (range 6.5–19.6) with diabetes duration of 0.5–12.3 years, who are followed regularly at the Diabetes Centre of the First Department of Pediatrics, University of Athens, were included in the study. All participants wore the Glucoday (Menarini Diagnostics Co) CGMS for 48 hours and their HbA1c values as well as their daily insulin requirements were assessed before and 3 and 6 months after the application of CGMS. **Result:** Mean HbA1c value of the participants before CGMS was  $8.56\%$  ( $\pm 1.2$ ) and decreased significantly to  $7.84\%$  ( $\pm 0.96$ ) 3 months and to  $7.81\%$  ( $\pm 0.8$ ) 6 months after the use of CGMS, respectively ( $p$ -value  $< 0.001$ ), although their daily insulin requirement remained stable ( $0.9 \text{ IU/Kg/day}$  versus  $0.905 \text{ IU/Kg/day}$ ).

**Conclusion:** The use of 48-hour continuous glucose monitoring in type 1 diabetic children led to recognition of hyperglycemia periods and resulted in improvement of glycemic control, which persisted for at least 6 months after the CGMS measurements without need of daily insulin dose increase.

P/WED/20

### The diabetes rollercoaster – riding the highs and lows

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**Objectives:** The aim of this study was to identify whether the range of symptoms commonly associated with hypo- and hyperglycaemia by paediatric diabetic patients differs from those recognised in medical literature.

**Methods:** All parents and the adolescents attending diabetic clinic were given questionnaires asking what symptoms they most often experience and associate with hypo- and then hyperglycaemia. From a list of 39 recognised symptoms they also indicated any experienced and which condition they associated it with.

**Results:** 24 parents from the pre-adolescent clinic, and 49 adolescents and their parents participated. 92% of parents of pre-adolescents felt they could always or usually identify hypoglycaemia

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compared to only 38% for hyperglycaemia. 92% of adolescents and 67% of their parents felt they could always or usually identify hypoglycaemia again with 53% & 54% respectively recognising hyperglycaemia. The most common hypoglycaemic symptoms were pallor, shaking, dizziness and tearfulness. In hyperglycaemia they were thirsty, urinary frequency and headache. Bad behaviour and tiredness were common in both conditions and only a few of the recognised symptoms were exclusive to one or other condition. Some patients described new and numerous symptoms.

**Conclusion:** This study shows that some patients experience the same symptoms during hypo- and hyperglycaemia and reinforces previous studies showing symptom variation between patients. It reinforces the need to educate patients and parents to identify their own symptom portfolio with confirmatory blood monitoring, and to not rely solely on recognised symptoms to identify hypo- and hyperglycaemia.

## Diabetes Acute and Chronic Complications I

P/WED/21

### Eye and renal complications in type 1 diabetes mellitus in National Hospital of Pediatrics in Hanoi – Vietnam

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We have 151 patients (52 males and 99 female) with T1DM, from 1 month to 16 years. Diabetes club meeting has been held annually for 8 years to share experience between patients & doctors. Insulin has been donated to 1/3 of our patients by NGO Assembly of God.

**Objective:** The study described clinical and laboratory features of eye and renal complication in diabetic patients, excluded patients who had eye or renal complications before having DM.

**Method:** A cross-sectional, descriptive study was retrospectively carried out to review 58 patients coming club meeting in 2006.

**Results:** Eye complication's found in 17.2% (10/58). Renal complication was noticed in 20.7% (12/58). In our patients, 36.2% had both complications in the eye and in the kidneys. Eye complication developed in the first five year of DM in 51.6%. Mean duration of DM when patients developed eye complication was  $6.2 \pm 5.1$  years. In eye complications, retinopathy was found in 38.7%, cataract in 22.6%. In the first five years of DM, non-proliferative retinopathy and cataract developed in 72.7% & 45.4%, respectively. In patients with HbA1c of less than 7.6%, retinopathy and cataract were found in 8.3% and 5.3%, respectively. Patients with HbA1c above 9%, retinopathy and cataract were found in 79.2% & 78.9%, respectively. In term of renal complication, edema, and hypertension, microalbuminuria above 100 mg/l were found in 24.2%, 27.2%, and 24.2%. In a good compliance group, 66.7% did not have complications, but in non-compliance group only 33.3% did not have complications. Renal complication with clearance creatinine of potential renal failure was seen in 72.7%.

**Conclusions:** The main factor affecting on eye and renal complication are poor compliance of the patients.

P/WED/22

### Onset of late complications is heavily influenced by the characteristics of postinitial remission in children with type 1 diabetes

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**Objectives:** Previously we have shown that in children with type 1 diabetes mellitus (T1DM), occurrence and length of postinitial

remission (PR) are mainly determined by glycated hemoglobin (HbA1c), endogenous insulin reserve (C peptide), and the presence of auto-antibodies at onset.

**Aim:** The aim of the present study was to analyze the effect of frequency and duration of PR on the onset of late complications.

**Methods:** Connection between metabolic parameters, characterizing PR and the occurrence of hypertension (HT) and microalbuminuria (MA) were studied. Children diagnosed with type 1 DM at our department between January 1995 and December 2004 (n = 227) were enrolled in the study. Patients were regularly screened for the occurrence of HT by ambulatory blood pressure measurement, for MA with immune nephelometry and for the signs of retinopathy (Rp) by ophthalmoscopy. Mean age and mean duration of diabetes at follow up were 14.0 (12.2–18.3) and 5.3 (4.5–8.3) years, respectively. Statistical analysis was performed by analysis toolpack and chi-square test.

**Result:** HT occurred in 59/227 patients (26 %), MA in 19/227 (8,3%) children, while no Rp was found. Mean age at onset of HT was  $13.7 \pm 1.4$  and that of MA was  $12.3 \pm 1.1$  years. HT was 1.5 times more prevalent in boys than in girls. Both complications have occurred after a mean duration of 5.1 years. There was a significant negative correlation ( $p < 0,05$ ) between the occurrence and magnitude of MA and duration of PR. Significant negative correlation ( $p < 0,05$ ) was found between HbA1c at onset and occurrence of both HT and MA. Frequency of MA was 4 times, while magnitude of albumin excretion was 2 times higher in non-remitters compared to remitters. HT occurred only in 25% in remitters, while in 75% of non-remitters.

**Conclusion:** In conclusion, occurrence and length of postinitial remission have major impact on the onset of early signs of late complications in children with type 1 diabetes mellitus.

P/WED/23

### Acute complications continue as a major cause of death for children and young adults with type 1 diabetes

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**Objectives:** To examine mortality rates and cause of death amongst subjects diagnosed with type 1 diabetes (T1D) aged 0–29 years.

**Methods:** A population-based register with a 98% ascertainment rate was used to identify subjects diagnosed with T1D aged 0–14 years from Yorkshire (1978–2004) and 15–29 years from West Yorkshire (1991–2004). Death notifications were coded according to ICD-9 (1979–2000) and ICD-10 (2001–2005). Person-years at risk analysis calculated expected numbers of deaths using UK mortality rates and standardized mortality ratios (SMR).

**Result:** 3,349 and 897 patients diagnosed aged 0–14 and 15–29 years represented 50 472 person years of follow-up. Mean follow-up length was 12.8 years for 0–14 s and 8.3 years for 15–29 s. Only ten patients (0.2%) were untraceable. Overall 107 (2.5%) patients died and 76 (71%) were male. 73 (2.2%) deaths occurred amongst 0–14 s and 34 (3.8%) in the older group. The overall SMR was 4.6 (95% CI 3.8–5.6) and similar by sex. The SMR rose with increasing disease duration. 47 deaths (44%) occurred from diabetes complications: acute complications (n = 32) comprised 14 from DKA, 2 hyperglycaemia (without mention of DKA), 8 hypoglycaemia and 8 unspecified. Chronic complication deaths (n = 15) included 6 from heart disease, 1 stroke and 8 renal (6/8 were female). 24 (22%) deaths were due to accidents/violence (SMR 2.1; 1.4–3.2), of which 5 were from

suicide; the SMR was also higher for females (3.4; 1.4–6.9) than males (1.9; 1.1–3.0). 9% of deaths (10/107) were related to drug misuse (excluding insulin/alcohol) (SMR = 3.1, 1.5–5.7). 19 deaths were of other/unknown cause.

**Conclusion:** Long-term follow-up for 0–29 year olds demonstrated a 4.5-fold excess mortality risk, an effect which increased with disease duration. Almost half the deaths were from diabetes complications but with continued vigilance most of such future fatalities should be preventable. An emerging trend for young people with T1D to misuse drugs warrants further research.

P/WED/24

### Diabetic ketoacidosis among children with established type 1 diabetes during one year at a Norwegian University Hospital

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**Objectives:** The risk of diabetic ketoacidosis (DKA) is 1–10% per patient and year in established type 1 diabetes. We registered the number of patients who had presented with DKA in our clinic during one year, and evaluated severity and etiology.

**Methods:** The 131 children at our clinic with established type 1 diabetes who participated in the yearly national benchmarking study in 2006 were examined for DKA during the year prior the benchmarking visit in 2006. Results are given as (%), fractions and means (range).

**Result:** 7 patients (5.3%) fulfilled the criteria (hyperglycemia, ketonuria and a venous pH < 7.3) for DKA. The mean age of the patients was 10.8 years (7–15.5) and the mean duration of diabetes was 4.2 years (2.5–9.0), mean pH 7.1 (6.98–7.23), mean blood glucose 24 mmol/l, (11.9–42.0), mean HbA1c 10.2 % (8.0–12.0), 5 of 7 patients used insulin pumps, 3 of 7 patients presented with infections. The mean duration of having symptoms of hyperglycemia before contact was taken with the hospital was 3.6 days (1–6). It was not possible to evaluate how many patients had observed ketones in urine prior to hospitalization. None of the patients developed cerebral edema.

**Conclusions:** All of the patients with DKA had poor metabolic control (mean HbA1c 10.2%). The patients realized something was wrong 1–7 days before they contacted the hospital. The main etiology of DKA was omitting or not using adequate doses of insulin. Especially, the meal doses were often neglected. Three patients also had infections, but none of them were serious. As a consequence of this analysis, we will instruct our patients to contact the hospital at an earlier point when the blood glucose gets out of control. We also want to analyze each new case of DKA in a systematic manner and use the results to improve our diabetes care.

P/WED/25

### Oxidative stress is increased in type-1 diabetic children with good glycaemic control and glomerular hyperfiltration

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**Objective:** To investigate the relation between the glomerular hyperfiltration (HF) and systemic oxidative stress in children and adolescents with type 1 diabetes mellitus (DM1).

**Patients:** Twenty-nine young DM1 normotense, without retinopathy and HbA1c < 9% were selected for the study. A group of control subjects of healthy children of similar sex and age was included.

**Method:** Glomerular filtration (CCr) and microalbuminuria (MA) were measured with 24 h urine samples. Antioxidant activity was estimated by the erythrocyte glutathione-peroxidase (GPx), the reduced glutathione (GSH) and plasmatic concentrations of  $\alpha$ -tocopherol and  $\beta$ -carotene; the lipoperoxidation by malondialdehyde (MDA) and the oxidative damage to proteins through plasma protein carbonyl groups (PCG). Clinical and metabolic variables and oxidative stress were compared in patients with HF (CCr  $\geq$  150 ml/min/1.73m<sup>2</sup>) and with normal CCr (non-HF). The differences between the groups were measured through variance analysis and non-parametric tests (SPSS-12.0).

**Results:** See table (means  $\pm$  SD)

Variable	Controls (n = 13)	Non-HF < 150 ml/ min/1,73 m <sup>2</sup>	
		min/1,73 m <sup>2</sup> (n = 14)	HF $\geq$ 150 ml/min/ 1,73 m <sup>2</sup> (n = 15)
HbA1c (%)	4,75 $\pm$ 0,26	7,14 $\pm$ 0,67 a	7,96 $\pm$ 0,68 b,c
CCr (ml/min/1,73 m <sup>2</sup> )	116,65 $\pm$ 9,76	128,46 $\pm$ 11,07	166,39 $\pm$ 14,99 b,c
MA (mg/g creatinine)	5,96 $\pm$ ,61	10,98 $\pm$ 5,81 a	11,24 $\pm$ 5,96 b
GPx (U/g Hb)	91,58 $\pm$ 47,0	98,29 $\pm$ 44,80	96,20 $\pm$ 40,94
GSH (mmol/g Hb)	1,78 $\pm$ 0,48	1,71 $\pm$ 0,95	1,60 $\pm$ 1,04
alpha-tocopherol (nmol/g Co+Tg)	1,75 $\pm$ 0,40	1,49 $\pm$ 0,58	1,47 $\pm$ 0,50
beta-carotene (nmol/ml)	1,42 $\pm$ 1,15	1,11 $\pm$ 0,54	0,91 $\pm$ 0,39
PCG (nmol/mg prot.)	1,17 $\pm$ 0,20	1,38 $\pm$ 0,37	1,62 $\pm$ 0,65 b
MDA (nmol/ml)	25,31 $\pm$ 6,61	31,88 $\pm$ 10,74	36,36 $\pm$ 12,82 b

(a) p < 0,05 non-HF vs. Controls, (b) p < 0,05 HF vs. Controls, (c) p < 0,05 non-HF vs. HF.

**Conclusions:** Overall, with regard to the group of control subjects, the DM1 patients showed oxidative stress with increased (p < 0,05) MDA (34,20  $\pm$  11,84 nmol/ml) and PCG (1,51  $\pm$  0,54 nmol/mg protein), despite good glycaemic control (HbA1c = 7,56  $\pm$  0,79%). In the DM1 patients, those with HF showed greater oxidative damage (p < 0,05) and a slight increase of urinary albumin excretion, which suggest a narrow relation between oxidative stress and subclinic renal dysfunction in short evolution DM1.

P/WED/26

### Evaluation of the benefits of regular exercise on glycaemic control and on potentially acute risks (diabetic ketoacidosis, rate of severe hypoglycemia) in children with diabetes type 1

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**Objectives:** Regular physical activity is recommended to patients with diabetes type 1. To evaluate the benefits of exercise on glycaemic control (HbA1c) and on potentially acute risks (diabetic ketoacidosis [DKA], rate of severe hypoglycemia and of hypoglycemia with loss of consciousness) in children with diabetes type 1.

**Methods:** Anonymous data of 22.438 pediatric patients (age 3.0–19.9 years; 6859 girls) with diabetes type 1 were provided by the Pediatric Quality Initiative (DPV), including data from 233 centers in Germany and Austria. Patients were grouped by the frequency of their regular physical activity per week (FRPA) as follows: FRPA0 = none, FRPA1 = 1–2x/week, FRPA2 = > 2x/week.

**Result:** Frequency of regular physical activity was 0–9 (mean 1.6) times/ week. Mean HbA1 was 8.1%; mean rate of DKA was 4.9 per 100 patient years. Multiple regression analysis revealed that

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high FRPA was associated to lower HbA1c ( $p < 0.00001$ ) and a lower rate of DKA ( $p < 0.001$ ). This was found in both sexes and in all age groups older than 9 years. There was no difference between the FRPA groups concerning the rate of severe hypoglycemia or hypoglycemia with loss of consciousness.

**Discussion:** In children with diabetes type 1 regular physical activity is associated to a better glycaemic control including a lower HbA1c and a lower rate of diabetic ketoacidosis. There is no elevated risk of severe hypoglycemia or hypoglycemia with loss of consciousness in children exercising frequently.

P/WED/27

### Children presenting in DKA at diagnosis have higher HbA1c during the initial 8 years of type 1 diabetes independently of access to care and ethnicity

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**Objective:** Diabetic ketoacidosis (DKA) often heralds the diagnosis of type 1 diabetes (T1D) in children. We tested a hypothesis that children diagnosed in DKA experience worse glycaemic control later in the course of disease.

**Method:** We identified 508 T1D children diagnosed below age 18 in Colorado during 1998–2001 and followed at the Barbara Davis Center for Childhood Diabetes for at least one year, up to 8 years. Review of medical records found DKA (venous pH  $< 7.3$  or bicarbonate  $< 15$  mEq/l) at diagnosis in 158 (31%) of these children. HbA1c was measured at each visit, on average 17x/patient using the DCA2000 + (Bayer™). Individual average HbA1c was calculated as  $\Sigma$  (A1c x days between visits)/total days of follow-up. The initial 60 days after diagnosis were excluded. Medians of individual average A1c were compared using Wilcoxon rank sum test. Multiple linear regression was used to evaluate the effect of onset DKA on average HbA1c, controlling for other factors.

**Results:** In the linear regression, average follow-up A1c was increased if DKA was present at onset ( $p = 0.014$ ), independently of the effects of underinsurance (Medicaid, indigent plan or none) ( $p = 0.032$ ), gender ( $p = 0.026$ ), age at onset ( $p = 0.003$ ), ethnicity and duration of follow-up.

DKA at diagnosis	A1c at								Average (n = 508)
	diagnosis (n = 441)	Yr1 A1c (n = 488)	Yr2 A1c (n = 482)	Yr3 A1c (n = 457)	Yr4 A1c (n = 439)	Yr5 A1c (n = 405)	Yr6 A1c (n = 279)	Yr8 A1c (n = 73)	
Yes (n = 158)	11.7	8.2	8.7	8.9	8.8	8.8	8.8	9.8	8.8
No (n = 350)	10.6	7.9	8.5	8.6	8.6	8.5	8.6	8.9	8.5
p-value	< 0.001	0.021	0.162	0.011	0.036	0.018	0.131	0.071	0.003

**Conclusions:** DKA at diagnosis carries a risk of worse glycaemic control independent of access to care and demographic factors. Reduced residual insulin secretion may be a candidate factor for future studies.

P/WED/28

### Diabetic ketoacidosis in newly diagnosed children in relation to family history of type 1 diabetes

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**Objective:** To study the effect of family history of type 1 diabetes (T1D) on the frequency of diabetic ketoacidosis (DKA) in children with newly diagnosed disease.

**Method:** The study cohort comprised 1522 children under the age of 15 years (853 boys; 56.0%), who had been diagnosed with T1D in Finland between June 1, 2002 and May 30, 2005 and who have participated in the nationwide Finnish Pediatric Diabetes Register established in 2002 for patients with newly diagnosed T1D. Family history of T1D was recorded at diagnosis by the staff involved in the initial treatment of the child. First degree relatives (FDR) include the mother, the father and the siblings of the affected child. In addition the history of T1D among the grandparents was registered. DKA was defined as a pH  $< 7.30$ . Chi-square statistics, Student's two-tailed t-test and Mann Whitney U-test were used in the analyses.

**Results:** Children with an affected FDR (175/1387, 12.6%), had DKA less frequently than the other children (7.1 vs. 20.5%;  $p < 0.001$ ). Among children whose mother had T1D (40/1416, 2.8%), the frequency of DKA was 5.1 vs. 19.5%, ( $p = 0.025$ ), if the father had T1D (82/1398, 5.9%) the frequency of DKA was 7.6 vs. 19.7% ( $p = 0.008$ ), and if a sibling was affected (69/1420, 4.9%) the frequency of DKA was 7.7 vs. 19.7% ( $p = 0.017$ ) when compared to the others. If a grandparent had T1D (in 76/1159 family, 6.6%), but there was no affected FDR, the frequency of DKA was 14.3 vs. 19.3% ( $p = 0.354$ ).

**Conclusions:** The frequency of DKA was markedly lower among newly diagnosed children with an affected FDR. The effect of grandparents with T1D on the DKA frequency in the index cases remained non-significant.

P/WED/29

### Neuropsychological changes over a 6-month period in children with newly diagnosed type 1 diabetes mellitus (T1DM) and diabetic ketoacidosis (DKA)

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**Objectives:** DKA is a known complication of initial presentation with T1DM. Evidence from magnetic resonance imaging (MRI) studies suggests that children with DKA demonstrate abnormal signals in the medial frontal lobes in the acute phase. However, little is known about the impact of DKA on cognitive functioning after recovery. We aimed to delineate neuropsychological effects of DKA in children with T1DM over 6 months.

**Methods:** Four children aged 9–17 years with newly diagnosed T1DM were recruited on admission to Royal Children's Hospital, Melbourne. To examine effects of DKA on cognitive profiles, one child with severe DKA and cerebral edema (CE) (pH = 7.00), one child with severe DKA (pH = 6.70), one child with moderate DKA (pH = 7.10), and one child without DKA (pH = 7.35) were recruited. Mental status, attention and new

learning were assessed at day 1, 5, 28 and 6 months following admission.

**Results:** On day 1, DKA children demonstrated compromised mental status, and all children showed mild to significant difficulties on some attention and new learning tasks. Across the first 28 days cognitive improvement was observed in all children. While severe DKA-CE and non-DKA demonstrated appropriate cognitive skills, severe and moderate DKA continued to experience attention difficulties. Two children have completed 6-month follow-up. Severe DKA continues to show mild difficulties in divided and inhibitory attention, while no cognitive deficit was observed in non-DKA.

**Conclusions:** Findings suggest that children with newly diagnosed T1DM experience cognitive difficulties in the acute phase of admission. Severe DKA is associated with persisting difficulties at 6 months, while no residual cognitive deficit is evident in non-DKA. Attentional difficulties have implications for ongoing mastery of a range of new cognitive skills in a rapid phase of cognitive and brain development. Our study highlights the importance of long-term neuropsychological follow-up of children with DKA.

## Diabetes Acute and Chronic Complications II

P/WED/30

### Gastric emptying and its relation to microalbuminuria in children with type 1 diabetes mellitus

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**Objectives:** Disordered gastric emptying is a frequent and clinically important complication of diabetes mellitus (DM). There is little information about gastrointestinal motility abnormalities in children with type 1 DM. The aim of this study was to determine gastric emptying time in children and adolescents with type 1 DM, and to investigate the relationship between gastric emptying time and microalbuminuria in these patients.

**Methods:** Gastric emptying time with solid meals was measured in 33 diabetic children and adolescents and 28 age matched healthy controls. Three consecutive timed overnight urine collections were used to calculate microalbuminuria. Increased albumin excretion rate was defined as a median albumin excretion rate greater than or equal to 7.5 µg/min (microalbuminuria ≥ 7.5). Data were evaluated using Mann Whitney U analysis, Kruskal Wallis analysis and Pearson's correlation tests.

**Result:** Gastric emptying time was slower in healthy control group (151.72 ± 154.46 minutes) compared to diabetic patients (308.39 ± 549.82 minutes). There was no significant difference between the groups (p = 0.63). Patients were divided into two groups according to duration of diabetes as longer than 5 years and less than 5 years. Gastric emptying time in patients with diabetes longer than five years didn't differ significantly compared to patients with diabetes shorter than five years and control group (p > 0.05). There was no significant difference between gastric emptying times among patients who have higher and lower microalbumin level (p > 0.05). There was no correlation between gastric emptying time and duration of diabetes and microalbuminuria (p > 0.05).

**Conclusion:** In children and adolescents with type 1 DM, there are not significant changes in gastric emptying times. No correlation was detected between microalbuminuria that is a marker of diabetic nephropathy and gastric emptying time.

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### Relationship between diabetic complications and past glycemic controls in the first cohort of the Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes (JSGIT) – multi-center prospective analysis

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**Background:** As Hvidore study is well known as a study for a difference among international centers in glycemic in a study of children and adolescents with type 1 diabetes, JSGIT established in 1994 to improve the quality of therapy for type 1 diabetes (T1DM) in children, had two nationwide cohorts; one started from 1995 and finished in 1999 and the other started from 2000. Aim of this study is to investigate the relationship between diabetic complications of the first cohort in 2006 and the HbA1c of 1995–1999 and impacts of the change of physician in charge from Pediatricians to Internists and the puberty.

**Method:** 1995 cohort recruited 546 children from 29 centers who were born from 1987 to 1988 and developed T1DM before the end of 1995. The medical record including HbA1c was collected every 4 months. In 2006, a survey according to HbA1c and the presence of diabetic complications was performed under written informed consent of each patient.

**Results:** The age and duration of patients were 24.0 ± 3.3 years and 16.3 ± 4.0 years, respectively. Averaged HbA1c of all centers (averaged no = 13.8 ± 12.4) from 1995 to 1999, and 2007 was 8.6 ± 1.6, 8.0 ± 1.5, and 7.8 ± 1.5 %, respectively. The rate of change of doctor in charge was 28% (24.2 ± 3.0 years of age). Photocoagulation was done in 18 patients (age and duration: 26.3 ± 3.0 years and 19.1 ± 4.4 years, the rate of the change: 33.3%). Albumin > 30 mg/gCr was present in 17 patients (24.5 ± 3.3, 17.4 ± 3.4, 29%). HbA1c levels of patients with/without complications in 1995, 1999, and 2006 had 8.4 ± 1.7, 8.6 ± 2.2, and 8.8 ± 1.4% / 8.3 ± 1.6, 8.1 ± 1.5, and 7.7 ± 1.5%, respectively (p = 0.051 in 2006).

**Conclusions:** This study reveals that it is difficult to show metabolic memory clearly in Japanese patients with childhood-onset type 1 diabetes during puberty.

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### Serum lipids profile peculiarities in children with diabetes mellitus type 1

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**Purpose:** Studying of a lipid profile in children with diabetes mellitus type 1.

**Patients and methods:** 48 children (27 girls and 21 boy) 2–17 years old with diabetes type 1 were investigated, from them 14 children with first time revealed diabetes (1 group), 16 persons with duration of disease from 1 to 5 years (2 group) and 18 children with duration of disease more than 5 years (3 group). Serum blood cholesterol, LPHD, LPLD, LPVLD, triglycerides, HbA1c% were measured.

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**Results:** In all groups increase of total cholesterol and index of atherogeneity was revealed, in children of groups 2 and 3 the increase of LPLD, in children of group 3 also increase of LPVLD and triglycerides was found. The analysis of lipid profile and level of HbA1c% showed that decompensation of carbohydrate metabolism increases atherogenic risk.

**Conclusions:** Atherogeneity of blood correlates with duration of disease and lack of compensation of carbohydrate metabolism in children with diabetes mellitus type 1.

### P/WED/33

#### Associated pathology to diabetes mellitus type 1

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**Aims:** To value the complexity of attention of these children due to associated pathologies: A) describe the most frequent pathologies, B) study the evolution of frequency on secondary complications.

**Methods:** From 1985 to 2006, 303 patients were transferred to adult endocrinology at the age of 18 years old. 54.6% men.

**Result:** At the onset the mean age was:  $9.36 \pm 3.56$  years. Diabetes duration until their transfer:  $9.12 \pm 3.77$  years. 60% had associated pathology 36% had secondary complication. A) Associated pathology: Other pathologies: 2.6%; 2 cases varicocele, 1 case of aortic stenosis, osteocondroma, osteosarcoma, hepatitis B, huge ovary cyst, sacrococcygeal fistula. Genetic syndromes: 1.6%; Apert, Marfan, Down, Neonatal Diabetes syndrome. Deaths before 18 years old: 1.32%; 1 sclerosis multiple, 1 osteosarcoma, 1 leukemia and 1 with unknown cause. B) Complications: Limited joint mobility-thickening of hand skin palms: 12% (diabetes evolution: 10.9 years). Reduced nervous conduction: 11.2% (9.71 years). Microalbuminuria: 10.5% (9.44 years). Retinopathy: 1.3% (12 years) and cataract in 2 patients. The frequency of complications divided in five years is: 1985–1990, 1991–1995, 1996–2000, 2001–2006: LJM: 4.6%, 12%, 12.9%, 9.8%. Nervous conduction speed reduction: 29.2%, 10%, 6.5%, 2.2%. Microalbuminuria: 16.9%, 8%, 8.6%, 8.7%. Retinopathy: 5.3%, 0%, 1.1%, 0%.

Endocrinopathy: 16.1% - Thyroiditis/TPO(+)-autoanti bodies: 9.6% - Obesity/overweight: 5.6% - Addison illness: 0.3% - Pubertal delay: 0.3% - Growth retardation: 0.3%	Psychiatric illness: 6.2% - Eating disorders: 2.9% - Major depressive disorder: 2.3% - Behavior alteration: 0.7% - Anxiety: 0.3%	Metabolic alteration: 6.2% - Hypercholesterolemia: 6.2%
Neurologic: 4.6% - Epilepsy: 1.3% - Becker dystrophy: 0.3% - Carpal tunnel syndrome: 0.7% - Multiple sclerosis: 0.7% - Charcot-Marie-Tooth: 0.7% - Migraine: 0.3% - Brachial plexopathy: 0.3% - Hemimegalencephaly: 0.3%	Dermatology: 4% - Necrobiosis lipoidica: 2% - Pityriasis versicolor/Onychomycosis: 1.3% - Alopecia: 0.3% - Lentiginosis: 0.3%	Digestive: 3.5% - Celiac disease: 1.3% (low valued) - Cholestasis: 0.7% - Lymphoidiculo hyperplasia: 0.6% - Liver illness: 0.3% - Rectal gland: 0.3% - Esofagitis: 0.3%
Haematologic: 2% - Chronic anaemia: 1% - Polyglobulia: 0.7% - Hemochromatosis: 0.3%	Kidney pathology: 2.6% - Hypercalciuria: 2% - Hyperuricuria: 0.3% - Hematuria: 0.3%	Pathology breathing: 1.3% - Asthma: 1.3% (low valued) - Tuberculosis (1 case)
HTA: 1.1%	Skeletal: 1% - Scoliosis: 1%	

**Conclusion:** High percentage of patients with DM-1 present associated pathology before 18 years old. The most frequent associated pathology is the endocrinological followed by the psychiatric. The frequency of complications has progressively decreased. We have observed that the first complications appear at around 10.5 years of diabetes duration.

### P/WED/34

#### The role of pro- and anti-angiogenic factors in the angiogenesis processes in children with diabetes mellitus type 1

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**Objectives:** The aim of our study was to assess the relation between pro- and anti-angiogenic factors and the presence of retinopathy in children diagnosed with diabetes mellitus (DM) type 1.

**Materials and methods:** We examined a group of 186 children with DM type 1 from the Diabetological Department Clinic of Paediatrics, Haematology, Oncology and Endocrinology at the Medical University of Gdańsk, Poland. The control group consisted of 64 healthy children. The children with DM type 1 had their daily urine albumin excretion, C-reactive protein, HbA1c, C-peptide measured, 24 hrs blood pressure monitoring and ophthalmologic examination. Additionally, all of them had serum IL-6, IL-12 and VEGF measured using highly-sensitive ELISA tests.

**Result:** The unadjusted analysis revealed that the risk of retinopathy was dependent with declining power on CRP [(OR 2.55; 95%CI 1.54–4.20)  $p = 0.0001$ ], HbA1c [(OR 1.58; 95%CI 1.22–2.06)  $p = 0.0004$ ], IL-6 [(OR 1.52; 95%CI 1.11–2.07)  $p = 0.007$ ], VEGF [(OR 1.42; 95%CI 1.23–2.0)  $p = 0.003$ ], duration of DM [(OR 1.39; 95%CI 1.39–1.18)  $p = 0.005$ ], age [(OR 1.25; 95%CI 1.07–1.46)  $p = 0.02$ ], systolic blood pressure [(OR 1.29; 95%CI 1.02–1.63)  $p = 0.02$ ], albumin excretion rate [(OR 1.01; 95%CI 1.0–1.03)  $p = 0.03$ ]. Moreover, a negative statistically significant correlation between IL-12 and VEGF in children with diabetic retinopathy was found.

**Conclusion:** On the account of our studies we suggest, that proinflammatory factors are engaged in neoangiogenesis regulation of diabetic retinopathy children.

### P/WED/35

#### Gastric emptying and postprandial glucose excursions in adolescents with type 1 diabetes

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To investigate the impact of the energy content of a meal on gastric emptying and postprandial glucose excursions in adolescents with type 1 diabetes mellitus (T1DM). Nine adolescents with T1DM ingested two different test meals in a randomized order on separate days following an overnight fast. The meals consisted of pasta with a sauce of tomatoes and ham with or without rape-oil, 640 and 320 Kcal, respectively. The subjects were normoglycemic at the start of the test and were given a sc injection of insulin aspart 7 IU preprandially. Blood samples were taken before and repeatedly after the ingestion during 240 min. Gastric emptying was assessed with the paracetamol absorption method (Willems et al. Dig Dis Sci 2001). The areas under the curve (AUCs) for glucose and paracetamol concentrations were calculated and paired samples t-test, Wilcoxon Signed Ranks test, Pearson's correlation, Spearman's rho and simple linear regression analyses were used. Time to peak in paracetamol concentration was delayed after the high energy meal compared to the low (120 vs. 60 min,  $p = 0.035$ ). The AUC for paracetamol concentration was larger during the whole study period after the low energy meal compared to the high

( $p = 0.045$ ) and even larger during the first 60 min ( $p = 0.008$ ). The AUC for glucose concentration was larger the first two hours after the low energy meal compared to the high ( $p = 0.032$ ). Gastric emptying is delayed and postprandial glucose excursions are less prominent after a high compared to a low energy meal in adolescents with T1DM. The preprandial insulin dose needs to be adjusted to the total energy content of a meal in order to reach postprandial normoglycemia.

P/WED/36

### Erythromelalgia associated with acute diabetic neuropathy in an adolescent with insulin-dependent diabetes mellitus

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Erythromelalgia is a rare clinical condition of unknown etiology characterized by severe burning pain in the distal limbs, accompanied by pronounced erythema and increased skin temperature are precipitated by heat or activity and can be improved by cooling the affected part. It can be divided into primary, which begins spontaneously at any age, and secondary, which is associated with infrequently diabetes mellitus but its significance is little known. We report the occurrence of acute diabetic neuropathy in an adolescent diabetic patient presenting erythromelalgia. A 15 year-old girl was diagnosed with insulin-dependent diabetes mellitus 4 months ago was referred for evaluation of progressive severe bilateral feet pain of 10 days duration. She had continuous burning sensation exacerbated by walking and worse at night, associated with redness and warmth in the painful regions. The finding of digital thermometer showed higher body temperature on peripheral area than central area of feet. Neurological examination showed no deficits in sensory or motor function and normal deep tendon reflexes. Nerve conduction studies revealed large fiber polyneuropathy. Various medications including gabapentin and constant immersion of her feet in ice water slowly relieved her discomfort.

P/WED/37

### Method of correction of autonomous nervous system disorders in children with diabetes mellitus type 1

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**Aim:** To study frequency of disorders of autonomous nervous system (ANS) in children with diabetes mellitus type 1 and effectiveness of transcranial magnitotherapy in correction. Patients and methods: 75 children and adolescents with diabetes mellitus type 1 7–17 years old were examined. Autonomous nervous system status was evaluated by heart rate variability analysis, diagnosis of diabetic cardiac neuropathy (DCAN) was provided with standard methods. Estimation of general state, self-esteem, activity and mood was carried out in every child. Transcranial magnitotherapy (TCM) was carried out with use of 'Amo-Atos' device, running alternating magnetic field, 1–10 Hz, time of procedure 7–12 min., overall number by the course is 10–12.

**Results:** Children with first time detected diabetes mellitus type 1 (12 patients among 75) had compensation of metabolic processes ( $HbA1c = 7,14 \pm 0,6\%$ ). Other patients had sub- and decompensation of diabetes (average level of  $HbA1c = 9,4 \pm 0,8\%$ ). 60 children (80%) had autonomous dysfunction, in 27 patients (36%) DCAN was diagnosed. After TCM the improvement of autonomous status was registered: increase of the number of children

with normal tonus of ANS, normal autonomous reactivity and activity of subcortical nerve centers, stable regulation. Some patients had tendency to improvement of indexes, typical for DCAN. Normalization of psychological status was also achieved.

**Conclusions:** 1) 80 % of children had autonomous dysfunction, in 27 patients (36%) DCAN was revealed. 2) TCM can be used in treatment of children with diabetes mellitus type 1 with autonomous dysfunction for influence on regulative structures of ANS.

P/WED/38

### Reduced baroreflex gain is a sign of early autonomic neuropathy in children with type 1 diabetes: preliminary results

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**Objectives:** Diabetic autonomic neuropathy (DAN) is a frequent and severe complication of diabetes. This fact underscores the clinical importance of DAN prevention. Thus, the timely detection of DAN and the use of effective means to postpone the progressive deterioration of autonomic function becomes of utmost importance. In this contest cardiovascular autonomic neuropathy (CAN) is of prominent focus because of its negative impact on quality of life in people with diabetes. The purpose of our study was to assess whether initial signs of CAN can be found in children and adolescents with type 1 diabetes (T1DM).

**Methods:** We evaluated 36 consecutive asymptomatic children and adolescents, aged  $15.1 \pm 3.8$  years (range 6.2–22.1), with T1DM from  $7.5 \pm 4.3$  years. Autonomic regulation was inferred from spectral analysis of RR interval and systolic arterial pressure variability (SAP), and by estimating time and frequency domain measures of baroreflex gain (BRS and index  $\alpha$ , respectively). We evaluated an age- and sex-matched control group.

**Results:** We observed a significant impairment in BRS and index  $\alpha$  in T1DM vs. control group (BRS:  $15.9 \pm 1.7$  mmHg vs.  $30.6 \pm 5.6$  mmHg,  $p = 0.002$ , and index  $\alpha$ :  $20.4 \pm 2.1$  mmHg vs.  $28.6 \pm 2.8$  mmHg,  $p < 0.05$ , respectively). No difference was observed in spectral indices of RR and SAP variabilities in the two groups. Furthermore, in T1DM patients, BRS and index  $\alpha$  showed an inverse correlation with disease duration:  $r = -3.48$  ( $p = 0.04$ ) and  $r = -0.47$  ( $p = 0.013$ ), respectively. No correlation was observed with glycemic control, evaluated as glycated haemoglobin.

**Conclusions:** In children and adolescents with T1DM, CAN seem to be initially characterized by selective baroreflex impairment. The severity of this dysfunction appears to be related to disease duration than glycemic control. A larger study is now on going to confirm these results.

## Type 2 Diabetes, Diabetes and Obesity I

P/WED/39

### Simple versus sophisticated measures of body fat in children and their relationship to insulin resistance

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**Objectives:** The relationship between visceral fat (VF) and insulin resistance (IR) is established in adults, but less is known in healthy prepubertal children. Simple but reliable methods for assessing

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obesity-related diabetes risk in children are important. Our aims were: 1. To compare different measures of body fat as predictors of IR and 2. To estimate the contribution of VF to IR, independent of subcutaneous fat (SF), in 9-year-old children.

**Methods:** Participants: 236 healthy children from the EarlyBird Study: 117 boys, 119 girls, mean age 8.9 years (SD 0.3). Children were recruited from randomly selected schools stratified by socio-economic status.

**Measures:** Insulin resistance (HOMA-IR); abdominal % fat by DEXA; % fat by bioelectrical impedance; BMI (SDS); waist circumference; waist-hip ratio (WHR); sum of five skinfolds.

**Results:** 1. 21% boys and 22% girls were overweight or obese (BMI  $\geq$  91st centile). 2. All anthropometric measures (except WHR) were associated with DEXA % abdominal fat ( $r > 0.76$ ,  $p < 0.001$ ). 3. All measures (except WHR) had similar predictive values for IR (table).

Predictors in model:	Boys R <sup>2</sup>	Girls R <sup>2</sup>	Fat type
Waist-hip ratio	0.01	0.16 ( $p < 0.001$ )	VF + SF
BMI SDS	0.17 ( $p < 0.001$ )	0.31 ( $p < 0.001$ )	VF&SF
%fat (bioelectrical impedance)	0.17 ( $p < 0.001$ )	0.30 ( $p < 0.001$ )	VF&SF
Sum 5 skinfolds	0.18 ( $p < 0.001$ )	0.36 ( $p < 0.001$ )	SF
Waist circumference	0.18 ( $p < 0.001$ )	0.40 ( $p < 0.001$ )	VF&SF
Waist circumference & SF	0.18 ( $p < 0.001$ )	0.40 ( $p < 0.001$ )	(VF&SF)-SF
% abdominal fat (DEXA)	0.19 ( $p < 0.001$ )	0.29 ( $p < 0.001$ )	VF&SF
% abdominal fat (DEXA) & SF	0.19 ( $p < 0.001$ )	0.36 ( $p < 0.001$ )	(VF&SF)-SF

**Conclusion:** In young children, a simple measure of waist circumference predicts IR as reliably as sophisticated measures of abdominal fat. The influence of VF, independent of SF, is apparent in girls but not boys, at this age.

### P/WED/40

#### Children and adolescents with type 2 diabetes: are clinical features linked to presence of autoantibodies?

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**Objectives:** Autoantibodies (AB) to islet-cell cytoplasm (ICA) and glutamic acid decarboxylase (GAD) can be found in up to 30% of adult patients with T2D. This study examined 471 children/adolescents (7–18 years) with clinically diagnosed T2D to determine the association of AB with T2D.

**Methods:** Children/adolescents were screened; included were tests for AB, C-peptide, and standardized glucose stimulation test (Boost-Test™).

**Result:** 10.2% were positive for at least 1 AB (GAD + 4%, ICA + 1.7%; both AB + 4.5%). From this group, 8.3% had typical acanthosis nigricans vs. 23.5% of the AB - group, 62.5% were over the 75th weight percentile (sex & age adjusted) vs. 86.7% of the AB - group and 41.7% were over the 90th weight percentile (sex & age adjusted) vs. 75.4% of the AB - group. Mean AB + pt age was lower than AB - pts (12.9 vs. 13.5 years), more pts were < 12 years (35.4 vs. 22.0%,  $p = 0.445$ ), and the female/male ratio was 1:1.2 (AB+) and 1.8:1 (AB-). Mean time since diabetes diagnosis was 6.97 (AB+) and 6.91 months (AB-). Boost-Test showed FPG lower in AB+ children (mean FPG, 7.65 [AB+] vs. 9.67 mmol/L [AB-]). By 120 min there was significantly greater increase in mean stimulated blood glucose: 14.7 (AB+) vs. 11 mmol/L (AB-),  $p < 0.05$ . Mean stimulated C-peptide levels (90 min) were 1200 (AB+) vs. 2030 pmol/L (AB-) and insulin levels were 166 (AB+) vs.

346 pmol/L (AB-). Lower C-peptide and insulin secretion after stimulation are consistent with lower pancreatic  $\beta$ -cell reserve, indicating the Boost-Test was highly dependent on AB status. Medians of HOMA resistance index were 3.7 (AB+) and 7.2 (AB-) and release index was 44.3 (AB+) and 93.5 (AB-). Incidence of autoimmunity in children/adolescents was comparable to adults. AB + group were more insulinopenic during glucose stimulation, although some pts had insulin resistance.

**Conclusion:** A diabetes subtype with features of T1D and T2D is present in pediatric diabetes patients and may require a long-term evaluation of therapeutic regimens. Supported by Sanofi-Aventis.

### P/WED/41

#### Characteristics of the metabolic syndrome is prevalent in children with newly diagnosed type 2 diabetes

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**Objective:** Assessment of characteristics of the metabolic syndrome (MS) in children with type 2 diabetes at the time of diagnosis.

**Methods:** The study involved 156 Japanese children, 68 males and 88 females, aged 7–15 ( $12.9 \pm 1.6$ ) year, diagnosed as having type 2 diabetes. They were identified by the urine glucose screening program at schools during the period from 1980–2006. Body weight, blood pressure and fasting levels of serum triglycerides (TG) and HDL-cholesterol (HDL-C) were examined at the time of diagnosis of diabetes. Characteristics of the MS were defined as follows; obesity: percent overweight more than 20.0%, TG: above 120 mg/dL, HDL-C; less than 40 mg/dL, systolic blood pressure over 125 mmHg and/or diastolic blood pressure over 70 mmHg. The presence of any two of the four criteria makes the diagnosis of the MS (Criteria for Japanese children aged 6–15 years by the Ministry of Health, Welfare and Labor in Japan, 2007). Correlation between lipid abnormalities and fasting levels of blood glucose, HbA1c, serum insulin and HOMA-IR was also evaluated.

**Results:** 82.5% of the patients had obesity; 89.7% of males and 76.1% of females were obese ( $p = 0.051$ ). The prevalence of high TG was 48.7% and that in low HDL-C was 17.8% among the patients. Elevated blood pressure was identified in 13.2% among the patients. There were no statistical differences of these frequencies in gender. The overall prevalence of the MS in addition to diabetes was 48.7%; 58.8% of males and 40.9% of females were affected (NS). Serum TG and HDL-C levels significantly correlated with serum insulin levels and HOMA-IR that reflect insulin resistance. On the other hand, there was no significant association between serum lipids levels and HbA1c and fasting blood glucose levels.

**Conclusions:** We found high prevalence of the MS in children with newly diagnosed type 2 diabetes. Prevalent lipid abnormalities may be associated with insulin resistance caused by obesity and glucose intolerance.

### P/WED/42

#### Insufficient compensation of acute insulin response to glucose as an essential pathogenesis in Japanese adolescent T2DM

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**Objectives:** It has been reported that the impairment in both insulin sensitivity and beta cell function is essential in the

development to T2DM. Furthermore, Arslanian's group and ours have suggested that the magnitude of the derangement is greater in beta cell function as acute insulin response (AIR) than insulin sensitivity (SI) comparing with that in obese control subjects, although these reports dealt with non-near-glycemic T2DM. We aim to clarify whether either AIR or SI or both is essential in diabetic development in patients following elimination of glucose toxicity.

**Method:** Forty-three T2DM, 21 obese, and 56 non-obese non-diabetic control adolescents underwent with frequently sampling intravenous glucose tolerance test (FSIGT) for the minimal model analysis (MM). T2DM patients were all obese comparable with non-diabetic obese group and were in near-normoglycemia, HbA1c below 5.8% and FPG below 110 mg/dl at the time of FSIGT. Parameters of FPG, Ib (basal insulin), SI, AIR and GDI (glucose disposition index) were examined between these three groups.

**Results:** The levels of FPG and HbA1c were not significantly different between three groups. Levels of Ib in both obese and T2DM groups were higher than in controls, but not different between obese and T2DM groups. T2DM group showed significantly lower AIR than obese group, but not than controls. SI in T2DM and obese groups were not different. Thus GDI in T2DM was significantly lower than in other two groups, while no significant difference between control and obese groups.

**Conclusion:** We have demonstrated that insufficient compensation of acute insulin response to glucose is an essential pathogenesis, rather than insulin resistance, even in Japanese obese T2DM. From aspect of hyperbolic relationship between SI and beta cell function by AIR, not by Ib, Japanese adolescents may, at least, have an increased risk of developing and worsening diabetes, even if they have only a mild increase of their body weight.

P/WED/43

### Prevalence of impaired glucose tolerance and type 2 diabetes and their determinants in obese Italian children and adolescents

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**Objectives:** Recent studies reported an increased prevalence of impaired glucose tolerance (IGT) and type 2 diabetes mellitus (T2DM) in children and adolescents with obesity. The aim of this study was to determine the prevalence of insulin resistance and impaired glucose regulation and their determinants in a cohort of Italian obese children and adolescents living in Latium.

**Methods:** A total of 270 subjects (129 boys, 141 girls; mean age:  $11.3 \pm 5.4$  years) with a BMI > 95th percentile (mean BMI z-score:  $2.4 \pm 0.8$ ), were studied. A 2-h oral glucose tolerance test was performed before entering a weight-loss program and capillary blood glucose and insulin concentrations were measured. Patients were categorized into normal glucose tolerance (NGT), IGT and T2DM. Insulin resistance was estimated by homeostatic model assessment (HOMA-IR) and beta-cell function by calculating disposition index and insulinogenic index (IGI). The whole body insulin sensitivity index (WBISI) was used to assess insulin sensitivity.

**Results:** Insulin resistance was detected in 57.4% (n = 155), IGT in 12.6% (n = 34), T2DM was present in 1.1% (n = 3) of the patients. All together, in 13.7% (n = 37) of the patients, IGT or T2DM were identified. Compared with the NGT, patients with IGT-T2DM were more insulin resistant ( $p < 0.0001$ ) and had lower disposition index ( $p < 0.001$ ) and WBISI ( $p < 0.001$ ). No significant differences resulted in BMI z-score and IGI.

**Conclusions:** Impaired glucose tolerance and type 2 diabetes are an emerging problem among children with obesity. IGT and T2DM

are associated with insulin resistance and a decreased beta-cell function, but overt T2DM is usually silent at the diagnosis. Therefore an OGTT is required in all subjects at high risk. Although IGT is a recognized complication of childhood obesity, longitudinal studies are needed to identify the metabolic precursors and the natural history of the development of type 2 diabetes in these patients.

P/WED/44

### The study of screening for type 2 diabetes and impaired glucose regulation in children and adolescents

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**Objective:** To analyze the results of screening for type 2 diabetes (T2DM) and impaired glucose regulation (IGR) in Beijing school children, providing evidence for screening protocol.

**Methods:** The survey population was selected as a stratified cluster sample from 8 urban and 10 rural areas in Beijing. Fasting capillary blood glucose (FCBG) were performed in 19 593 children and adolescents aged 6–18 years in 4 urban and 3 rural areas. The screening test was fasting capillary blood glucose (FCBG), oral glucose tolerance test (OGTT) were performed in those with positive measurements (FCBG  $\geq 5.6$  mmol/L). Diabetes and IGR were diagnosed using WHO criteria.

**Results:** There were 19 112 (97.5%) individuals with complete records were studied, 469 had positive screening results and only 225 (48.0%) agreed to perform OGTT, 32 were diagnosed as T2DM/IGR, 6 were T2DM, all of them were girls, aged 9–15 years old, 3 had acanthosis nigricans, 2 had family history of T2DM. BMI, blood pressure, blood lipid, HOMA-IR were higher in T2DM/IGR subjects than those with normal glucose regulation. The odds ratio (OR) of overweight, obese, family history, puberty, acanthosis nigricans for T2DM/IGR was 1.88, 3.65, 2.20, 1.67 and 6.77 respectively. There were no differences about mean age, gender distribution, rates of obesity, acanthosis nigricans and puberty when compare completed with all positive children.

**Conclusions:** In general population, the prevalence of T2DM and T2DM/IGR was 0.6/1000 and 3.5/1000 respectively, it is may be reasonable to recommend screening in high-risk children, especially the obese and those with acanthosis nigricans. T2DM/IGR had much metabolic disorders and probably developed cardiovascular disease in the future. It is critical to screen and treat T2DM/IGR in children, in order to reduce the incidence of chronic disease in adults.

P/WED/45

### Comparing the practicability and operability of screening protocol for T2DM between Beijing study group applied and ADA recommended

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**Objective:** To compare the practicability and operability of screening protocol for type 2 diabetes (T2DM) between American Diabetes Association (ADA) recommended and Beijing study group applied.

**Methods:** A total of 17 113 school children aged 8–18 years old were included in our study, screening for T2DM and IGR in overweight/obese children who had more than one risk factor (family history of T2DM, acanthosis nigricans, puberty), the screening test was fasting capillary blood glucose (FCBG), those with positive results underwent OGTT; 997 subjects aged 10–18 years who were examined in health maintenance visits in

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clinic were included in Drobac's research, ADA recommended protocol of screening for type 2 diabetes was applied.

**Results:** There was no difference between ADA recommend and Beijing study group applied protocols about the number of risk factors contained in questionnaire and anthropometric. Beijing study group had much higher call back rate than Drobac's study (59.62% vs. 33.51%). The final diagnosis rate were both low in two screening programs (6.42/1000 and 15.5/1000). Different from Drobac's study, there were no significant differences about age, gender, obesity rate, acanthosis nigricans and family history of diabetes between completed and uncompleted group ( $p > 0.05$ ) in Beijing research.

**Conclusion:** The protocol of FCBG firstly and then OGTT performed should be recommended in screening for T2DM and IGR in Beijing children.

### P/WED/46

#### Increased adiposity after diagnosis in Italian children with type 1 diabetes mellitus

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The purpose of the study was to test the accelerator hypothesis in Italian children with type 1 diabetes. Obesity-induced insulin-resistance may upregulate  $\beta$ -cells, which become more susceptible to autoimmunity in genetically predisposed individuals. It has been reported that in pediatric type 1 diabetes younger age at diagnosis was associated with higher BMI-SDSs. We measured BMI-SDS, at 2–12 months after diagnosis, in 174 insulin-treated patients (106 male, 68 female) followed between 1990–2005. Patients, aged 1 to 15.7 years, were divided into 3 groups, according to age at diagnosis: G1: 1–4.99 years, G2: 5–9.99 years, G3: 10–15.7 years. In all patients, BMI-SDS was not different among the 3 groups of patients ( $p = 0.61$ , F test; ANOVA), and did not change over 1990–2005 (Pearson's correlation coefficient ( $r$ ): 0.052,  $p = 0.50$ ). There was no significant interaction between age category at diagnosis and category of year of diagnosis ( $p = 0.75$ ); there was no correlation between age and year at diagnosis ( $r = 0.09$ ;  $p = 0.23$ ). In 92 patients longitudinally evaluated, BMI-SDSs at diagnosis wasn't higher in G1 than both G2 and G3 ( $p = 0.75$ ; ANOVA). Five years after diagnosis, BMI-SDS was similar across the 3 age-groups ( $p = 0.46$ ; ANOVA). BMI-SDSs increased from diagnosis to 5 years (effect of time:  $p = 0.001$ ; ANOVA). In contrast to Accelerator Hypothesis, obesity is not a common finding in Italian children at type 1 diabetes diagnosis. As regards BMI as a risk factor in diabetes pathogenesis, it should be established whether patients are more insulin-resistant than controls, and whether greater BMI during childhood could explain insulin-resistance. There might be a threshold at which obesity determines earlier onset of type 1 diabetes, already not reached in our Italian patients. The increased BMI-SDS 5 years after diagnosis could be related to overinsulinization due to intensive therapy, and represents a risk factor for the late development of microvascular complications.

### P/WED/47

#### Roles of diabetes and obesity on adiponectin levels in children and adolescents with type 1 diabetes mellitus

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**Objectives:** To clarify the reason why adiponectin level in patients with child-onset type 1 diabetes mellitus (T1DM) is almost comparable with non-obese and non diabetic subjects.

**Methods:** Total adiponectin (TA) was measured in 51 non-obese T1DM without retinopathy/nephropathy (22 boys, age at onset:  $7.4 \pm 3.7$  years old duration:  $7.5 \pm 5.5$  years), in comparison with 17 patients with child-onset type 2 obese diabetes mellitus (T2DM: 7 boys), 18 obese children (obesity: 12 boys), and 42 non-obese/non-diabetic children (controls: 20 boys). Variables of obesity include body mass index (BMI) and obesity index (OI). Blood specimen was tested for triglyceride (TG), total cholesterol (TC), HDL-cholesterol (HDLc), LDL-cholesterol (LDLc), HbA1c, and high-sensitive CRP (hs-CRP), the arteriosclerosis index (AI) calculated as well. TA and leptin were measured by ELISA and RIA.

**Results:** (1) There was no obese subject in T1DM and controls. (2) TA in T1DM was significantly lower than those in T2DM and obesity ( $13.0 \pm 4.4$  vs.  $5.8 \pm 2.9$ ,  $5.6 \pm 2.4 \mu\text{g/ml}$ , respectively), but significantly higher than in controls ( $10.8 \pm 4.4 \mu\text{g/ml}$ ). (3) In T1DM, TA had a positive correlation with HDLc, so that negatively with AI ( $p < 0.05$ ). However, there was no correlation of TA with age, duration, BMI, OI, HbA1c, hs-CRP or leptin. In controls, TA was positively correlated with HDLc, and negatively with TG and AI in T2DM. (4) There was no significant difference in BMI, OI, LDLc, or AI between T1DM and controls. These parameters in T1DM and controls were significantly higher than those in T2DM and obesity. HDLc in obesity was significantly lower than in T1DM and controls.

**Conclusions:** We demonstrated that even in hyperglycemic state TA in T1DM was significantly higher than that in T2DM, as the same relationship was noted in normoglycemic state between obesity and control. These results suggest that adiponectin level may be affected by obesity rather than by diabetic hyperglycemia.

### P/WED/48

#### Validation of percentiles for insulin sensitivity indexes in healthy Caucasian children: WBISI and HOMA-IR

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Insulin resistance (IR) is tightly linked to adiposity and is considered a strong predictor for type 2 diabetes mellitus and metabolic syndrome. The epidemic of childhood obesity claims for urgent need to target IR subjects from the very beginning in order to individualise therapeutic management. Although euglycemic clamp is the gold standard to determine IR, more practical methods have been validated. The most widely used are HOMA-IR, which takes into account fasting glucose and insulin, while WBISI estimates glucose and insulin excursion after oral load. For both, HOMA-IR and WBISI, normal values have been elaborated for adults while no data exist for the paediatric population. The purpose of this study was to determine percentile patterns for HOMA-IR and WBISI in prepubertal Caucasian children. After physical examination including anthropometric measures and overnight fasting, a standard OGTT was performed on 118 prepubertal normoweight healthy children (62M/56F; age =  $8.20 \pm 2.44$  years, BMI =  $15.93 \pm 1.14 \text{ kg/m}^2$ ; SDS-BMI =  $-0.04 \pm 0.78$ ). HOMA-IR [(FG FI)/22.5] and WBISI [ $10000/\sqrt{\text{FI} \cdot \text{FG}}$ ] (MPG-MSI) were calculated. Before setting the percentiles, statistical analysis were performed. No differences for age ( $p = 0.771$ ), BMI ( $p = 0.276$ ), SDS-BMI ( $p = 0.457$ ), HOMA-IR ( $p = 0.612$ ), WBISI ( $p = 0.698$ ) and DHEAS ( $p = 0.563$ ) were found between males and females, thus all subjects were analyzed as a single group. Correlation analysis performed was not significant excluding confounding factors [age vs. HOMA-IR ( $p = 0.258$ ) and WBISI  $p = 0.321$ ; BMI vs. HOMA-IR ( $p = 0.502$ ) and WBISI ( $p = 0.051$ ); SDS-BMI vs. HOMA-IR ( $p = 0.810$ ) and WBISI ( $p = 0.162$ )]. These reference data are useful to easily detect IR subjects within the Caucasian

population helping to target those who need intensive therapeutic counselling.

ISI	Subjects n	Range	3rd	10th	25th	50th	75th	90th	97th
HOMA-IR	118	0.57–2.71	0.57	0.64	0.85	1.16	1.53	2.20	2.71
WBISI	118	4.34–16.41	4.34	5.73	6.86	8.97	12.90	15.09	16.41

## Monogenic Forms of Diabetes

P/WED/49

### Diabetes mellitus in children with Down's syndrome

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**Objectives:** Children with Down's syndrome have an increased risk of type 1 diabetes. However, the reports regarding the prevalence of Down's syndrome in children with diabetes are few. The aim of this study was to describe the prevalence of Down's syndrome among children with diabetes in Sweden. Another aim was to describe the insulin treatment regimens and metabolic control in children and adolescents with diabetes and Down's syndrome.

**Methods:** Data were collected by a questionnaire that was distributed to all paediatric diabetes centres in Sweden. Data on Down's syndrome in the background population was obtained from the Swedish birth defect registry.

**Result:** 41 out of 43 clinics answered the questionnaire representing 7083 subjects with diabetes. In April 2007, 15 subjects with Down's syndrome were identified. Median age was 15.6 (range 4.5 – 20.0) years, with a median duration of diabetes of 5.0 years. All children were treated with insulin, mainly with multiple insulin injections (10/15). Three children used insulin pump and two children were treated with twice daily insulin injections. One child was also treated with metformin. The median daily insulin dosage was 0.76 U/kg/d (range 0.05 – 1.7 U/kg/d) and HbA1c (Mono-S, upper reference limit 5.3%) was 6.3% (range 4.1 – 7.9%). Coeliac disease was reported in 5 and thyroid disease in 8 children. Simultaneous hypothyroidism, diabetes and celiac disease were noted in two children with Down's syndrome. We identified a prevalence of Down's syndrome in patients with diabetes of 0.21%, whereas the prevalence of Down's syndrome in new-born children in the background population is estimated to 0.13%.

**Conclusion:** The prevalence of Down's syndrome in children with diabetes seems to be increased in Sweden. Intensive insulin therapy is possible in children and adolescence with Down's syndrome and the metabolic control is often satisfactory. Registry validated studies are needed to confirm our findings.

P/WED/50

### Cardiovascular involvement in Wolfram syndrome

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Wolfram syndrome (WFS) is a genetic disease with recessive autosomic transmission, also known with the acronym DIDMOAD (central diabetes insipidus, diabetes mellitus, optical atrophy, sensorineural deafness). Additional manifestations are atonic bladder, psychiatric illness, cardiovascular and gastrointestinal autonomic neuropathy. Heart malformations have exceptionally been described. We report a five-generation Sicilian family with WFS, which represents the largest pedigree described. The family was ascertained through a patient born to healthy consanguineous

parents, who had all the DIDMOAD clinical features and suddenly died at 18 years. The proband had three unaffected sisters, two affected sisters and one affected brother. Other three patients (5th generation), were two siblings and one first degree cousin. All the patients shared two common ancestors and were born from three first cousin couples. Sequencing of the WFS1 gene (on chromosome 4p16) showed in all the patients a homozygous 16 base-pair deletion in exon 8 which causes a TAG stop codon in position 454. One affected sister of the proband had surgery for Tetralogy of Fallot, whereas the affected sister and brother manifested resting sinus tachycardia (HR 110–115 b/m), probably expression of cardiovascular autonomic neuropathy. One of the two affected siblings had a large secundum atrial septal defect. Signs consistent with cardiovascular autonomic neuropathy have been described in WFS patients, while few data concerning congenital heart disease are reported. A Lebanese report detected pulmonary stenosis or ventricular septal defect in 16.1% of the WFS cases; some patients with ventricular septal defect were described in a Turkish family. We believe that heart malformations are new features that may be present in WFS; their pathogenesis is unclear, but their presence in selected families emphasizes the clinical heterogeneity of the disease and can help to better understand the function of gene-product.

P/WED/51

### A boy with Wolfram syndrome presenting with diabetes mellitus and marked polyuria, bilateral hydronephrosis and hydroureter mimicking obstructive uropathy

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Wolfram syndrome (WFS) is a rare hereditary neurodegenerative disorder which consists of DI, DM, optic atrophy (OA) and deafness. We report a case of WFS who presented with marked polyuria, bilateral hydronephrosis and hydroureter with preexisting DM.

**Case report:** A 13 year-old Thai boy presented with polyuria and incontinence for 1 month. He has been diagnosed with type 1 DM and receiving insulin since 4 years old. His glycemic control was poor. Labs showed: BUN 24 mg/dl, Cr 1.5 mg/dl, Na 131 mEq/L, K 4 mEq/L, Cl 93 mEq/L, CO<sub>2</sub> 25 mEq/L, urine Na 66 mEq/L, urine sp. gr. 1.010, no protein, sugar 4+. During admission, his urine volume was 4–5 L/day. Despite adequate glucose control, polyuria persisted. Pelvic U/S showed bilateral hydronephrosis and hydroureter along ureteric course with thickening walls of urinary bladder. Our initial thought was that his polyuria and urinary salt loss was due to tubular dysfunction 2 to either obstructive uropathy or high-grade VUR. However, IVP did not show any evidence of urinary tract obstruction and VCUG showed only grade 1 of left VUR. Meanwhile, eye exam to look for diabetic retinopathy showed pale optic discs consistent with optic atrophy. Hearing test indicated that the boy had bilateral high frequency hearing loss. IQ test showed borderline mental retardation. After Na replacement, therapeutic Dx of central DI was done by giving intranasal DDAVP. Urine volume significantly decreased > 50% which was consistent with central DI. The diagnosis of WFS was then made.

**Conclusion:** We describe a boy with WFS characterized with DM, central DI, OA and deafness. He presented with pre-existing DM with marked dilatation of urinary tract and polyuria mimicking obstructive uropathy. In this patient, central DI did not preclude the presence of hyponatremia 2° to urine Na loss from tubular dysfunction. WFS should be considered in any diabetic patient with polyuria despite adequate glucose control.

P/WED/52

**Clinical parameters for molecular testing of maturity onset diabetes in the young (MODY)**N. Datz<sup>1</sup>, C. Nestoris<sup>1</sup>, W. von Schütz<sup>1</sup>, T. Danne<sup>1</sup>, A. J. Driesel<sup>2</sup>, M. Maringa<sup>2</sup> & O. Kordonouri<sup>1</sup><sup>1</sup>Children's Hospital at the Bult, Diabetes Centre for Children and Adolescents, Hannover, Germany, <sup>2</sup>IntegraGen GmbH, Bonn, Germany

**Introduction:** Children and adolescents with monogenic forms of diabetes are often diagnosed by chance, due to the variety of clinical presentation and limited experience of diabetologists. Aim of this study was to evaluate clinical parameters that could lead to an efficient screening for MODY.

**Methods:** Clinical parameters were: negative diabetes-specific antibodies at onset of diabetes, positive family history of diabetes, and low to moderate insulin requirements after one year. 39 of 292 patients were negative for GADA and IA2A, but only 8 (20.5%) patients fulfilled both other criteria and were included into the molecular screening programme. Molecular testing was performed through sequencing of the programming regions of HNF-4alpha (MODY1), glucokinase (MODY2) and HNF-1alpha/TCF-1 (MODY3). Additionally, in one patient with renal cysts, the HNF-1beta/TCF2 region (MODY5) was tested.

**Results:** In total, 8 patients (5 boys; mean age  $9.5 \pm 5.0$  years; diabetes duration  $2.8 \pm 2.9$  years; insulin requirements  $0.47 \pm 0.14$  U/kg/d) underwent molecular testing. Positive molecular results were found in five (63%) patients (two patients with MODY2, two with MODY3, one with MODY5). Three patients had no genetic mutation. At diabetes onset, the mean age of the 5 patients with MODY was  $10.6 \pm 5.3$  years (range 2.6–15 years) and HbA1c was  $8.4 \pm 3.1\%$  (6.5–13.9%). The mean diabetes duration until diagnosis of MODY was  $3.3 \pm 3.6$  years (0.8–9.6 years) with insulin requirements of  $0.44 \pm 0.17$  U/kg/d (0.2–0.6 U/kg/d). Patients with MODY3 were changed from insulin to repaglinid, those with MODY2 were recommended discontinuing insulin treatment, while therapy was not changed in the patient with MODY5.

**Conclusion:** In the majority of patients with negative diabetes-specific antibodies, positive family history, and low to moderate insulin needs, MODY has been diagnosed by molecular screening. Watchful consideration of these clinical parameters may lead to an early genetic testing, and, hence, to an adequate treatment in these patients.

P/WED/53

**Maturity-onset diabetes of the young type 3: a case report of a female child responsive to a low dose of sulfonylurea**M. Jesic<sup>1</sup>, S. Sajic<sup>1</sup>, V. Zdravkovic<sup>1</sup>, M. Maringa<sup>2</sup>, M. Jesic<sup>3</sup> & D. Micic<sup>4</sup><sup>1</sup>University Childrens Hospital, Endocrinology, Belgrade, Serbia and Montenegro, <sup>2</sup>IntegraGen GmbH, Genetic, Bonn, Germany, <sup>3</sup>University Childrens Hospital, Neonatology, Belgrade, Serbia and Montenegro, <sup>4</sup>Institute of Endocrinology, Diabetes and Diseases of Metabolism, Endocrinology, Belgrade, Serbia and Montenegro

**Objective:** To investigate whether typical maturity onset diabetes of the young type 3 due to mutation in the HNF-1alpha gene is responsive to a low dose of sulfonylurea.

**Methods:** We describe a nonobese girl aged 10.5 years (BMI 20 kg/m<sup>2</sup>) with signs of initial sexual maturation whose mother and maternal father (died in August 2006) had insulin treated diabetes mellitus since early adolescence. Due to genetic familial history, the mother decided to check the girl's glycemia which was found to be considerably increased, both on a fasting stomach (up to 6.9 mmol/l), and particularly postprandially (up to 16.2 mmol/l). The girl was tested for oral glucose tolerance and blood analysis for

antibody presence to portions of pancreatic cells, and their products was also done. Genetic testing for MODY was performed by analyzing maternal and daughter's DNA. All of the exons were polymerase chain were amplified on the intron sequences. The obtained genetic fragments were then sequenced.

**Results:** Oral tolerance test to glucose with insulinemia showed insulinopenia (maximal insulin rate in 60th min. was 18,6 mUI/mL at glucemia 16,9 mmol/l), while antibodies (GAD, anti IA2) were negative. HbA1c was 7.9% (normal < 6.5%). Using genetic analysis in mother and child, we identified identical mutation that has not been described in the literature until now - TCF 1 exon 2 c.368 > C p.Leu 123 pro heterozygote - mutation sequence HNF - 1alpha, the variant type MODY3. Treatment with small doses of sulphonylurea, gliklazid (20 mg/daily) was initiated, and after 3 months the impression was that therapy gave good results; glycemia was practically normalized, there was no hypoglycemia, and after initial 7.9% HbA1c it decreased to 5.8%.

**Conclusion:** Treatment with small doses of sulphonylurea - gliklazid, can be successful, not only in children with MODY3, but also in vertical line diabetic relatives previously on long-term insulin therapy, however, its long-term efficacy will have to be confirmed.

P/WED/54

**High prevalence of TCF1 and NEUROD1 common variants in combination with GCK mutations among Spanish children and adolescents with MODY**

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Maturity-onset diabetes of the young (MODY) is an early onset (< 25 years), autosomal dominant form of non-insulin dependent diabetes mellitus (DM) due to a primary functional defect of pancreatic  $\beta$ -cells. MODY is clinically and genetically heterogeneous. To date, at least six genes have been associated with different subtypes of MODY. Mutations in *GCK* (MODY2) and *TCF1* (MODY3) are predominant among the European population.

**Aim:** Since common variants in MODY genes may contribute to the risk of DM we investigated their prevalence among MODY patients by performing consecutive mutation and sequence variant screening of *HNF-4 $\alpha$*  (MODY1), *GCK* (MODY2), *TCF1* (MODY3) and *NEUROD1* (MODY6) in a group of Spanish families with clinical evidence of MODY.

**Methods:** The coding sequences, intron/exon boundaries and known regulatory regions were amplified by PCR and screened for mutations and known polymorphisms by dHPLC and DNA sequencing.

**Results:** 12/17 patients (70.6%) had mutations in *GCK*, 5 of which were novel. Two patients presented with previously described mutations in *TCF1* (R200Q) and *HNF-4 $\alpha$*  (IVS5-2delA), respectively. In 3/17 patients (17.6%) no mutation was identified (MODY-X). Up to 90% of the patients with *GCK* mutations also presented with one (33%) or  $\geq 2$  (58%) non-synonymous common variants in *NEUROD1*: T45A, (83%); *TCF1*: I27L (50%); A98V (6%); S487N (41.7%) or *HNF-4 $\alpha$*  T130I (6%).

**Conclusions:** Our results reveal the existence of complex combined genotypes in MODY that may explain the phenotypic variability. The *TCF1* I27L and A98V variants have been respectively associated with insulin resistance and impaired serum C peptide and insulin responses after OGTT. Likewise, some studies have postulated that the *NEUROD1* T45A and *HNF-4 $\alpha$*  T130I variants may represent risk alleles for DM1 and/or DM2, respectively.

Further functional studies and a closer follow-up of these families will help to address the genotype/phenotype correlations of these combinations.

P/WED/55

### Permanent neonatal diabetes mellitus - sulphonylureas treatment

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**Aim:** A particular case of diabetes mellitus with onset in early infancy, born SGA is presented. Based on clinical signs, an excellent response to sulphonylurea treatment, although the genotype and specific antibodies could not be determined, the diagnose of permanent neonatal diabetes mellitus (PNDM) was established. Case description: B. Sebastian (now 1 year 10 months old) was diagnosed with diabetes mellitus at the age of 3 months. The HbA1c at onset was 15,2%. First the patient received insulin therapy in a multiple injection regimen. Glycemic control was poor, pre- and postprandial variations were high due to alimentation difficulties (entirely lactate appropriately for the age of 3 month). At 10 months old the child was successfully, progressively in 3 days, switched to sulphonylureas oral treatment. The clinical and metabolic improvement was excellent. Currently the diabetes control is obtained with glibenclamide (0,16 mg/kg/d - 3 doses). After six months of sulphonylureas HbA1c was 6,6% with small glycemic variations.

**Conclusions:** The aetiology of diabetes mellitus with onset before 6 months of age is genetic (47% a mutation of the KCNJ11 gene, Kir 6.2 subunit). The metabolic balance obtained, HbA1c, pre- and postprandial glycemic variations were superior under sulphonylurea therapy compared to insulin regimen. In case of impossibility of determining the genotype, based on clinical signs for PNDM and a positive sulphonylurea test, a progressive replacement of insulin with sulphonylurea is preferred. It is the first case of PNDM treated with oral antidiabetes in Romania.

P/WED/56

### Activating mutations in the KCNJ11 gene encoding the Kir 6.2 subunit in patients with permanent neonatal diabetes of Greek and Turkish Cypriot origin

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Permanent neonatal diabetes mellitus (PNDM) may be caused by heterozygous activating mutations of the KCNJ11 gene encoding the Kir 6.2 subunit of the KATP-channel of pancreatic beta-cells.

**Objective:** To assess the contribution of genetic factors in Cypriot patients with PNDM and possibly alter treatment.

**Methods:** KCNJ11 gene was sequenced in two insulin treated diabetic patients diagnosed before 6 months of age.

**Results:** In both patients we identified heterozygous missense mutations of the KCNJ11 gene. The first patient (PtA) a 2.5 year Turkish Cypriot male carries a de novo R201H mutation. He was diagnosed at the age of 7 weeks presented with severe ketoacidosis and was achieving moderate glycaemic control (HbA1c 7.2–9.6%) on an insulin dose of 11U/kg/d. Pancreatic ultrasonography revealed normal appearance. He was recently successfully

transferred to oral sulphonylureas with an adequate c-peptide response to OGTT (1493 pmol/l in 120'). The second patient (PtB), a 6 month Greek Cypriot male has the R50Q mutation and is only the second to be reported with this defect. He presented with severe DKA at the age of 42 days and developed cerebral edema during resuscitation complicated with epilepsy. EEG was reported normal though. He is still receiving insulin (0.5IU/kg/d) and is planned to be transferred to sulphonylureas in due course. Birth weight was 2200 g in PtA and 2610 g in PtB. In both patients pancreatic autoimmunity (ICA, GAD, IA2) has been negative since diagnosis and c-peptide was undetectable at diagnosis. There is no family history of diabetes in none of them although preliminary genetic results of Pt.B mother suggest that she also has the R50Q mutation without having impaired neither glucose tolerance nor pancreatic secretory dysfunction.

**Conclusion:** PNDM patients of Cypriot origin are found to have genetic defects impairing the Kir6.2 subunit of the KATP-channel. R50Q mutation is the second to be reported and may be related with different extrapancreatic effects if expressed as a mosaic.

P/WED/57

### Genetic polymorphism of HLA region in anti-islet autoantibody seroconversion observed in permanent neonatal diabetes caused by mutations in the KCNJ11 gene

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**Objectives:** It is well documented that humoral markers of autoimmune type 1 diabetes (T1DM) are absent at the onset of permanent neonatal diabetes (PNDM). Recently, we have demonstrated that carriers of the KCNJ11 (Kir6.2) mutation presenting with PNDM may show seroconversion for islet antibodies after at least 10-year duration of the disease (Diabetes Care in press). In the present study we aimed to evaluate whether genetic polymorphism of HLA region is associated with autoimmune process observed in PNDM.

**Methods:** To address this question 16 diabetic carriers of heterozygous activating Kir6.2 mutations confirmed by direct DNA sequencing, 216 patients with T1DM and 178 healthy individuals were included in the study. The alleles of HLA-DRB1, -DQA1 and -DQB1 genes were evaluated using PCR-ASO method.

**Results:** The case-control approach confirmed that DRB1\*04-DQA1\*0301-DQB1\*0302 and DRB1\*0301-DQA1\*0501-DQB1\*0201 haplotypes are associated with predisposition to T1DM in the polish population; OR (95%CI) = 5.1 (3.2–8.1) and 1.8 (1.3–2.4), respectively. The most common protective haplotypes were DRB1\*1501-DQA1\*0102-DQB1\*0602 and DRB1\*1101-DQA1\*0501-DQB1\*0301; OR (95%CI) = 0.02(0.01–0.11) and 0.3 (0.2–0.5), respectively. The distribution of HLA alleles and haplotypes in the PNDM group was similar to that observed in control group. Interestingly, the DRB1\*1501-DQA1\*0102-DQB1\*0602 protective haplotype was statistically more frequent in PNDM (25%) than in T1DM (0.5%),  $p_c < 10^{-5}$ . However, the alleles and haplotypes of HLA-DRB1, -DQA1 and -DQB1 were almost equally distributed among islet antibody positive and negative PNDM patients.

**Conclusions:** As reported by others, HLA region do not contribute to pathogenesis of PNDM. Moreover, occurrence of islet antibodies in patients with PNDM was independent of HLA haplotypes predisposing to type 1 diabetes. Thus, HLA region

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seems to have no involvement in autoimmune response that can be triggered in patients with mutated Kir6.2 protein.

P/WED/58

### Family report on two siblings affected by transient neonatal diabetes - a novel SUR1 mutation inherited from the father

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**Objective:** Family report on two siblings affected by transient neonatal diabetes - a novel SUR1 mutation inherited from the father. Patient 1 was diagnosed with hyperglycaemia, dehydration and ketoacidosis at the age of 7 weeks. Insulin therapy was needed until the age of 4.5 months. Patient 2 was born six years later and was diagnosed with hyperglycaemia at the age of 3 weeks. Insulin treatment lasted until the age of 2.5 months. The two patients are now 8 5/12 und 2 7/12 years respectively and are still without insulin therapy.

**Methods:** Chromosome 6q24 abnormalities were excluded by genetic testing. Further analysis of the KCNJ11 gene which encodes the Kir6.2 subunit of the pancreatic KATP channel showed no mutation. To complete molecular genetic testing analysis of the ABCC8 gene encoding for the SUR1 of the KATP channel was performed and showed a mutation in the two affected siblings.

**Results:** Both children with transient neonatal diabetes and the father are heterozygous for a novel ABCC8 gene mutation. This T > C mutation at nucleotide 1352 (c.1352T > C) results in the substitution of proline for leucine at codon 451(p.Leu451Pro). This leucine residue is conserved across species. It is therefore most likely, that this missense mutation is pathogenic. The unaffected sister and mother are negative for the mutation. The analysis from the unaffected brother is pending.

**Conclusions:** The results of molecular genetic testing might be important in case of relapse of diabetes. Due to the gain-of-function mutation in the SUR1 subunit of KATP channel these patients are likely to respond to sulfonylurea treatment.

## Miscellaneous I

P/WED/59

### Clinical profile and autoantibody status in younger onset diabetes in Bangladesh

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**Objectives:** To examine the clinical profile and GAD and IA2-ic antibody (Ab) status in different clinical subtypes of 193 diabetics under 18 years attending BIRDEM, a tertiary centre in Bangladesh.

**Methods:** A cross sectional study from January 01 to December 03. Patients were classified based on clinical features. Type 1 (Group 1) patients were younger and had short duration of classical symptoms or presented with diabetic ketoacidosis (DKA); Patients with fibrocalculous pancreatic diabetes (FCPD/Group 2) had evidence of pancreatic stones; patients with malnutrition modulated diabetes (MMDM/Group 3) were malnourished with prolonged symptoms of

diabetes without ketosis. Two type 2 diabetics were excluded from the analysis using either ANOVA or the  $\chi^2$  test.

**Results:** Among 136 newly detected patients 41.2% had type 1 diabetes, 23.5% FCPD and 33.8% MMDM. Anti-GAD Ab positive patients had lower C-peptide ( $p = 0.01$ ) and relatively shorter duration of symptoms ( $p = 0.06$ ). Cataracts were present in 1.4%, 18.7% and 27.5% in Group 1, 2 and 3 subjects respectively ( $p = 0.0001$ ). Microalbuminuria was present in 10.1% in Group 1, 17% in Group 2 and 23.1% in Group 3 ( $p = 0.12$ ). Neuropathy was present in 1.4%, 12.7% and 18.8% in the three groups respectively ( $p = 0.01$ ).

	Group 1	Group 2	Group 3	p value
Age at diagnosis (years)	9.29 ± 4.1	13.54 ± 2.1	13.84 ± 2.33	0.0001
Duration of symptoms at diagnosis (months)	1.45 ± 1.28	5.6 ± 8	10.16 ± 8.05	0.0001
DKA	11/52 [21.1%]	0/31	0/45	
BMI (kg/m <sup>2</sup> )	14.05 ± 3.8	13.06 ± 2.2	12.76 ± 2.7	0.0001
HbA1c (%)	14.75 ± 2.84	17.62 ± 2.05	16.37 ± 2.96	0.0001
C-peptide (ng/ml)	0.54 ± 0.51	0.47 ± 0.23	0.66 ± 0.67	0.70
GAD Ab positive	20/50 [40%]	2/12 [16.6%]	8/43 [18.6%]	0.08
IA2-ic Ab positive	15/50 [30%]	1/12 [8.3%]	10/43 [23.25]	0.14

**Conclusion:** Although the three groups differ clinically, the C-peptide and antibody status do not discriminate between the types of diabetes defined by clinical criteria. Autoimmunity is also present in FCPD and MMDM indicating an overlap with T1D in these groups.

P/WED/60

### Medication induced diabetes during treatment of pre-B cell and T-cell ALL: prevalence, risk factors and characteristics in a population of ALL patients at The Hospital for Sick Children

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Medication induced diabetes (MID) occurs in 11% – 30% of patients receiving chemotherapy for acute lymphoblastic leukemia (ALL). It is usually temporary and few patients require insulin therapy. Older age, obesity, family history of diabetes and Down syndrome are risk factors for MID. The course of the disease and the effect of various treatment regimens on its development have not been clearly described.

**Objectives:** To determine the prevalence of MID during therapy for ALL and to study the associated demographic and treatment variables.

**Methods:** Patients treated for pre-B or T-cell ALL at The Hospital for Sick Children between 1998 and 2005 were identified retrospectively. Their medical charts were reviewed to estimate the prevalence and describe the course of MID (defined as two or more blood glucose values > 11.1 mmol/L). Each patient's complete medical course was examined for episodes of MID including all cycles of chemotherapy, admissions for fever and neutropenia and therapy for relapse including bone marrow transplant. Associations between the presence of MID and a number of demographic and treatment variables were assessed.

**Results:** 373 patients were diagnosed with ALL during the study period. One patient was excluded because of pre-existing type 1 diabetes. 110 patients (29.4%) developed MID during therapy. 56 patients developed their initial episode of MID during induction. 19 patients were treated with insulin (5%). Patients who developed

MID were older ( $8.3 \pm 4.9$  vs.  $5.5 \pm 3.7$  years,  $p < 0.001$ ), and had a higher body mass index (BMI) Z score ( $0.33 \pm 1.24$  vs.  $-0.01 \pm 1.36$ ,  $p = 0.04$ ). Gender was not associated with MID. Within the group that developed MID, older age, initial MID episode during induction and recurrent episodes of MID, but not BMI, were associated with insulin treatment.

**Conclusions:** Older patients and those with a higher BMI are more likely to develop MID during ALL therapy. This suggests a role for insulin resistance in the development of MID.

P/WED/61

### Neuronal cells *in vitro* produce taurine in response to a hyperosmolar environment - a paradigm for diabetic cerebral oedema and its therapy

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Clinical neurochemical data from children with type 1 diabetes mellitus and hyperosmolarity due to diabetic ketoacidosis (DKA) suggests a role for idiogenic osmoles such as taurine as an essential neuro-osmoregulator. *In vivo* studies of children with DKA have shown focal neuronal swelling and neurochemical changes in the fronto-medial, hippocampal and parietal subcortical neurons. This study investigates these changes further in an *in vitro* setting using the neuronal SH-SY5Y cell line. Under conditions of increasing glucose and sodium concentrations in cell culture medium, cell morphology and mitochondrial function (MTT assay) were documented, and taurine handling was observed using radiolabelled taurine tracer and HPLC to determine taurine production and release. Under graded hypertonic conditions, cell morphology and mitochondrial function deteriorated, radiolabelled taurine was released from the pre-labeled SH-SY5Y cells in a time-dependent biphasic manner and intracellular taurine production increased parallel with the intensity of hyperosmolar insult. Re-exposure of cells to hypotonic fluid, mimicking inappropriate fluid therapy, led to cell death. We have shown for the first time that neuronal cells facing a hypertonic environment *in vitro* generate taurine as a protective intracellular osmolyte. Our finding that subsequent exposure to hypotonic fluid is detrimental to cell survival leads us to speculate that such generation of idiogenic osmoles contributes to cerebral oedema following therapy for ketoacidosis with hypotonic fluid.

P/WED/62

### HOMA and QUICKI reflect hepatic but not peripheral insulin action in adolescents

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**Objectives:** Insulin stimulates muscle glucose uptake and inhibits hepatic glucose production. Measures of insulin sensitivity or resistance must take both of these actions into account. HOMAIR and QUICKI are two simple measures of insulin resistance and sensitivity that are derived from fasting glucose and insulin levels as such it is likely that they primarily reflect hepatic insulin action and not muscular effects.

**Methods:** To prove this hypothesis the relationships of HOMAIR and QUICKI to peripheral insulin sensitivity (PIS) and hepatic insulin resistance (HIR) were assessed in 36 adolescents (age  $13.5 \pm 2.9$  years, BMI  $23.0 \pm 5.7$ , mean  $\pm$  SD). PIS and HIR were determined using the stable labeled frequently sampled

intravenous glucose tolerance test (250 mg total glucose/kg, 13% 6,6-d2-glucose). PIS were calculated using the one compartment minimal model and stable glucose concentration. HIR was determined over the last hour of the study by multiplying hepatic glucose production (Steele's equation) by mean plasma insulin concentration. **Results:** As expected HOMAIR and QUICKI were significantly related to HIR (log HOMAIR and log HIR,  $r = 0.43$  and  $p = 0.01$ ; QUICKI and log HIR,  $r = -0.43$ ,  $p = 0.01$ ) but not PIS. When both PIS and HIR were included in the equations only the relationships to logHIR were significant. (log HOMAIR,  $p = 0.015$ , QUICKI,  $p = 0.014$ ).

**Conclusions:** These results demonstrate that in adolescents HOMAIR and QUICKI assess hepatic but not peripheral insulin action.

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### International Diabetes Federation "Life for a Child" Program

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In developed countries, people with diabetes can access full care and so generally lead healthy and productive lives. In contrast, in many developing countries insulin is often unavailable or unaffordable. Health centres may have no ability to measure blood glucose, and very few people can afford to self-monitor. Expert care may be unavailable, and some countries do not have any capacity to measure HbA1c. Many children die soon after diagnosis, or have poor control and quality of life and develop early and devastating complications. The International Diabetes Federation "Life for a Child" Program helps these children by assisting diabetes centres to provide cost-effective standard diabetes care. The program commenced in 2000, and is run from Sydney with the assistance of Diabetes Australia-NSW and HOPE worldwide. Core funds come from individual donors in Australia, the Netherlands, USA, and other countries - generally people with diabetes or their families. Funds are also donated by companies and associations. Partners include Insulin for Life, Rotary International, and Diabetesvereniging Nederland. We now support the care of 585 children in 13 countries: Tanzania, Rwanda, DR Congo, Nigeria, Azerbaijan, Uzbekistan, Nepal, India, Sri Lanka, Philippines, Papua New Guinea, Fiji and Bolivia. Support is provided to recognised diabetes centres. Priority needs (insulin, syringes, monitoring, education, training) are determined, a budget is decided, and specific lists of the neediest children are supported. The cost to support a child is US\$200-400/year. Health outcomes and financial trails are carefully monitored. Some highlights in various countries include: country-wide approaches, implementation of self-monitoring, extension of support from capitals to provincial centres, provision of HbA1c and biochemistry machines, establishment of registers, first recognition of type 2, and inaugural camps. We also conduct extensive in-country and international advocacy.

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### Month of birth seasonality in children with celiac disease differs between genders and from that in the general population

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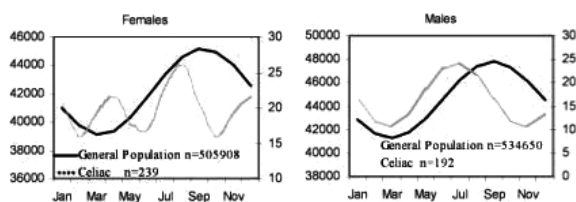
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**Introduction:** Celiac disease (CD) is an immune-mediated disease of multifactorial etiology, triggered by the ingestion of gliadin. It is closely associated with type 1 diabetes mellitus (T1DM) with the incidence of both diseases rising in recent years.

**Objectives:** Having previously shown that children with T1DM have a month of birth (MOB) seasonality different from that of the general population (GPop), we aimed to test the MOB pattern in a cohort of children with CD.

**Methods:** 431 children with CD (239F; 192M) from 2 children's hospitals in Israel were studied. 73% of the patients and 22% of first-degree relatives had other autoimmune diseases, predominantly T1DM. The yearly pattern of MOB was submitted to "cosinor" analysis.

**Results:** Female children with CD had a different pattern of MOB (3 peaks) from that in male patients (peak in summer) and the GPop in Israel (peak in autumn) ( $p < 0.01$ ) (Fig.). In the GPop both males and females showed a 12 months (mos) rhythm in MOB ( $p < 0.01$ ), peak in Sept ( $R = 0.85, 0.86$  respectively) while in CD female patients had a 4 + 8 mos rhythm (mesor 20.2 Amp4 = 3.8, Amp8 = 2.3  $R = 0.74$ ;  $p < 0.01$ ) with peaks in March, Aug and Dec. Male CD's had a 8 mos rhythm (mesor 17.46 Amp = 6.8  $R = 0.95$ ,  $p < 0.01$ ) with one peak in July. There was also a significant difference between the MOB pattern in CD children with or without CD in the family and in females diagnosed before or after age 2 years. [Laron Fig]



**Conclusions:** Children with CD have a different pattern of MOB than in the GPop. CD patients have excess births in summer as found for children with T1DM (Laron et al., JPEM 1999; 12:397-402). This supports a viral component in the etiology (Stene et al. Am J Gastro 2006; 101:2333-40).

P/WED/65

**Fulminant onset (Japanese) type 1 diabetes in a Caucasian boy, triggered by Lyme disease?**

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**Introduction:** Type 1 diabetes (T1D) results from autoimmune destruction of pancreatic  $\beta$ -cells. Markers of the immune destruction include autoantibodies to islet cell (ICA), insulin (IAA), glutamic acid decarboxylase (GAD 65), and tyrosine phosphatases (IA-2 and IA-2B). These autoantibodies are present in 90% of individuals with T1D. In Belgium, antibody-negative Caucasian patients presenting with a more severe metabolic decompensation, higher insulin needs, and less preserved  $\beta$ -cells mass were associated with higher HbA1c levels and did not show any sign of high amylase activity. In Japan (20% of acute onset T1D), but also in other Asian countries, several cases have been reported where islet-related autoantibodies were negative and the onset of diabetes was acute. The characteristics of rapid (or fulminant) onset (Japanese) T1D are: abrupt onset with ketosis or ketoacidosis; high plasma glucose with almost normal HbA1c; elevation of pancreatic enzyme levels; absence of islet-associated autoantibodies; rapid decrease in C-peptide secretion. There is no evidence of Japanese onset T1D in Caucasian patients.

**Case:** We report on a 5 1/2 year-old Caucasian Belgian boy who had been complaining for 2 weeks, mainly about abdominal pain and polydipsia. He was 115.5 cm tall (P3-10) and weighed 17 kg

(P10-25). Table 1 summarizes some biological characteristics. Serum was negative for ICA, IAA, GAD 65 and IA-2. The HLA-DQ genotype was protective for T1D. At admission to the hospital, the patient showed painful swelling of joints in the legs. Serologic testing was positive for *Borrelia burgdorferi*.

	Day 1	Day 2	1 month
Glycaemia (mg/dl)	403		
HbA1c (%)	5.3		5.6
C-Peptide ( $\mu$ g/l)	6.5 (glycaemia: 80 mg/dl)	1 (glycaemia: 105 mg/dl)	0.8
Amylase (IU/l)	106 (n < 100)		49
Lipase (IU/l)	131 (n < 60)		23
pH	7.25		
HCO <sub>3</sub> - (mmoles/l)	16.2		

**Conclusion:** This could be the first case of fulminant (Japanese) T1D in a Caucasian child since he displayed the main characteristics: abrupt onset with acidosis; high glycaemia with normal HbA1c; elevation of pancreatic enzyme levels; rapid decrease of serum C-peptide; absence of islet cell auto-antibodies. The concomitant Lyme disease could be a trigger factor.

P/WED/66

**Metabolic health in UK children is unrelated to social inequality (The Earlybird Diabetes Study)**

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**Objectives:** Health interventions increasingly target poor neighbourhoods in the belief that inactivity, obesity and diabetes risk are linked to deprivation. We tested this assumption in a cohort of 224 healthy children from 53 schools across a wide social range.

**Methods:** Home deprivation was based on individual home postcode and school deprivation by the percentage of pupils entitled to free lunch at the school attended. Physical activity (PA) was monitored objectively by accelerometry, and the mean of 4 recordings, each over 7 days, at ages 5, 6, 7 and 8 was used to estimate the child's habitual PA. Body mass index sds (BMI) was measured at 8 year. Metabolic risk (METrisk) was assessed at 8 year using the mean z-score of four markers: insulin resistance (HOMA), triglycerides, cholesterol/HDL ratio and blood pressure.

**Results:** In boys, PA was unexpectedly higher in those living in deprived areas ( $r = 0.17$ ,  $p = 0.05$ , substantially so in those attending more deprived schools ( $r = 0.26$ ,  $p = 0.004$ ). Neither index of deprivation was significantly related to BMI (home  $r = -0.16$ ,  $p = 0.07$ ; school  $r = -0.04$ ,  $p = 0.64$ ). Similarly, deprivation was not associated with METrisk, even after adjusting for BMI (home  $r = -0.01$ ,  $p = 0.94$ ; school  $r = -0.04$ ,  $p = 0.66$ ). METrisk was, however, weakly related to habitual PA ( $r = -0.17$ ,  $p = 0.05$ ). In girls, neither index of deprivation was related to PA (both  $r < 0.05$ ,  $p > 0.66$ ), or BMI (both  $r < 0.08$ ,  $p > 0.43$ ) or to METrisk (both  $r < \pm 0.04$ ,  $p > 0.70$ , even after adjusting for BMI). METrisk was unrelated to PA ( $r = -0.10$ ,  $p = 0.35$ ). Crucially, METrisk, even at this young age, was closely related to BMI in both girls and boys ( $r = 0.47$  and  $0.50$  respectively, both  $p < 0.001$ ).

**Conclusions:** We can find no evidence, in contemporary children, that metabolic disturbance is associated with social inequality. Excess weight gain seems to be the overriding factor, irrespective of socio-economic status. These findings may have economic implications in health care targeting.