INVITED SPEAKERS

Metabolomics – A New Route to Type 1 Diabetes

INV01

Metabolome en route to type 1 diabetes

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Serum metabolome was investigated prospectively in children who later progressed to type 1 diabetes as well as in the non-obese diabetic (NOD) mouse. Serum metabolite profiles were compared between sample series drawn from 56 children who progressed to type 1 diabetes and 73 controls who remained non-diabetic and permanently autoantibody negative. The controls were matched for time and site of birth, gender and genetic risk. Additionally, serum samples were collected every week from 80 (35 female, 45 male) NOD mice starting at 3 weeks of age.

Individuals who developed diabetes had reduced serum levels of succinic acid and phosphatidylcholine at birth, reduced levels of triglycerides and antioxidant ether phospholipids throughout the follow-up and increased levels of proinflammatory lysophosphatidylcholines several months prior to seroconversion to autoantibody positivity. The lipid changes were not attributable to HLA-associated genetic risk. The appearance of insulin and GAD autoantibodies was preceded by diminished ketoleucine and elevated glutamic acid. The metabolic profile was partially normalized following the seroconversion. Phospholipid changes observed prospectively in progressors to type 1 diabetes were also observed in female NOD mice who later progressed to T1D. Similarly as observed in children, lysophosphatidylcholines were elevated in insulin autoantibody (IAA) negative mice that later progressed to T1D, but were at normal levels in IAA positive mice in the same group. Autoimmunity may therefore be a relatively late response to the early metabolic disturbances. Recognition of these pre-autoimmune alterations may aid in studies of disease pathogenesis as well as open a time window for novel type 1 diabetes prevention strategies.

Translational Research in Pediatric Diabetology

INV02

The concept of systems biology in pediatric diabetes

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Diabetes mellitus is a serious chronic disorder of childhood and its incidence is increasing, thus representing a major public health problem. Diabetes is a complex disease resulting from the interaction between multiple genetic and environmental factors. Given the complexity of the disease, a systems biology approach is needed to better understand the pathogenesis of diabetes and its complications, and to identify potential new therapeutic drugs for primary or secondary prevention. Systems biology is defined as the quantitative analysis of the dynamic interactions between several components of a biological system through the combination of mathematical modeling and experimental biology, with the aim of understanding a system as a whole. This is obtained through the combination of several 'omics' sciences: genomics, transcriptomics, proteomics, metabolomics. A genome wide association-approach has been used in diabetes and has led to the identification of several genetic loci associated with the disease. This approach also represents an important starting point for new biomarkers discovery in diabetes. Proteomic studies in diabetes have focused on *in vitro* and *in vivo* experiments, finding evidence for cytokine- and cellular-mediated autoimmunity as a primary event in β-cell destruction. Increased morbidity and mortality in patients with diabetes are mainly attributable to vascular complications. Functional genomic studies of kidneys have been performed in rodent models and identified specific genes expressed in the context of diabetes. Urinary and plasma proteomics have unraveled specific protein patterns associated with diabetic nephropathy. Further advances in genomics, proteomics and in other 'omics' and the integration of the findings of these different sciences will hopefully allow a better understanding of the pathogenesis of diabetes and its complications in the near future and will potentially lead to a personalized medicine for young patients with diabetes.

INV03

CGM – translating research trials to clinical practice

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Children and adolescents with T1D are using newest technologies for their diabetes treatment. The number of pump users is increasing steadily, and more and more patients are using insulin analogues. Patients are measuring their blood sugar more than 10 times daily. But still patients lack of exact informations about postprandial hyperglycemias and nocturnal hypoglycaemia, about blood sugar (BS) excursions during sport activities and acute illness. Real-time (RT) continuous glucose monitoring (CGM) systems may completely change the treatment of T1D. RT-CGMS helps us to understand the dynamic of BS oscillations in different situations. It helps patients to improve their diabetes treatment. In the last five years the number of clinical investigations using CSII or CGM systems increases steadily. Majority of them showed that continuous use of CGM-systems helps to lower HbA_{1c} levels and to reduce the number and length of hypo and hyperglycaemia of patients with T1D in different age groups. RT-CGM is known to be safe and well tolerated and provide readings that are close to BS measurements with commonly used meters. The new generations of CGM systems give patients more information then ever. Alarms inform about borderline sugar values, trend arrows give information's about future sugar excursions, exact sugar values can be seen on the screen at any time. Guidelines for proper use of sensors in different age groups are needed. Lessons from clinical studies should give informations how to use the system properly. The accuracy and efficacy of different RT-CGMS were analyzed in several studies, but still more studies are needed to support widespread use of different CGM devices. The benefits in different groups of patients as toddlers, teenagers or pregnant woman should be of special interest. Continuous use of sensors for longer period of time should be encouraged since research showed that regular use of sensors helps mostly in achieving good metabolic control.

New Developments in Nutritional Management

INV04

Nutrition for competitive athletes with type 1 diabetes

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Patients with T1D may profit from regular physical exercise, especially when this is coupled with self-monitoring of blood glucose. However the management of athletes with T1D is still seen as an issue, even if they have been able to achieve success at all

levels of competitions in recent years. In order to reach their goals athletes with T1D require adequate amounts of macronutrients and energy to support their training and sustain performance during regular exercise and during competitions. This however may alter glucose levels, which in turn may create the need for glucose monitoring during sport training and performance in order to avoid hyper and hypoglycaemia. According to the National Athletic Trainers' Association Position Statement 2007, keeping a near-normal BG levels (100 to 180 mg/dL or 5.5 mmol/L to 10 mmol/L) reduces the risk of dehydration, lethargy, hypoglycaemia, and autonomic counter regulatory failure. Athletes should be instructed to always monitor their BG before training and performance since they should avoid physical activity if fasting BG levels is above 250 mg/dL and ketosis is present, and use caution if glucose levels is above 300 mg/dL and no ketosis is present. On the other hand they should take extra carbohydrate if glucose levels are below 100 mg/dL. They should learn carbohydrate counting and carbohydrate-to-insulin ratio. Carbohydrate counting for athletes has application in several settings: during daily training, for the week before a competitive event, in the preceding hours before competition, during competition, and in the 24 hours after competition. For each of these time periods, appropriate carbohydrate and insulin dosages must be determined to maximize performance and keep blood glucose levels within the patient's therapeutic goals.

In this lecture we review the state of the art in this field and discuss recent experience using Continuous Glucose Monitoring System (CGMS) in managing athletes with type 1 diabetes.

INV05

Estimating the prandial glucose rise: do children need to count carbs, fat and protein?

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At present, most patients with type-1 diabetes are using multiple daily injections or insulin pump therapy according to the basal-bolus principle. In both forms of treatment, calculations of prandial insulin boluses are based on the amount of carbohydrates (CARB) of the meal. Despite of correct bolus application, a high proportion of late postprandial hyperglycemic excursions is observed in some patients, particularly after ingestion of meals rich in protein and fat.

Insulin pumps offer nowadays the possibility of applying 3 different kinds of boluses: standard, square-wave and dual-wave bolus. Few studies have shown that the use of dual-wave bolus could lead to a better postprandial glycemia than the use of standard bolus in carbohydrate- and fat-rich meals. However, until now there are no established strategies to adjust prandial insulin calculations according to the different components of food intake. Pankowska et al. (Pediatr Diabetes, 2008) recently described an empiric algorithm for the calculation of prandial insulin dose taking into consideration the energy delivered from all three components, CARB, protein, and fat as well. Although they report positive results and good glycemic control in patients using this algorithm along with pump therapy, there is a lack of systematic studies for the evidence and effectiveness of this procedure.

Therefore, we initiated a prospective, randomized clinical trial (Pediatric Pizza-Salami Study) to evaluate the effectiveness of insulin dose adjustments of CARB-based compared with CARB-, protein- and fat-based methods using standard or dual-wave bolus for insulin delivery. Primary measure is the 6h postprandial glucose profile after a standardized age/gender- and energy-adjusted test meal as assessed by continuous glucose monitoring system. The study population consists of pump users aged between 6 and 21 years with type-1 diabetes for a least 1 year. First results will be reported.

INV06

Impact of Nutrition on Type 1 Diabetes Management and Outcomes

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Medical nutrition therapy is a fundamental part of diabetes management. The major focus of the nutritional management of diabetes rests in carbohydrate counting to allow the careful matching of prandial insulin with carbohydrate intake. Youth with type 1 diabetes (T1D) also need to follow general pediatric nutrition guidelines regarding daily intake of protein, carbohydrates, fats, and other nutrients to ensure normal growth and development and reduced risk of cardiovascular disease. Recent data suggest suboptimal dietary quality in youth with T1D with excessive intakes of saturated fats and cholesterol and inadequate intakes of fiber and vitamin D. In fact, up to 75% of youth with T1D have insufficient or deficient levels of vitamin D.

Recent data also link dietary management with diabetes outcomes in youth with T1D. Increased adherence to nutrition has been associated with lower HbA1c in the pediatric population with T1D. Investigators from the Barbara Davis Diabetes Center have reported that fewer than 1 out of 4 adolescents with T1D accurately estimate carbohydrates. In addition, our research group has identified the importance of carbohydrate estimation consistency rather than carbohydrate counting accuracy for optimizing glycemic control.

The current era of intensive insulin therapy, affording physiologic insulin replacement and greater flexibility, has potentially undermined the fundamental importance of overall healthful eating aimed at optimizing weight and lowering risk for cardiovascular disease.

Opening Ceremony

INV07

ISPAD history

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International society for pediatric and adolescent diabetes (ISPAD) was established as International Study Group for diabetes in children (ISGD) on June 12th 1974 in Paris by 16 pediatric-diabetologists led by Prof. Henry Lestradet. Mayor reason for establishment was lack of attention for childhood diabetes by other diabetological associations – EASD, ADA and IDF - which focused mostly on type 2 diabetes in the adults.

The main purpose of the organization was promotion of care for children and adolescents with diabetes. It has encouraged and supported basic, clinical, epidemiological, health economic and all other relevant research concerning pediatric and adolescent diabetes. The objectives were accomplished through scientific meetings, training programs, collaborative studies and promotion of education and research on children diabetes.

In the first decade ISGD was attended mostly by pediatric-diabetologists from Western Europe and USA. Following meetings in Miscolc, Hungary and Bled, Yugoslavia (Slovenia) activities of ISGD spread also to Eastern Europe, Asia, Australia and South America.

On September 4th 1993 ISGD was transformed during the 19th meeting on the Island of Kos, Greece into ISPAD. At that time, the members proclaiming their commitment to implementation of the St Vincent Declaration to promote optimal health, social welfare and quality of life for all children and adolescents with diabetes.

One of the greatest successes of ISPAD was the implementation of the ISPAD consensus guidelines on the treatment of diabetes in the young in 1995, which were later renewed. In 2005 Pediatric Diabetes became the official journal of ISPAD.

39th ISPAD meeting will be held in Slovenia again after 20 years. At that time it was organized by one of the founding members of ISGD–ISPAD Prof. Leo Matajc.

In the presentation some of the most important former ISPAD annual meetings, staff members and achievements of the society will be presented.

Pediatric Type 2 Diabetes – Screening, Treatment and National Programs

INV08

Incidence and clinical characteristics in childhood type 2 diabetes (T2DM)

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Various reports have demonstrated that the incidence of childhood T2DM has increased all over the world in recent years. The recent incidence of childhood T2DM in Japan is estimated to be approximately 3.0–3.5/100 000/yr. The incidence in junior high school students (0.7) is three to six times higher than that in primary school students (5.0–8.0). In Tokyo, the incidence of T2DM in school children in 1980–2004 (2.9) reveals significantly higher than that in 1975–1980 (1.7). More than 80% of children with T2DM are obese, and boys are more likely to be obese than girls. It is speculated that the increase in the incidence of childhood T2DM over the decades may be a consequence of the increase in the frequency of obesity among school children. However, this trend of increasing incidence of childhood obesity has recently become weaker, and perhaps as a consequence, the incidence of T2DM has decreased after the year 2000. Besides, 60–70% of the patients have a family history of T2DM in second- and first-degree relatives. The family history plays a crucial role in the majority of children developing T2DM. On the other hand, several studies have demonstrated that intra-uterine environmental factors could affect the development of T2DM. The Japanese Society for Pediatric Endocrinology investigated the associations of weight at birth, weight at diagnosis of T2DM, and clinical characteristics of T2DM. 11.3% of the patients had low birth weights (<2500 g) and 9.7% had high birth weight (>4000 g). The frequencies of low and high weights were higher among children with T2DM than among a control group. This U-shaped relationship was more evident in non-obese than in obese patients with T2DM. The frequency of a family history of T2DM was lower among low-birth weight patients. In contrast, high-birth weight patients had a higher prevalence of diabetic mothers. Differences in clinical characteristics were demonstrated among patients with T2DM with low and high birth weights.

INV09

Treating postprandial hyperglycemia in young with type 2 diabetes

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Prandial glucose regulation (PGR) is an emerging approach to treating type 2 diabetes that emphasises the need for moderating the acute surges in plasma glucose levels that follow meals. Mechanistic and epidemiological studies indicate that postprandial glucose (PPG) contributes significantly to overall glycemic exposure and helps drive the complications of diabetes. In particular, post prandial hyperglycemia is the most important contributor to HbA1c, particularly when is lower than 7.5%. Therefore, targeting postprandial hyperglycemia is mandatory for the achievement of HbA1c targets. Numerous prandial therapeutics are now available, and an ever-growing literature on their use shows that they are safe, effective, and convenient and that they may offer distinct clinical benefits not found with treatments that target basal (fasting) glycemia. IDF guidelines recognize the significance of PPG and the need to measure and treat it. In these guidelines the cut-off for PPG is indicated in 7.8 mmol/l (140 mg/dl).

INV10

Treatment of type 2 diabetes in youth: what do we know and what's on the horizon

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Historically, type 2 diabetes mellitus (T2DM) has been a disease of adults and older individuals and not a pediatric condition. However, recently there has been an alarming trend of increasing cases of youth T2DM in the USA and the rest of the world. The majority of these youths are obese, in mid puberty, have a strong family history of T2DM and have conditions associated with insulin resistance, such as metabolic syndrome, PCOS etc. The pathophysiology of T2DM in youth involves peripheral and hepatic insulin resistance together with defective b-cell function and relative insulin deficiency. With the increasing rates of obesity in the general population as well as in youth with type 1 diabetes, the distinction between ''true'' T2DM and obese type 1 diabetes may not be possible on the basis of clinical features. Thus, not infrequently obese children with type 1 diabetes may be clinically diagnosed as having T2DM. Despite the wealth of approved therapeutic options in adults with T2DM, currently available therapies in pediatrics are very limited and include metformin and insulin. In this lecture data will be presented in regards to: 1) the pathophysiology of T2DM in childhood; 2) the metabolic differences between those patients with vs. without pancreatic autoantibodies; 3) the management strategies for youth T2DM; and 4) future innovative drug therapies in development.

Diabetes in Africa

INV11

A global view of diabetes in Africa and the African diaspora

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Of the 41 IMF classified heavily indebted poor countries (debt/revenue ratio $>280\%$) 32 are in Africa. These countries face the double burden of high mortality from communicable and non-

communicable diseases. As economies improve non-communicable diseases take over as the major cause of mortality. Estimated adult type 2 diabetes prevalence rates in Sub-Sahara Africa will increase by 80% from 2007 to 2025 (from 10.4 to 18.7 million) and by 75% in North Africa (from 8.3 to 14.5 million) (1).The estimated prevalence of children with type 1 diabetes is 38.8 thousand in Sub-Saharan Africa (probably over-estimated) and 29.1 thousand in North Africa. Incidence rates of type 1 diabetes in North Africa are 7.3–10.1 (per 100 000 < 15 year) whilst the rates in Sub-Saharan Africa are largely unknown (1). Many die or have poor control. The IDF Life for a Child Program assists children in Rwanda, Tanzania, DR Congo, Nigeria, Zimbabwe, Mali, Sudan and Morocco. Ketosis-prone type 2 diabetes (also described as Atypical, Flatbush diabetes) is a well-described form of diabetes in people of African origin which can cause life-threatening ketoacidosis followed by prolonged normoglycaemia on minimal or no therapy (2).

The estimated African diaspora population is 168 million: North America (USA) 39 million, South and Central America 101, Caribbean 22, Europe 8.0. There is a gradient of increasing age-standardized diabetes prevalence among groups of African origin with increasing Westernization (rural Cameroon 0.8%, urban Cameroon 2.0%, Jamaica 8.5%, and UK 14.6%) (3). While genetic influences exist the predominant factors for the increase in diabetes relate to diet, physical activity and social determinants.

References:

1. IDF Atlas 3rd Ed 2006.
2. Choukem S-P et al. Diabetes Care. 2008; 31: 2332–2337.
3. Mbanya JC et al. Diabetes Care. 1999; 22: 434–440.

INV12

The story of Antony and his family – could it be different?*

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As it is well known already, childhood diabetes exists in Africa. Whether it is a rare disease or it has specific features, no one could tell for sure. All the published resources state that diabetes among children is characterized by high mortality and that the occurrence of diabetic ketoacidosis is inevitable. The terms ''availability and affordability'' always accompany comments about insulin supplies. This means that even if there is some insulin around, maybe it is out of the reach of the affected child's family. There are so many infectious, parasitic and malnutrition diseases that diabetes seems somewhat outrageous, even to pediatricians. Epidemiological data are elusive, and trained pediatric endocrinologists are virtually non-existent at most settings. The historically emerged compound mixture of witch-craft and prejudice, Christianity and touches of cutting-edge technology makes it almost impossible for foreigners to figure out how they could be of help. But what if you were born in Nairobi, were lucky enough not to have AIDS and all of a sudden develop this sophisticated disease? Antony is a nice 15 year-old student, the brightest in his class, who developed diabetes before his forth birthday. He survived the initial DKA and never omitted insulin, just occasionally a meal when unavailable. Antony hasn't experienced a hypo that he could remember and doesn't grumble over diabetes. He is reconciled with his fate, just dreams to be allowed to eat fruit or rice sometimes. His parents are proud of him. They have just begun to worry why he doesn't grow as his peers do. His unemployed father is grateful that Antony doesn't get sick often – he still remembers the initial 3 months hospital stay that starved out the whole family, although as he recalls the hospital taxes were not high. What would be Antony's life like? Could it be different? That is worth discussing.

*V.I. was 2008 July's tutor for the Pan-African ESPE Pediatric Endocrinology Training Program in Kenya.

INV13

Paediatric diabetes in Tanzania: problems and perspectives

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Introduction: Tanzania is currently experiencing a rise in childhood diabetes as the rest of the world. Diabetes exerts a considerable burden on health resources of the developing countries which are already stretched to the limit by infections such as malaria, tuberculosis and HIV/AIDS. The economic cost of diabetes and its complications cannot be met by most of the individuals and families in these countries. Activities to raise public awareness helped in improving the management resulting in early diagnosis of children with diabetes. The improvement in paediatric diabetes care in Tanzania is largely attributed to sponsorship from IDF and WDF. Tanzania was among the country which benefited from IDF child sponsorship programme and World Diabetes Foundation. There about 265 children in five WDF.

Challenges: Despite the provision of free insulin these children still have poor glycaemic control indicated by high HbA1c.These could be due to poor compliance of insulin, injecting wrong dosages since most of the children lack parental/adult support and guidance. Most families have financial constrains, causing them to miss clinics appointments, miss a meal hence skip insulin. Poor storage of insulin in many families may cause decrease of insulin potency. Many families have no refrigerator, or have no reliable supply of electricity so use other local alternatives which may not be so effective. Currently there is no epidemiological data, on incidence and prevalence of diabetes in children – hence it is difficult to convince the government and donors on how big is the problem. The ratio of number of patients to health care provider trained in the field of diabetes in Tanzania is too high.

Way Forward: Provision of psychosocial support as well as parental guidance. Scaling up of T1DM the initiative that will be supported by Novo Nordisk. We are currently preparing the education material and adopting the ISPAD guideline to suit our local circumstances.

The Loop Club: New Approaches to Artificial Pancreas

INV14

Noninvasive glucose MONITORING with a Multisensor System under different conditions – what to expect

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A non-invasive Multisensor device for continuous glucose monitoring, based on dielectric spectroscopy, combined with additional sensors for optical, sweat/moisture and temperature measurement has been developed. The motivation for the multisensory device is based on the understanding that various temporal fluctuations of the properties of skin, can introduce significant perturbations to the actual glucose related measurement.

In the course of this development, several experimental clinical studies have been performed to a) investigate the performance of the concept in the individual development steps, b) verify on the impact of the introduced miniaturization steps, c) test the concept under increasingly more demanding experimental conditions and d) repeat a standard experiment to compare and benchmark the individual development steps with each other.

Within a period of 4 years conditions have been taken from highly controlled to nearly unrestricted daily life experimental conditions. At the same time individual sensors have been stepwise merged onto one substrate, arriving at a fully integrated Multisensor device with the dimensions of 54 x 64 x 14 mm. Typically, the Multisensor is attached to the upper arm with an elasticated arm band. Sensor signals are transmitted vie Bluetooth to either a computer or a Pocket PC. In the meantime several hundred study days have been performed within different development steps. Results will be shown from these development steps as well as from different experimental conditions. Effects and challenges will be illustrated and discussed according to the findings in these studies. Furthermore, an outlook will be given on how to address these challenges and what steps are needed for this system to move from a miniaturized concept to a prototype level that can then eventually move towards clinical validation.

INV15
Application of immunoisolation in the treatment of diabetes

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Many have been the efforts to design technologies to transplant pancreatic islets in the absence of immunosuppression. Most of these approaches are still far from clinical application. A promising technology that is gaining increased attention during recent years is microencapsulation of pancreatic islets. The technology is based on the principle that foreign cells are protected from the host immune system by an artificial membrane. Inspite of the simplicity of the concept, progress in the field of immunoisolation has been hampered for many years due to biocompatibility issues. During the last years important advances have been made in the knowledge of the characteristics and requirements capsules have to meet in order to provide optimal biocompatibility and survival of the enveloped tissue. Novel insight shows that not only the capsules material but also the enveloped cells should be hold responsible for loss of a significant portion of the immunoisolated cells and, thus, failure of the grafts on the long term. Microcapsules without cells can be produced as such that they remain free of any significant foreign body response for prolonged periods of time in both experimental animals and humans. New approaches in which newly discovered inflammatory responses are silenced bring the technology of transplantation of immunoisolated cells close to clinical application.

INV16
Continuous glucose monitoring utilizing a FRET-based method – The P.CEZANNE project

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Continuous glucose monitoring (CGM) is a prerequisite for utilizing insulin pump therapy in an efficient manner, and is still deemed a worthy aim in preventing diabetes complications in spite of the limited success reported in the NEJM study (NEJM 359;14:1464–76, 2008). The main groups of CGM devices can be grouped into transcutaneous and corneal optical devices (both noninvasive), subcutaneous electrochemical devices (minimally invasive), and implanted devices (such as the P. Cezanne device). The optical devices use a variety of technologies including near and mid infrared and Raman spectroscopy. The corneal devices are bases on colorimetric glucose measurement utilizing phenylboronic acid. Currently the most common utilized systems include the Medtronic Guardian RT, the Minimed Paradigm and the Abbott Freestyle Navigator, based on glucose oxidase-electrochemistry. These systems enable continuous monitoring of glucose for a limited time, but their acceptability is still hobbled by the high costs of consumables and by technical constraints. We will review these systems and give an overview of the various approaches that are used to follow the variations glucose concentrations. We shall also present recent advances in the P. Cezanne Fluorescence Energy Transfer (FRET)-based continuous glucose monitoring solution. The core of our system consists of a bacterial glucose-binding protein hybridized with two fluorescent proteins (GBP-fluo) that exhibit a FRET response to varying glucose concentrations. An animal cell line has been developed that stably expresses GBP-fluo. Solutions are being found for the energy source for the sensor, the microelectronics and the hydrogel-based waveguiding sensing chamber. Biocompatibility issues and antifouling of the sensing membrane are problems that require further research. When finally operational, we hope that our implantable system and its associated telemedicine network may provide a truly autonomous and durable solution to CGM.

Diabetes Interacting with Other Hormonal Axes

INV17
Androgens and type 1 diabetes

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Abnormalities of androgen levels have been described in patients with type 1 diabetes (T1DM). Recent clinical information about pubertal development in boys with T1DM shows that despite receiving intensive treatment some delay of pubertal development still is observed in them. This clinical data suggests that partial androgen deficiency is present during puberty in boys. However, studies evaluating the levels of testosterone in adolescents with T1DM have shown conflicting results. A possible mechanism explaining this delay in puberty is that insulin has a role in the central nervous system, and that hypogonadotropic hypogonadism occurs associated with insulin deficiency. Insulin receptors present in the hypothalamus have a permissive role on gonadotropin secretion and experiments performed in animals have shown that under insulin deficiency, hypogonadism mediated by a decrease in kisspeptin expression in the hypothalamus occurs.

Hyperandrogenism has been classically associated with insulin resistance and type 2 diabetes, but increasing evidence shows that T1D women may also exhibit this abnormality. Girls with T1DM exhibit increasing androgens and signs of incipient functional ovarian hyperandrogenism at the end of puberty. In adult women a prevalence of 40% of clinical or biochemical hyperandrogenism has been shown, but this problem has a milder magnitude compared with non-diabetic PCOS women. An association of hyperandrogenism with intensive insulin treatment, but not total daily insulin dose, and with premenarcheal onset of DM has been described.

This talk will review clinical data, physiopathology and treatment of abnormalities of androgen levels in patients with T1DM.

INV18

Thyroid function in type 1 diabetes

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Autoimmune thyroid disease (AITD) is frequently observed among children and adolescents with type 1 Diabetes (T1D) as well as among their first degree relatives. The overall incidence of positive thyroid auto-antibodies in T1D children and adolescents, even at diabetes onset, ranges from 15% to 30%, with a higher preponderance among girls, and up to 50% of such patients progress to clinical AITD. The progression of thyroid auto-antibodies positivity to TSH increase mostly occurs within 5 years, ranging from the time of diabetes onset to several years of follow-up, with a higher incidence around puberty. It is well known that hormonal thyroid abnormalities, even at a subclinical stage, may interfere with glycaemic metabolic control and may increase insulin requirements, however, studies in both type 1 diabetic children and adolescents and in pregnant type 1 diabetic women indicate that the presence of thyroid auto-antibodies without thyroid dysfunction has no negative effect on the patient's glycaemic control.

Patients developing both T1D and AITD are considered to have an autoimmune polyglandular syndrome type 3 variant (APS3v). As a result of this strong association between AITD and T1D, two organ-specific T-cell mediated diseases, genetic studies searching for common loci/genes for susceptibility for both diseases demonstrated the presence of three loci on chromosomes 2p, 6p and Xp in patients affected from both endocrine disorders, revealing a strong shared genetic susceptibility to T1D and AITD, with most shared genes involved in immune regulation, suggesting that immune dysregulation plays an important role in the joint susceptibility to T1D and AITD. Due to the high incidence of thyroid auto-antibodies among T1D patients and the high incidence of progression to subclinical or clinical hypothyroidism and rarely to Grave's disease, annual screening of all diabetic children and adolescents for thyroid auto-antibodies as well as measurement of TSH is recommended.

SWEET Dreams: Structure, Process and Outcome Quality in Europe

INV19

Heterogeneity of pediatric diabetes care in Europe

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Introduction/objectives: Diabetes is one of the most frequent chronic diseases affecting children and adolescents. The main objective of SWEET Project is to improve control of diabetes all types in children by supporting the development of centers of reference for pediatric diabetes in the EU. Here we present results of work package 1 of this project aiming to describe current situation on pediatric diabetes care in EU.

Methods: Data were collected using two questionnaires. The first one distributed among leading centers of pediatric diabetes (one per country) was aimed to establish an overview of systems, national policies, quality control and financing of pediatric diabetes care. Responses were received from 26/27 EU countries. The second questionnaire was widely disseminated among 354 ISPAD members from EU countries and included questions related to individual pediatric diabetes centers. A total of 108 datasets were collected and processed from health care professionals caring for more than 29 000 children and adolescents with diabetes.

Results: There is considerable heterogeneity in the delivery of care for children with diabetes across Europe. Only 13/26 EU countries have a pediatric diabetes register. Seventeen countries have officially recognized centers for pediatric diabetes, but only eight of them have defined criteria for becoming such a center. A system of quality control of pediatric diabetes at the national level was reported from 7/26 countries. Twelve countries have reported national diabetes plans. Moreover, in only four countries deals this plan specifically with children. Two countries are addressing children at risk of type 2 diabetes by focusing on childhood obesity.

Conclusions: The dataset forms an important basis enabling the development of strategies towards better and more equal access to modern pediatric diabetes care across Europe.

INV20

The SWEET Project – a model for Europe and beyond?

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'SWEET' is an acronym standing for 'Better control in paediatric and adolescent diabetes: working to create Centres of Reference' and is based on a partnership of established national and European diabetes organizations (www.sweet-project.eu): ISPAD (with paediatric centres from the Czech Republic, France, Germany, Greece, Hungary, Italy, Luxembourg, the Netherlands, Poland, Portugal, Romania, Sweden, UK to start with), IDF Europe, FEND, and PCDE. Co-funding was granted by the European Public Health Executive Agency with additional funds from corporate partners and foundations.

Outcomes of the project will be a better knowledge of paediatric diabetes in Europe, recommendations for minimum treatment and care standards, for patient education programmes and for paediatric training programmes for health professionals. Finally, a toolbox supporting the creation of Centres of Reference for paediatric and adolescent diabetes will be put in place. It will include a platform that allows any participating centre to import and input data online using a standard diabetes data set for paediatric diabetes patients. Those centres that do not currently have an electronic medical record system can enter their data directly into the database and manage patient information. Aggregate data is de-identified and exported to the SWEET

project for longitudinal data analysis, training and ongoing delivery and improvements in the quality of patient care. In a first step the SWEET Online platform will allow 12 countries in 11 languages to connect to one unified diabetes database.
The goal is to develop joint recommendations for structure, process and outcome quality with regard to the treatment strategies and standards for paediatric diabetology, as well as training programs for diabetes experts and patients. The SWEET project hopes to extend from the initial group of centres within countries and throughout Europe and beyond with the help of the ISPAD network.

INV21
How sweet is SWEET? – better control in pediatric and adolescent diabetes: working to create centres of references

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The increasing incidence of T1DM in children and decreasing age at onset, has been reported almost everywhere in Europe. The disease itself and its late (micro- and macrovascular) complications may cause major burden both personally and financially as well as for society. With optimal care from diagnosis and onwards, the long term complications may be prevented or delayed.
Identification of current standards of treatment and care of children with diabetes in the EU, and the recommendations for better control in paediatric and adolescents diabetes is one of the objectives of the SWEET project.
Through a mail questionnaire, information was obtained on practice guidelines, structure of diabetes teams and their services.
In most countries the ISPAD Clinical Practice Consensus Guidelines 2006–2008 was used as basis for the national recommendations of diabetes care and treatment.
Although treatment goals may be comparable, and care through multidisciplinary teams is supported, for none of the team members, EU wide recognised professional training exists. Recognized team members, their roles, their availability and the services provided, differ significantly between the countries.
The aim of the SWEET study is to address these differences as well as create recommendations of Diabetes Care and Treatment to enhance equal standards of treatment and care of children with diabetes within Europe.
This is SWEET!

Translational Research in Early Micro- and Macrovascular Complications in Pediatric Diabetes

INV22
The neuropsychological impact of type 1 diabetes in childhood and adolescence

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The attainment of optimal mental health and neurocognition is arguably the pre-eminent developmental task of childhood and adolescence. The potentially deleterious impact of a chronic disease such as type 1 diabetes upon brain development is therefore highly significant. Given the dependency of neural ontogeny and function upon stable and adequate blood glucose levels, there is a strong theoretical concern that type 1 diabetes in childhood and adolescence may impact upon neurocognitive development. Recent DCCT publications found no deterioration in cognitive function in adults or adolescents. Children and younger adolescents however have different neurophysiological requirements. Acute effects on cognition in childhood by either high or low blood glucose levels have been documented. The issue of the chronic impact of type 1 diabetes on the developing brain remains an open question. Controlled twelve year prospective data from diagnosis of type 1 diabetes from childhood through to neuromaturation published by our group showed that patients experienced significant decreases in verbal, performance and full scale IQ with concomitant morphological and chemical changes consistent with lower neuronal density, increased gliosis and demyelination (particularly in the frontal lobes and basal ganglia) and decreased brain volume. The same cohort of patients demonstrated markedly reduced rates of secondary school completion and higher rates of DSM-IV psychiatric diagnoses. Thus type 1 diabetes does appear to have significant neurocognitive, psychological and functional consequences in childhood and adolescence.

INV23
Risk modelling for diabetes complications: predictors and confounders

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Prospective observational studies offer the possibility of risk modelling for long-term vascular complications. Foremost among the risk factors are glycaemic control and blood pressure. By their very design, however, predictors may be rendered less relevant for current patients by temporal trends in other factors and differences in ethnicity.
Interventional studies provide the next step in risk modelling. Improved HbA1c in the DCCT/EDIC modified the risk for all vascular endpoints. During the DCCT the effect of HbA1c and duration accounted for only 22% of the variance in retinopathy, indicating that other factors must modify microvascular complications. Renin–angiotensin system inhibition resulted in successful reduction in retinopathy but not the primary renal endpoints in DIRECT-1 or RASS. Intervention studies control for known risk factors, but may not always be able to control for those unidentified confounders or genetic predisposition.
If our younger children are heavier because insulin resistance has accelerated the onset of diabetes itself, it is likely that there will be a greater contribution of central obesity associated factors on complication development. Visceral adiposity adversely affects blood pressure and lipids and increases inflammatory markers. As a measure of insulin resistance, the estimated glucose disposal rate (eGDR) derived from hypertension, HbA1c and waist-hip ratio was a better predictor for cardiac disease than HbA1c, and a better predictor than the metabolic syndrome in the Pittsburg Epidemiology of Complications Study.
Whilst the EDIC results confirm the effect of metabolic memory, the glucose excursions themselves may be important contributors to complications. A possible model is type 2 diabetes treated with diet or oral agents, so without fluctuation in exogenous insulin. The glucose peak, fasting insulin and HbA1c accounted for 26% of the variation of carotid intima thickness, an early marker of atherosclerosis.

INV24
Complication-causing pathways in macrovascular disease

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Diabetes mellitus is one of the most potent risk factors for coronary artery disease (CAD). This effect results from an acceleration of atherosclerosis induced by hyperglycemia and other aspects of the diabetic milieu. To decrease the cardiovascular burden of this disease, a better understanding of the mechanisms linking diabetes to atherosclerosis is needed, so that new interventions specifically targeted to diabetic subjects can be developed. Several mechanisms have been thus far proposed to explain the acceleration of the atherogenic process in response to high glucose. One involves the buildup of advanced glycation end-products (AGE); another involves the activation of protein kinase C. An increased production of superoxide resulting from increased availability of intracellular glucose in insulin-independent tissues has been proposed as a mechanism underlying the activation of these as well as other glucose-induced pathways. While these mechanisms have been demonstrated to occur in vitro and in animal models, their contribution to the increased risk of CAD observed in humans with diabetes is uncertain as is the translation of these findings into new therapies. A powerful approach that is currently pursued to expand knowledge in this field is to systematically search the genome for variants that are associated with an increased risk of CAD in diabetes and use information about the location and function of these variants to infer about the mechanisms involved in the diabetes-induced acceleration of atherogenesis.

A Heavy Problem: Treating Overweight in Adolescents with Type 1 Diabetes

INV25
Prevalence of obesity in youth type 1 diabetes

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Background: Different studies have showed an increase in the incidence of Type 1 Diabetes in youngsters at earlier ages. This phenomenon has been related to the weight gain in the said population.
In our Diabetes Unit, we found that in the last 30 years there has been an increase in the onset in children and adolescents.
It seems that there has been an increase in the onset in children and adolescents.
Due to the increase in weight in the young population, this could be associated with the increase in frequency and the earlier age at diagnosis within that group.
Aim: To test this phenomenon in the context of the major increase in T1DM at our centre.
Methods: Data from 106 males and 108 females diagnosed with T1DM during three different periods were retrospectively reviewed and classified as Group1: 67 patients from 1976 and 1977; Group 2: 85 patients from 1986 and 1987; and Group 3: 79 patients from 2008.
Results: BMI standard deviation score (SDS) was: Group 1: BMI SDS - 0.7 +/− 1.5; Group 2: −0.4 +/− 1.2; Group 3: 0.1 +/− 1.8 being this increment statistically significant (F 5.7, $p < 0.004$).
Age at diagnosis: Group 1: 8.52 yr +/− 3.74; Group 2: 8.51 yr +/− 3.68; Group 3: 10.57 yr +/− 3.68.
Weight at birth: Group 1: 3.38 kg +/− 0.57; Group 2: 3.38 kg +/− 0.50; Group 3: 3.23 kg +/− 0.52.
Keto-acidosis onset: Group 1: 41.8%; Group 2: 48.2%; Group 3: 42.6%.
Conclusions: Our results showed an increase in BMI from 1970s to 2000s, but this increase was not associated with an earlier onset age among our patients. We saw neither significant changes in birth weight nor in percentage of ketoacidosis onset.

ISPAD/JDRF Symposium

INV26
A clinical staging system for type 1 diabetes is necessary because

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Scientific research advances knowledge of disease and its specific treatment by systematic delineation of qualitative and quantitative trait differences that distinguish entities by their clinical, biochemical and molecular characteristics. Such differences form the basis of rational therapy. The ultimate goal is to guide optimal decision making for each individual afflicted by a disease complex, based on a full understanding of the interaction of the disease mechanism with that individual's personal genome. The historical evolution of our views concerning the syndrome we call diabetes mellitus (DM) mirrors these concepts; careful clinical description complemented by distinguishing via chemical or other laboratory markers such as the levels of residual insulin, the presence of autoimmunity, and an expanding array of therapeutic options such as insulin secretagogues, incretins, designer insulins and increasingly sophisticated systems for insulin delivery. However, the inadequacies and limitations of our current knowledge are reflected in the classification systems we use for DM, including T1 DM. The common assumption that T1 DM is an autoimmune disease is challenged by finding similar clinical patterns in children without any evidence of autoimmunity. Nor is autoimmunity always associated with disease. Phenotypic overlap is evident in recent discoveries on the molecular control of insulin secretion; patients deemed ''insulin dependent'' only a decade ago now are known to be insulin independent when treated by sulfonylureas. Therefore, a clinical staging system for T1 DM is necessary for a number of reasons. We really do not know why this disease occurs in children. We must not assume that T1 DM in a toddler is the same as that in a child or adult. We need to understand how individual genotypes affect the clinical phenotype. In short, a clinical staging system for T1 diabetes is necessary because of our fundamental ignorance about this disease.

Summer Camps: Combining Pleasure with Therapeutic Education

INV27
Diabetes camps in Austria or how to teach children about carbohydrate-counting and nutrition

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Diabetes Camps for children and adolescents with diabetes mellitus type 1 (DMT1) have a long tradition in Austria. The first one was organised more than 50 years ago.
The camps in Austria are mainly organised by lay-organisations and there is a variety of different camps taking place every year.

Most of them are only for children and adolescents with DMT1, some are for the whole family. Very often these camps are the only possibility for children to meet peers with the same problems they are experiencing themselves, which helps them to get a different perspective on their own situation and to handle their diabetes better in their everyday life.

The majority of these camps are taking place in the summer-time, but there are also ski-camps in the winter. The main idea is to offer these kids a vacation kids together with a team of professionals, but also to include diabetes education. This education starts with teaching the young ones to inject insulin themselves, up to talking about the prevention of diabetic late complication with adolescents. It turned out to be very effective to teach children more in everyday life situations, than in a setting like a school-class, e.g. the effect of sports on the BG-level on a hiking-trip.

One important part is to educate the children about healthy nutrition and carbohydrate-counting. In younger children the carb-counting in mainly done by the mothers, in the camp-situation, they easily learn how to weight their carbs themselves. Other options are e.g. a quiz or games, where they have to estimate the amount of carbs.

Altogether these playful attempts to combine a vacation with a diabetes-education are helping the children and adolescents to be more independent and to reach their metabolic goal.

INV28

Summer camp for children and adolescents with T1D in Slovenia

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The first known summer camp for children with diabetes was introduced by Dr. Leonard F. C. Wendt in the year 1925 in Michigan, USA. Since then specialized camps for children with T1D ore organised all over the world. In Slovenia the first summer camp for children with diabetes was organized by the nester of the Slovenian pediatric diabetology Dr. Lev Matajc in 1967. Children attend the camp with the aim of obtaining new knowledge about diabetes and meeting peers with diabetes.

Organisation of the Summer Camp: Children in the camp represent almost 50% of all school-aged children with T1D in Slovenia. Group counselors - older T1D patients who are specially trained in diabetic education and younger T1D patients (16–18 years old), who will be trained as a future volunteer educators for the needs of the camp are taking care for small groups of children. Counselors organise sport activities, fun games, swimming lessons, singing... A diabetic team (diabetologists, registered nurse specialist - educators, other registered nurses with special knowledge in T1D, a dietician and psychologist) is present all the time. They follow the goal of achieving good metabolic control and proper education for all children.

Educational Plan for the Camp: All children are taking part in the scheduled group educational program. They form small groups according to age and prepare lectures about diabetes, diet together with members of the diabetic team. Since most of the children are using CSII they learn how to use the pump correctly. The correct treatment of hypoglycaemia is discussed. Children finish special posters about diabetes. A special educational program is held for the youngest, who learn about T1D through educational games, stories, painting and writing. At the end of the summer camp all children write a test about diabetes. After the summer camp families of the children who showed a low level of knowledge are invited for another educational session to the out patient clinic.

INV29

Summer camps for children with T1DM on the light of advanced technology

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Managing children with diabetes requires a complex strategy in treatment process, which is provides in clinic as well as in schools, kindergartens or by organizing a leisure time. Now today when the significant improvement in quality of treatment was done, we can ask: does it make a sense to organize a camp for children with diabetes? Moreover Intensive insulin therapy combine with new technology like a insulin pumps and continuous glucose monitoring significantly decreases the risk of sever hypoglycemia (SH). In Warsaw Center, despite that the majority of patients have spent a summer time with non-diabetic children; the camps still have been commonly organized for children and adolescent patients. The analyse of summer camps from last two years shows that most of patients have been on the insulin pumps, we also realized that acute complications like DKA and SH have occurred occasionally and there were not the diabetes-related medical problems, thereby medical staff has taken an opportunity to train children in diabetes skills. It was established a training in proceeding in various life situation. The program includes a practical training in adaptation of insulin dose for exercises by using temporal basal rate, suspending insulin pumps with measuring metabolic outcomes (CGMS). The patient's adherents in implementing new function of insulin pumps has been assessed. The second one part is training in food counting and meal insulin dosing by using age-related games. Moreover bolus calculator as a tool for adjusting of prandial insulin has been introduced. Usually the practices have been provided in group for 10–12 children, moreover its has often become spontaneously supported group in which many of patients have been enhanced in self management.

Conclusions: ummer camps, where advanced technology are commonly used allow to enhance patent's adherences to their right insulin adjustment and diabetes-related decision making every day.

INV30

Henri Lestradet's Heritage: a 50 year experience in diabetes camps

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Henri Lestradet organized the first diabetes camp in 1953 and founded the Aide aux Jeunes Diabétiques (AJD, Help to Young Diabetics) in 1956. Diabetes education has been and is still the first and main aim of AJD, and the first name of the association was ''School for diabetic children''. For more than 50 years, 1200 children and adolescents have attended the camps every year, in summer (about 800) and during small vacation periods. Sessions with parents of younger children have been opened for more than 15 years. About one-third of the participants come for the first time, the mean total number of attendancies being 2.4. The camps are managed as hospitals and expenses are in great part covered by the social security, the charge for the families being around 200 Euros for a 3 week session, with possibilities of social welfare for the most deprived. The camp staff is made of 2 MDs, 1 activity manager and 1 nurse, 1 medical assistant per 15–20 children and 1 qualified youth leader per 6–8 children, representing a total of more than 300 temporary staff per year. Camps are a privileged experience and training for young MDs and other health professionals. Procedures for running the camps have been fully written and accredited. Twenty-five sessions are offered in 9 centres (2 in Normandy, 1 in Britanny, 2 in the southwest, 3 in the Alpes and 1

in Réunion Island), from 1 to 3 weeks duration, each session being for a specific group of age, from 3 (with parents) to 18 years of age. A great variety of physical and play activities are offered : hiking, cycling, canoeing, sailing, skiing, swimming, camping, dancing ... Education at camps consists in both individual and practical, at the time of analyses/injections, and in structured group sessions. To harmonize the treatment practices between children and adolescents coming from every part of the country in all centres, reference documents for education have been elaborated by a national educative committee and validated by a nationals survey using a knowledge questionnaire, showing that attendancy at the camps was associated with increased knowledge. Camps have been a privileged ground to conduct large clinical research studies; the most recent ones have been the screening of retinopathy by fundus photography in 504 adolescents, showing mild non proliferative retinopathy in 23, and the follow-up of insulin treatment regimens over the last 10 years, showing a great contrast between major changes in practice and limited improvements in HbA1c. The camps are the cornerstone for education, care and associative activities of young with diabetes and their families.

Translational Research in Psychology: Changing Behaviour in the "Difficult" Adolescent

INV31

Risky behaviors, suicidal and self-injurious behavior in adolescents with type 1 diabetes – implications for future research, prevention and treatment

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Objectives: The influence of psychosocial issues on the course of T1D has long been under research. It is shown, that T1D increases the risk for eating disorders in females. The connection between T1D and other types of psychopathology is not that clear. Risky behaviors, suicidal and self-injurious behavior begin in adolescence and are often symptoms of underlying psychopathology. Present study assessed whether adolescents with T1D engage in risk-taking, suicidal and self-injurious behavior as frequently as their healthy peers.

Methods: A self-report questionnaire containing questions on demographic and family characteristics, risky behaviors, suicidal behavior, and self-injurious behavior was administered to a representative cohort of adolescents with T1D and to healthy controls.

Results: Questionnaires were returned by 126 patients (75 females, 51 males; aged 16.9 ± 1.7y) and 499 control subjects (307 females, 192 males; aged 16.9 ± 1.2y). Females with T1D compared to female controls reported lower prevalence of cigarette smoking (< 0.05), drinking liquors (< 0.001), being drunk (< 0.01), higher prevalence of bingeing (< 0.01), and frequently engaging in sports (< 0.001). Males with T1D compared to male controls reported lower prevalence of running away from home (< 0.05), cutting class (< 0.05), cigarette smoking (< 0.001), drinking beer (< 0.001), wine (< 0.05), liquors (< 0.001), being drunk (< 0.001), using soft drugs (< 0.001), and sexual intercourse (< 0.01). There were no differences in the prevalence of suicidal and self-injurious behaviors in females. Compared with male controls, males with T1D reported lower prevalence of all suicidal and self-injurious behaviors; the differences were statistically significant for suicidal ideation (< 0.05) and intended suicide (< 0.05).

Conclusions: T1D was protective for most adolescent risky behaviors in both genders, for suicidal and self-injurious behaviors in males. T1D posed a risk for disordered eating in females.

INV32

Inter- and Intrapersonal barriers to achieving the goals of diabetes self-management

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The Ecological Perspectives Model postulates that all health outcomes depend on factors operative in 5 domains: societal, community, institutional, interpersonal and intrapersonal. This presentation will focus on the microenvironment, highlighting the interpersonal and intrapersonal factors which either facilitate or mitigate against the achievement and maintenance of the goals of diabetes self-management. In the interpersonal realm, attention will be paid to the relationship between teens with diabetes and their parents and health care providers. Family factors that impact include: ineffective or inadequate parental support; single parent families; low socio-economic status; parental mental illness, addiction or alienation; family disorganization, conflict and poor cohesion. Intrapersonal factors that are of important include: mental health issues (eating disorders, depression, anxiety), teen addiction, learning or behavior disturbance and fear of hypoglycemia.

Review of the literature is not at all encouraging in providing interventions that effectively reverse poor control in these teens. Focus will be paid to analysis of what factors may be most important in informing interventions.

INV33

Behaviour change in young people with diabetes

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Poor adherence to therapy is a common problem for adolescents living with diabetes, frequently producing adverse metabolic and psycho-social outcomes. A variety of psycho-educational interventions targeting this problem have been shown to produce modest benefits in both HbA1c and quality of life measures though most require either highly trained psychologists or investment of significant resources.

Motivational interviewing (MI) is one such counselling approach designed to resolve ambivalence about behaviour change. The principles underpinning MI appear particularly suitable for teenagers with diabetes as the method identifies 'readiness to change' thinking by the patient who selects relevant goals and is in charge of the agenda. Limited advice or information is given by the therapist and the process avoids confrontation. Studies have shown MI to be effective in the management of both adults and young people with diabetes.

Arising from the principles underpinning MI, a 'guiding' style has been shown to be most effective counselling technique for facilitating behaviour change. The DEPICTED Study has developed a training package for health-care professionals which focuses on agenda-setting and promoting a guiding counselling style to help young people with diabetes modify their self-management to improve outcomes. The intervention is designed to be applicable to routine clinical consultations without significant resource implications. The effectiveness of this training programme is currently being tested in a randomised controlled trial in the UK which will be measuring outcomes in 697 subjects from 26 clinics.

Food Fight: Diabetes and Eating Disorders

INV34

The role of education programs in the prevention and treatment of eating disorders in youth

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While the comorbidity of type 1 diabetes and anorexia nervosa is extremely rare, the assumption of a higher prevalence of clinical bulimia nervosa is still discussed controversially. On the other hand it is estimated, that around 10% of adolescent girls meet the criteria for an eating disorder not otherwise specified (EDNOS) (DSM-IV, 1994), the rate is twice as common as in metabolic healthy girls. Data on the frequency of ''insulin purging'' (provoking insulin omission to effect weight loss) are varying in a wide range, depending on sample selection, survey instruments and age groups involved.

But even erratic meal patterns or subclinical eating disorders worsen metabolic control and increase the risk of serious acute (DKA) or late complication. Preventive interventions, e. g. diabetes specific education, screening for psychosocial adjustment problems and psychotherapeutic advice for young people at risk of eating problems should be provided especially to prepubertal and pubertal girls.

According to the psychosocial and biological changes of puberty, specific interactive educational modules for small groups have been developed as part of a diabetes education programme for adolescents: 1) ''Who is normal?'': knowledge about pubertal maturation, normal weight gain, insulin dose in puberty, body image and the individual optimal body weight. 2) Skills for healthy food choices, flexible insulin dosing for age-specific eating habits, self regulation of snacking and prevention of episodes of binge eating. 3) Supporting physical activity to prevent excessive weight gain by training the adaption of insulin doses instead of eating additional carbohydrates. 4) ''I'm okay!'': coping with emotional stress and ravenous appetite; supporting a positive body image, self-confidence and self-efficacy in diabetes therapy. 5) Basic information on eating disorders and access to therapeutic help. 6) Appropriate involvement of parents in diabetes management and constructive communication.

INV35

Identifying and preventing eating disorders in youth with diabetes

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Although there is controversy whether there is a greater prevalence of clinically diagnosable eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder) in young women with diabetes, it is well-documented that eating disorders and ''disordered eating'' are associated with poor metabolic control, problems in adherence, and increased rates of microvascular complications in women with diabetes. Moreover, recent research has shown that young women with diabetes have 2.4 times the risk of developing an eating disorder than age-matched women without diabetes. Importantly, several studies have shown that about 30% of all women taking insulin struggle with ''sub-clinical'' symptoms of 'disordered eating,'' such as restrictive eating, a preoccupations with weight and shape, feelings of guilt after eating, and strategic misuse of insulin for weight control. A range of variables—genetic, cultural, individual temperament, self-esteem, family interactions, etc.–contribute to the development of eating disorders. For youth with Type 1 diabetes, several classic warning signs will be reviewed which may be seen by the diabetes clinician and may mark the identification of an eating disorder or disordered eating: As important as it is for diabetes clinicians to be able to identify and recommend appropriate treatment for an eating disorder, it is more critical for the pediatric diabetes provider to take steps towards preventing the development of eating disorders, especially in young female patients with Type 1 diabetes. Prevention tips will be reviewed which may help to reduce the risk of an eating disorder or disordered eating in pediatric patients. In summary, it is important for pediatric and young adult providers to understand how to identify an eating disorder or 'disordered eating'', as well as how to work with the patient and family to prevent the development of an eating disorder secondary to the diagnosis of diabetes.

INV36

Diabetes and eating disorders: challenges and opportunities

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The close relationship between the physical and mental health of individuals with diabetes has been clearly demonstrated. This is evident in the case of eating problems, which range from mildly disturbed eating behaviour to clinical eating disorders, particularly in girls and women with diabetes. Eating problems, which include weight dissatisfaction, dieting, binge-eating, insulin omission and other disturbed eating behaviour, are common and persistent in individuals with diabetes, and often go unrecognized and untreated. Disturbed eating behaviour can interfere with the tasks of diabetes management, contribute to suboptimal metabolic control, and lead to short-term and long-term diabetes-related medical complications. This talk will introduce some of the mechanisms of association between diabetes and eating problems. Clinical warning signs of a significant eating problem, an approach to managing eating problems in the diabetes clinic setting, and indications for referral will be discussed. Psychological themes commonly present in individuals with diabetes and eating problems will be outlined.

ISPAD/EURODIAB Symposium on Childhood Type 1 Diabetes

INV37

Type 1 diabetes time trends over a 23 year period in Sweden – a population based study covering the 0–34 year age range

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Objective: To study time trends of type 1 diabetes in a nationwide setting over a 23 year period in the under 35 year age-group and to analyze the incidence patterns by age, sex, time period and cohort. **Study population and methods:** Data from more than 18 000 individuals were obtained by combining two prospective research registers, the Swedish Childhood Diabetes Register (SCDR) and the Diabetes in Sweden Study (DISS) over the period 1983–2005. The data set covers birth cohorts 1949 to 2005. Poisson regression was used to fit age-period-cohort models.

Results: Incidence in the 0–14 year age group during the period was 32.3 (95% CI 31.5–33.1) per 100 000 boys and 30.8 (95% CI 30.0–31.6) per 100 000 girls. Incidence rates increased significantly during the period in both sexes in the 0–4, 5–9 and 10–14 year age groups. Mean male incidence rate in the 15–34 year age group was 16.4 (95% CI 15.9–16.9) while female incidence was significantly lower 9.2 (95% CI 8.8–9.5) cases per 100 000 population. Incidence did not increase over time in this older age-group, and in both sexes there were small but significant decreases in the 25–29 and 30–34 year age-groups. Looking at birth cohorts a clear shift to younger age at onset was seen for birth cohorts born after 1985. For birth cohorts 1949–1965 there was rather a decrease in incidence. Poisson regression modeling showed significant age, period and cohort effects but the best fitting model required inclusion of only age and cohort in the model.
Conclusions: This large, nationwide and study covering age groups 0–34 years demonstrates a clear shift to a younger age at onset Rates increased in prepubertal age groups over time but decreases were observed in the oldest age groups. A cohort effect dominates over a time period effect, indicating that exposures occurring early in life may influence a child's risk of developing diabetes later in life.

INV38
Clinical characteristics at presentation – analysis of 1444 prospective incidence cases of the hungarian registry (2002–2008)

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Objective: To describe the duration of symptoms before diagnosis, the clinical presentation of type 1 diabetes at onset in children aged under 15 yr, and the prevalence of diabetic ketoacidosis (DKA) at presentation.
Methods: The Hungarian Childhood Diabetes Registry has prospectively collected demographic and clinical data of all newly diagnosed children with type 1 diabetes using a standardized questionnaire from January 1, 2002 to December 31, 2008.
Results: 1444 incident cases were identified. Polyuria, polydipsia, fatigue and weight loss were the main presenting symptoms in all age categories. The median duration of symptoms prior to diagnosis was 14 weeks and the mean blood glucose level at diagnosis was 26.3 ± 12 mmol/l. Diabetic ketoacidosis (DKA) ($pH < 7.3$) occurred in 30% overall. Nine percent of the children ($n = 132$) had a pH value < 7.1. The youngest children (0–4 years) had shorter median duration of symptoms (7 weeks) and higher blood glucose levels (29.5 ± 13.2 vs. 25.7 ± 11.1 in 5–9yrs vs. 25 ± 11.4 in 10–14yrs; $p < 0.001$) and more frequently presented with DKA (45% vs. 32% in 5–9 yrs vs. 28% in 10–14 yrs; $p < 0.001$). Children diagnosed under 2 yrs of age had more severe metabolic decompensation.
Conclusions: The frequency of DKA in children with newly diagnosed type 1 diabetes is still very high, especially in the youngest children. The very young (under 2 yrs) are more difficult to diagnose and are more likely to present with DKA.
Recent incidence trends reveal that the highest rate of increase is occurring in the youngest age group. Consequently, the number of newly diagnosed children with type 1 diabetes requiring initial hospitalization is also expected to rise. Appropriate planning of hospital services is therefore of public health significance.

INV39
Perinatal risk factors revisited: a re-analysis of individual patient data from published studies

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Objectives: Researchers have proposed that events occurring early in life could be of particular importance in the aetiology of childhood onset Type 1 diabetes and several perinatal factors (such as birth weight, Caesarean section delivery, maternal age and birth order) have been implicated. The aim of this research was to systematically examine evidence of associations between perinatal factors and Type 1 diabetes in children by performing a series of meta-analyses (using individual patient data, where possible).
Methods: Relevant studies published before 2009 were identified from literature searches using MEDLINE, Web of Science and EMBASE. Authors of all studies containing relevant data were contacted and asked to collaborate in the various analyses. Researchers provided individual patient data (or conducted pre-specified analyses) and meta-analysis techniques were used to derive combined risk estimates, and investigate heterogeneity between studies.
Results: In total, authors of 27 studies agreed to collaborate in these meta-analyses. Preliminary results from the studies indicate that on average children with birth weight over 4 kg had an 11% increase in diabetes risk compared with children born 3 to 3.5 kg ($P = 0.002$). There was also a consistent 20% increase in the risk of diabetes in children born by Caesarean section ($P < 0.001$). Preliminary findings for maternal age and birth order will also be discussed.
Conclusions: Children who are heavier born and children who are born by Caesarean section have consistent increases in Type 1 diabetes risk.