Pediatric Diabetes

ISPAD International Society for Pediatric and Adolescent Diabetes

Pediatric Diabetes 2010: 11: 583–591
doi: 10.1111/j.1399-5448.2010.00746.x

Special Report

Report of the 36th ISPAD meeting, Buenos Aires, Argentina, 27–30 October 2010

Benitez-Aguirre P, Maahs DM. Report of the 36th ISPAD meeting, Buenos Aires, Argentina, 27–30 October 2010.
Pediatric Diabetes 2010: 11: 583–591.

Paul Benitez-Aguirre[a] and David M Maahs[b]

[a]Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Sydney, Australia; and [b]Barbara Davis Center for Childhood Diabetes, The Children's Hospital Denver, University of Colorado, Denver, Aurora, CO 80045, USA

Key words:

Corresponding author:
Paul Benitez-Aguirre, Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Sydney, Australia.
e-mail: paulb6ATchw.edu.au

Introduction

The 36th annual meeting of the International Society for Pediatric and Adolescent Diabetes (ISPAD) was held in Buenos Aires, Argentina, providing a forum for the annual exchange of research and updates in pediatric diabetes with the aim to improve care worldwide for children and adolescents with diabetes.

Wednesday, 27 October

Opening session – absence of chronic complications in youth: vision or reality?

Dr Olga Ramos, Argentina, reviewed the spectrum of diabetes complications faced by young persons with type 1 diabetes mellitus (T1DM) using illustrative cases both sobering and optimistic. She touched on the role of genetics, environment, and adherence to therapy.

Dr Thomas Danne, Germany, spoke on the global perspective and the vision of an international collaborative IT network for diabetes benchmarking and peer-review – The SWEET Project (1). He highlighted *T*eams, *T*argets, *T*echnology, and *T*herapeutic education (4T's) as key components to improve diabetes management. He also described the role of ISPAD in providing support to developing countries and capacity building through programs such as *Life for a child* and creation of educational materials including the ISPAD guidelines (2) and the training manual for health care professionals.

Dr Assam (Sam) El-Osta, Australia, illustrated the phenomenon of epigenetics with historical and basic science examples. He described changes in gene expression of NFκβ-p65 induced by short-term exposure to hyperglycemia (3). He explained how changes in genomic methylation, histone modification, and chromatin modeling may relate to metabolic memory (4). He concluded by suggesting that we may therefore be able to control gene expression and that the paradigm would be 'good or bad epigenetics' as opposed to 'good or bad genetics'.

He was followed by Dr Knut Dahl-Jorgensen, Norway, who reviewed the epidemiology of macrovascular disease in persons with T1DM and the increased awareness of higher risk of cardiovascular disease in females with T1DM. He suggested that improved metabolic control and lifestyle modification may result in a decrease in cardiovascular risk. However, evidence for the use of medications such as statins and

angiotensin converting enzyme inhibitors is lacking in the pediatric population. The multicenter Adolescent type 1 Diabetes cardio-renal Intervention Trial will assist to clarify the role of medical therapy in young persons with T1DM.

Plenary session I: a difficult start: the pregnant adolescent with type 1 diabetes mellitus

Dr Ethel Codner, Chile, gave a thorough review on the activation of the hypothalamic–pituitary–gonadal axis, the onset and progression of puberty and pregnancy outcomes in adolescents with T1DM. The onset of puberty and thelarche in females with diabetes has followed the secular trend, whereas menarche is delayed by around 6 months and associated with higher hemoglobin A1c (HbA1c) (4), body mass index (BMI), and a diagnosis of T1DM before the age of 10 yr (5, 6). Menstrual irregularities and hyperandrogenism are common in adolescents with T1DM and are more prevalent in those with worse glycemic control (7); however, the proportion of ovulatory cycles does not appear to differ compared to non-diabetic controls (P/041/ISPAD 2010). She described lowered LH/FSH patterns observed with insulin-deficient mouse models (5) and presented data on the role of kisspeptin in reversing low LH levels (8). Dr Codner highlighted the importance of making adolescents aware of a planned pregnancy. The data suggest that in adolescents with T1DM 75% of pregnancies were not planned (6), at least 50% had sexual intercourse without birth control (9), and risk taking behavior was no different than in the general population (10).

Dr Alicia Jawerbaum, Argentina, reviewed data on the impact of peroxisome proliferator-activated receptors' (PPAR) natural agonists as preventors of diabetic embryopathy and presented data testing the hypothesis that diets rich in PPAR ligands may prevent maternal diabetes-related malformations in mice. Diabetes-induced embryopathy depends on metabolic control and intra-uterine programing. Experimental models demonstrate that maternal diabetes alters the concentration of PPARs and their endogenous ligands (8). Early organogenesis, a most sensitive period, is affected by excess metabolic substrates, dyslipidemia, and oxidative stress. Increased nitric oxide production results in excess protein nitration and nitrosative stress, exacerbating morphogenesis (11). She described the role of matrix metalloproteinases (MMP-9 and MMP-2) as markers of a pro-inflammatory state in which lipoperoxidation and alterations in arachidonic acid bioavailability (important ligands in PPAR activity) increase risk of teratogenesis (12, 13). Finally, she presented data suggesting that diets enriched in PPAR ligands (oleic and linoleic acid) have the ability to prevent diabetic embryopathy (14) by regulating lipid metabolism and decreasing oxidative stress.

Dr Emilio Herrera, Spain, delivered a lecture on how under- and over-nutrition both in the intra-uterine environment and perinatally affect body composition and risk factors associated with type 2 diabetes, the metabolic syndrome, and cardiovascular disease. Examples from the literature include those from the World War II era famine in Holland as well as from animal models.

Plenary session II: avoiding real problems: the threat of DKA

Dr Julie Edge, UK, reviewed the epidemiology and pathogenesis of diabetic ketoacidosis (DKA) and cerebral edema (CE). Risk of DKA is greater in those with newly diagnosed T1DM. Of those with CE, the mortality rates across studies were between 20 and 25% and long-term neurological morbidity 15 and 26% (15). She reviewed risk factors for poorer outcomes and the proposed mechanisms involved in CE. She presented data showing that risk of CE was related to the administration of insulin within the first hour of presentation during fluid resuscitation, large fluid volumes in the first 3–4 h, and rapid lowering of plasma sodium. Interestingly, CE was not related to the rate of glucose fall (11).

Dr Desmond Bohn, Canada, elaborated on the role of effective osmolality as a clinical tool in the management of DKA (16). He proposed that CE in DKA is associated with too rapid a change in effective osmolality and may be related to the rate of insulin infusion. A recent study by Al-Hanshi suggests that lower dose of insulin infusion (0.05 μ/kg/h) may make it easier to lower the effective plasma osmolality gradually and might, therefore, reduce the risk of CE (17), but further studies are required.

Dr Mabel Ferraro, Argentina, reviewed the risk factors of CE in Latin America including the results of a multicenter study in which rates of CE and mortality in DKA were both 1.8%. In addition, Dr Ferraro reported a range of DKA at first presentation of T1DM between 10% and 90% in the pediatric population of Latin America.

Oral session I: new approaches in chronic complications

Dr M. Salem, Egypt, presented data on the use of plantar fascia thickness as a measure of tissue glycation and its association with microvascular complications in young persons with T1DM. She also presented data on the prevalence of ocular surface disorders in adolescents with T1DM which appears to increase with longer diabetes duration.

Dr A Tilmanne, Belgium, described the risk factors associated with sensory and motor polyneuropathy in T1DM, in particular HbA1c. She proposed the potential use of tibial nerve F wave latency to monitor polyneuropathy. Dr MJ Fritsch, Austria, presented data which demonstrated an association between reduced endothelial progenitor cells (EPC) and disturbed micro- and macrovascular function in children with T1DM. She postulated that hyperglycemia leads to depression of EPC which eventually may result in a diffuse endotheliopathy and vascular complications. She was awarded the best oral presentation prize for ISPAD 2010.

Dr HD Margeirsdottir from Norway presented data showing that even after relatively short diabetes duration (5.5 yr) and intensive insulin therapy, early atherosclerosis and low grade inflammation seem to be present in young persons with T1DM (mean age 13.7 yr). Dr L Iughetti, Italy, presented a longitudinal study, over a 2-yr follow-up period, which demonstrated early endothelial dysfunction and possible decrease in myocardial perfusion in children with T1DM compared to healthy controls. Dr A Dye, USA, presented data which described changes in forearm vascular resistance caused by hyperglycemia-induced vasodilation in adolescents with T1DM. She proposed that hyperglycemic vasodilation decreases the reserve capacity for further endothelial-mediated vasodilation to other stimuli.

Oral session II: novel findings in pediatric diabetes management

Dr E Bismuth presented a case history of a patient with type A insulin resistance syndrome who was treated with rhIGF-1 and developed severe retinopathy and raised the concern of whether this has implications for rhIGF-1 treatment in other disease states.

Dr REJ Besser presented data on the potential use of urinary C-peptide to creatinine ratio as being a more practical and less invasive method to estimate residual beta-cell function, although further data are required. Dr T Mouraux reported that in a Belgian Diabetic Cohort there was a low prevalence for both T2DM and MODY (1.7% for each).

Dr I Libman presented data indicating that increased age, BMI percentile, and lower HbA1c all predicted increased C-peptide levels. Dr Libman showed that C-peptide levels peaked at 2–3 months after diagnosis, but by 11–13 months after diagnosis, C-peptide levels had returned to values found at the clinical onset.

Dr J Ludvigsson provided an update on 4 yr of data on the effect of glutamic acid decarboxylase (GAD)-alum treatment in T1DM children (18, 19); no adverse events have been noted as a result of GAD-alum treatment and GAD-specific effects on the immune system have been noted.

Ms A Pham presented data on 185 youth with T1DM and celiac disease in Australia. Younger age at onset, female sex, and thyroid disease were all risk factors associated with celiac disease. Of those diagnosed with celiac, 77% were diagnosed within 5 yr of T1DM diagnosis and 37% of those diagnosed had been asymptomatic. Ms Pham estimated that approximately 1/20 youth with T1DM has celiac and that these data are supportive of current ISPAD screening guidelines (20).

Thursday, 28 October

Plenary session III: trends in obesity research

The Lestradet Award was given to Dr Barbara Anderson, PhD of Texas Children's Hospital, Houston, Texas. In her lecture, 'Putting the Evidence to Work for Advocacy and Education', Dr Anderson reviewed psychosocial and behavioral research in pediatric diabetes. The importance of ISPAD's declaration of Kos (21) has had a lasting benefit on pediatric diabetes care and research and calls to (i) make insulin available for ALL children and adolescents with diabetes; (ii) reduce the morbidity and mortality rate of acute metabolic complications or missed diagnosis related to diabetes mellitus; (iii) make age-appropriate care and education accessible to children and adolescents with diabetes as well as to their families; (iv) increase the availability of appropriate urine and blood self-monitoring equipment for ALL children and adolescents with diabetes; (v) develop and encourage research on diabetes in children and adolescents around the world; and (vi) to prepare and disseminate written guidelines and standards for practical and realistic insulin treatment, monitoring, nutrition, psychosocial care, and education of young patients with diabetes – and their families – emphasizing the crucial role of health care professionals – and not just physicians – in these tasks around the world. Dr Anderson stated that there were age-specific considerations that needed to be taken into account when managing children with T1DM and their families. For example, in children <6 years, the entire family is the "patient"; in 6–11 year old children with T1DM, school support is a critical factor; in 11–14 year old patients, sustaining parent involvement is crucial; and finally in 15–19 year old patients, psychological issues such as depression,eating disorders and diabetes "burn-out" must be considered.

Dr Ram Weiss, Israel, was entitled 'Insights into the Pathogenesis of Childhood Obesity' and reviewed data on the importance of the location of fat depots as they relate to pathophysiology. Hepatic

fat is associated with a more atherogenic phenotype, while the ratio of visceral to subcutaneous fat is also important. The mechanisms of lipid partitioning have important implications for the pathophysiologic consequences of obesity and are due to a variety of factors including diet, exercise, genetics, and in-utero exposure. Unfortunately, at present it has proven difficult to manipulate storage locations long term.

Dr Jill Hamilton, Canada, reviewed data on the pathogenesis and natural history of hypothalamic obesity. Approximately 10% of CNS tumors involve the pituitary and hypothalamus. The pattern of weight gain can be predicted if there is increased BMI at presentation, if hydrocephalus develops, or if there is hypothalamic damage. More metabolic syndrome, increased insulin secretion, and decreased insulin sensitivity contribute to weight gain. Treatment and prevention methods include diet, activity, medications, and bariatric surgery and this form of obesity has lessons for more general forms of obesity seen in pediatrics.

Symposium I: bad visions: substance abuse in youngsters with diabetes

Dr S Hofer, Austria, reported that ~5% of 11–15 yr olds and 30% of 15–20 yr olds with T1DM smoke (22) and 80% of smokers start by age 18, emphasizing the importance of smoking prevention efforts in adolescents. In addition, the deleterious metabolic effects of smoking on insulin sensitivity, glycemic control, hypertension, and lipids were highlighted.

Dr P Lee, Australia, reviewed data on the effects of substance abuse on metabolic control, including a case of ketamine-induced metabolic acidosis and DKA (23). The importance of this issue was highlighted by the results of an on-line survey in young adults with 504 T1DM, in which 77% reported some drug use. Effects of drug abuse on metabolic control and cognitive function are both acute and lasting up to a week (24). Dr K Berg-Kelly, Sweden, reviewed risk behaviors in adolescents with diabetes and the importance of screening for risk behaviors in all adolescents, but especially in those with erratic or deteriorating glycemic control.

Symposium III: the View from the beta-cell: a cure in sight?

Dr Catarina Limbert, Portugal, gave an overview of current and potential therapies for T1DM: from insulin delivery systems to microencapsulated islet cells and islet cell transplants and outlined their respective limitations. She presented data on the regeneration of beta-cell from mesenchymal cells through reprograming of human bone marrow stromal cells (BM-MSC) to insulin-producing phenotypes (20). BM-MSC have been observed to decrease acute graft-vs.-host disease after allogenic hematopoietic transplantation (25). Furthermore, certain immunophenotypes of BM-MSC are considered non-immunogenic allowing for the possibility of allogenic transplantation with no need for immunosuppresion.

Dr Matthias von Herrath, USA, presented data on differing human leukocyte antigen (HLA) haplotyptes and how the presence of CD8 T cell-driven insulitis may influence the natural history and evolution of T1DM (26, 27). He proposed that re-emergence of autoreactivity may be the main culprit underlying long-term islet graft failure and new strategies need to be tested to circumvent recurrent autoreactivity (28).

Dr Voltarelli, Brazil, presented data on autologous hematopoietic stem cell transplantation (HSCT) following high-dose immunosuppression in patients with a recent (<6 wk) diagnosis of T1DM (29). The majority of patients (21/25) showed a period of insulin independence. Of these, 7 remained insulin independent >5 yr post-transplant and 14 had resumed insulin which was weaned upon introduction of sitagliptin. The four who did not benefit from HSCT presented with DKA at diagnosis. Dr Voltarelli hypothesized that those with DKA had insufficient residual beta-cell mass to regenerate and regain adequate function, while those who remained insulin independent had significantly greater residual beta-cell mass. He also described the plans for transplantation with umbilical and mesenchymal stem cell which have been shown to be able to differentiate into insulin-secreting beta-cells and regenerate beta-cell mass. We keenly await results from these trials.

Symposium IV: looking healthy: exercise and diabetes

Dr Jan Aman, Sweden, emphasized that exercise is one of the three cornerstones of diabetes treatment and highlighted the evidence on the benefits of exercise on glycemic control and recommendations for children and adolescents to have less than 2 h of screen time and more than 60 min of moderate or more vigorous activity daily. With exercise, diabetes providers will be challenged to provide recommendations and education on how to adjust insulin and food intake so that glycemic control can improve in addition to insulin sensitivity and physical fitness.

Dr Michael Riddell, Canada, began his lecture with the provocative statement that exercise can make glycemic control worse given the current diabetes therapeutics. He summarized the differences in anaerobic and aerobic exercise and that these may require different management strategies as well as the concept of an exercise exchange, the importance

of bolus and basal adjustments with exercise, and techniques to avoid nocturnal hypoglycemia (24).

Dr Tadej Battelino reviewed data on continuous glucose monitoring use with exercise and the clear clinical need for more data on this topic, including randomized clinical trial data as well as evidence from clinical practice. Data in this area also have application in moving toward a closed-loop artificial pancreas.

Friday, 29 October

Plenary session IV: real numbers: data bases for pediatric diabetes research

Dr Michael Haller, USA, was awarded the Young Investigator Award and delivered a lecture on current trials at Florida on interventions in young children with T1DM, including a phase 2 trial of vitamin D, DHA, and autologous cord blood. Despite a greater than 3% increase annually in the incidence of T1DM in young children, few studies have been performed in this age group (30); he emphasized that safety is paramount in this age group.

Dr Jill Hamilton, Canada, presented data from the Canadian Prospective Non-Type 1 Diabetes Study (31) in which it was determined that rates of T2DM, medication-induced diabetes (MID), and MODY were 1.54, 0.4, and 0.2 per 100 000 in Canada. Obesity was the most important risk factor for both T2DM and MID, but that these youth displayed different phenotypes.

Dr Thomas Danne, Germany, updated the conference on the SWEET consortium that has focused on better control in pediatric and adolescent diabetes and is working on creating centers of research. Initial efforts have focused on Europe with plans to expand soon. Those interested in joining the SWEET consortium were provided the following e-mail address: aschemeier@hka.de.

Dr William Tamborlane, Yale, presented preliminary data on 815 patients from the US Pediatric Diabetes Consortium study that currently is focusing on treatment outcomes in diabetes in the first 24 months after diagnosis with initial data expected in 2011. Furthermore, the newly formed Pediatric Diabetes Exchange has begun recruitment and involves more diabetes centers.

Oral session IV: psychosocial issues and education in diabetic youth

Dr C Nadebaum presented novel data on the cognitive effects of DKA in newly diagnosed youth and that at day 1 and day 5 after diagnosis 42.5 and 18.6% had impaired mental state highlighting the implications for diabetes in patients newly diagnosed with T1DM who have been in DKA.

Dr AM Figueroa Sobrero presented data on 86 youths and families with T1DM and the importance of considering family functioning style and school performance when optimize each family's diabetes education program.

Dr RP Wadwa of the Barbara Davis Center reported that the majority of adolescents with T1DM were not aware of their HbA1c target, but that those who did achieve an HbA1c of <7.5% were more likely to think that their HbA1c goal was lower than 7.5% as compared to those who did not achieve the ISPAD goal of <7.5%. These data are complementary to findings from the Hvidoere study (32) and implications of goal setting for diabetes care were discussed.

Dr ER Pulgaron found that youth whose caregivers had lower self-management skills had a higher A1c, although no association was determined with numeracy or literacy.

Dr S Hofer reported data from the DPV (*Diabetes-Patienten-Verlaufsdaten*) study in which A1c tracks from T1DM onset to early adulthood and that A1c is lowest in prepuberty and then increases in puberty and postpuberty.

Dr E Boogerd, Netherlands, spoke on how an on-line digital treatment environment, 'sugarsquare', may lead to improved communication and treatment.

Dr Goethals, Belgium, spoke on the knowledge about diabetes and diabetes management in siblings of patients with T1DM.

Oral session V: unraveling the genetic basis of diabetes in children

Dr O Rubio-Cabezas, Spain – UK, presented evidence suggesting that testing for monogenic diabetes should be extended to include all those who present before 9 months of age. Extending the age of testing from the previously recommended 6–9 months of age increased the sensitivity of testing from 93.2 to 99.6%. Dr Mcdonald presented clinical characteristics which can help to discriminate MODY from T1DM or T2DM and thus improve selection of candidates for genetic testing. The key discriminator of T1DM and T2DM was insulin treatment from diagnosis (99 vs. 0.4%). Useful clinical discriminators included age at diagnosis, BMI, and family history of diabetes (parents).

Dr Noormets, Estonia, presented data on the sex differences in the development of diabetes in mice with deleted Wolframin (Wfs1) gene. In his models, male mice had increased risk of developing diabetes compared to female mice. An increased proinsulin/insulin ratio in Wfs1KO males suggested a possible disturbance in the conversion of proinsulin to insulin as the underlying mechanism.

Dr Dusatkova, Czech Republic, presented a study on two ancestral mutations in a large number of

Czech families with glucokinase (GCK) deficiency raising the question as to whether GCK mutation may represent a potential evolutionary advantage. Dr Szalapska, Poland, presented data on the frequency of polymorphisms of KCNJ11, INS VNTR, and NR3C1 genes in children born small for gestational age (SGA) in Poland. There were no significant associations found between these polymorphisms and SGA children in the Polish population. Dr Sugihara, Japan, presented data on the first nationwide multicenter study on the HLADRB1, DQB1, DPB1 genotypes in Japanese children with T1DM and their families. Dr M Borowiec, Poland, presented data on specific clinical pattern for glucokinase gene mutations in MODY families. Dr M White, Ireland, reported on a novel Wolcott–Rallison Syndrome mutation in two members of an Irish consanguinous family.

Oral session VI: update in clinical care of pediatric diabetes

Dr M Hefnawy, Egypt, presented data showing that subcutaneous insulin therapy was as effective as intravenous insulin infusions in the management of mild-to-moderate DKA of patients with good tissue perfusion.

Dr M Angulo, Spain, presented data demonstrating that in patients with T1DM, insulin pump therapy resulted in lower glycemic variability and less oxidative stress (as measured by TNFα) compared to multiple daily injection therapy. Dr G Storms, Germany, presented results suggesting improved glycemic control and patient satisfaction with the use of an integrated infusion pump system with a smart glucose meter. Dr R Slover of the Barbara Davis Center presented data on glucose excursions in children and adolescents in the STAR 3 study in which youth with elevated HbA1c on multiple daily injection therapy switched directly to sensor-augmented pump therapy improved glycemic control.

Dr J Johannesen, Denmark, presented data indicating that presentation of T1DM in DKA is associated with HbA1c in the future. Possible explanatory factors include residual beta-cell function and adherence to T1DM treatment. Dr MLM Andersen, Denmark, explored the use of historic cohorts as control subjects for intervention studies in which decline in stimulated c-peptide over time has been measured. Although such an approach has methodologic concerns, it might allow for a decreased sample size and for more subjects to be in the treatment arm of early intervention studies. Dr S Zucchini, Italy, presented data on long-term follow-up of 41 subjects with T1DM with abnormal urinary albumin excretion (UAE) of whom 80% regressed to normal UAE regardless of treatment with ACE inhibitors or not, similar to a recent paper in adults in which ACE inhibitors did not prevent diabetic nephropathy (33).

Symposium VII: new approaches to diabetes psychology for the real world

This session focused on the importance of psychosocial well-being and fostering of collaborative relationships between youth with diabetes, their families, and treating teams. Dr G Forsander, Sweden, highlighted the importance and benefits of including a psychologist as part of the diabetes management team early in the course of illness. These included equipping the family with coping strategies and supporting other members of the team in the work with the family.

Dr T Wysocki, USA, presented data supporting the family as the most appropriate focus of intervention and health promotion. He pointed out that fostering a constructive parent–adolescent relationship was paramount and should be a central goal of treatment.

Dr M Wit, Netherlands, supported the need for constant evaluation of psychosocial well-being. She pointed out that psychosocial evaluation tools can be used to assess the psychosocial needs of the young person and family and identify possible barriers to effective self-management. She presented data supporting regular monitoring and discussion of health-related quality of life as an effective intervention to improve patient management and satisfaction (34).

Symposium VIII: early complications: a nutritional view

Carmel Smart R.D. of Australia reviewed current understanding of nutrition and microalbuminuria with a focus on data on protein restriction in microalbuminuria including a Cochrane review in which protein reduction slightly, but not statistically significantly, slows progression of diabetic kidney disease (35). Current guidelines based on EURODIAB data recommend that protein account for not more than $<20\%$ of the diet. In youth with diabetes, sufficient nutrition for growth and development is a goal while encouraging fruits and vegetables as well as legumes, nuts, and fish as healthy sources of protein and limiting fat intake.

Dr I Libman, USA, reviewed data on how hypertension tracks from childhood into adulthood and that increases in weight over time are partly responsible for increases in blood pressure and specific data on diet, daily calorie intake, fat, fiber, and micronutrients Na, K, Ca, and Mg. The SEARCH for Diabetes in Youth study has shown that adherence to a DASH diet (dietary approaches to stop hypertension) is associated with less hypertension (36).

Dr M McGill, Australia, emphasized that rates of CVD are higher in T1DM and that atherosclerosis begins in childhood and dyslipidemia is common in T1DM worldwide. Children with T1DM are

frequently overweight and dyslipidemia is largely undiagnosed and under treated. Longitudinal data from Benitez-Aguirre demonstrate that elevations in Total Cholesterol track over 8 yr from adolescence to young adulthood (Benitez-Aguirre, unpublished data). Medical nutrition therapy is the preferred first line treatment for dyslipidemia as well as increases in physical activity. Further data are needed on this topic such as a CVD risk engine for T1DM and better evidence on when to start statins and their risk/benefit ratio in adolescents with T1DM.

Saturday, 30 October

Plenary session V: on the lookout for the right target: the current situation of diabetes prevention

Dr M Craig, Australia, reviewed data on the role of viruses and T1DM (and also that next year's ISPAD will include a symposium on viruses and T1DM: Viruses and Diabetes International Study Group). As early as 1971, the concept of a potential vaccine for T1DM was discussed (37). One piece of evidence to suggest that infections play a role in the rising incidence of T1DM comes from data in which a lower proportion of new onset cases are occurring in children with high-risk HLA genotypes (38). A recent meta-analysis of enteroviruses in T1DM demonstrated an odds ratio of 12.7 for enterovirus exposure in T1DM cases as compared to controls and an odds ratio of 3.7 for enterovirus exposure to the development of autoimmunity (Leung W-C et al., BMJ, in press). The pathogenesis of enterovirus infection in the development of T1DM has been reviewed recently (39).

Dr D Schatz, USA, reviewed immune-modulatory therapies for T1DM in 2010. He emphasized that there can never be a cure for T1DM without prevention and that a critical need exists for both reversal of beta-cell destruction and prevention. Although the status quo with increasing rates of T1DM is unacceptable, safety is necessary in any pediatric trial. The concept of T1DM as a disorder of failed immunoregulation was reviewed and included an illustrative figure from Bluestone (40) on the pathogenesis of T1DM and immune system targets and medications. A safe combination of therapies is needed and may include medications with the following effects: anti-inflammatory/immunomodulatory/antigen-specific/beta-cell stimulating or replacing.

Dr P Pozzilli, Italy, reviewed data that indicates diagnosis of T1DM is being made earlier in the pathophysiologic process and therefore patients with T1DM present with more preserved beta-cell function. He highlighted the following: (i) the importance of c-peptide as a measure of beta-cell function; (ii) data are needed on the relation of metabolic control and residual beta-cell function on long-term outcomes; (iii) c-peptide preservation is associated with a reduction in diabetic vascular complications and hypoglycemia in the DCCT; (iv) c-peptide is lower in young children than adolescents and adults; (v) c-peptide is the best surrogate marker for intervention studies aimed at modifying beta-cell destruction; and (vi) fasting c-peptide in children may be sufficient and not require a mixed-meal-tolerance test.

Symposium V: ethical viewpoint: what are the limits of pharmacologic intervention in the pediatric patients with DM?

Dr K Pillay, South Africa, reviewed principles of ethical decision making including autonomy, beneficence, non-maleficence, and justice; he added that dignity, truthfulness, and honesty are also important qualities for research in pediatric diabetes and that international research needs to address local needs and cultures and involve local collaborators.

Dr A Pulungan, Indonesia, gave his perspective on global inequalities in pediatric research by pointing out that only five articles on pediatric diabetes have been published by Indonesian investigators since 2000 and none in international journals. He stressed the importance of collaboration between developed and developing countries to improve research and care of children and adolescents with diabetes.

Dr J Ludvigson, Sweden, highlighted the complexity of ethical issues with intervention trials to prevent T1DM in pediatrics in which treatment benefits must be balanced vs. potential adverse effects in patients with evolving developmental capabilities. He presented data on how autonomy increases in children from 7 to 16 yr of age.

Dr C de Beaufort, Luxembourg, provided insight on the approach of regulatory bodies such as EMEA (European Medicines Agency) to new medications in pediatrics. Since 2007 there have been >100 pediatric applications with >11% of these related to pediatric diabetes or endocrinology. Better understanding of these processes is required to meet the goal of safer and more efficacious medications for our pediatric patients with diabetes.

Plenary session VI: looking at the genes – new insights

The final plenary session focused on the genetics, molecular diagnostics, and clinical approach to monogenic diabetes. Dr J Shield, UK, reviewed the molecular genetics and clinical characteristics of neonatal diabetes mellitus (NDM), both transient and permanent. Dr S Ellard, UK, discussed the topic 'How to Approach Monogenic Diabetes of

Unknown Etiology'. She reviewed the epidemiology, most common mutations, and clinical course of NDM and Dr Mlynarski, Poland, spoke on 'Monogenic Diabetes and Positive Antibodies: Double Diabetes?'. The latter proposed the possibility that positive antibodies in a patient with a monogenic form of diabetes may reflect that antibody formation could be secondary to beta-cell damage, rather than always reflecting autoimmune disease.

Poster sessions

There were lively poster sessions with excellent research presented by young and experienced researchers worldwide. Abstracts for each poster are provided in volume 11, supplement 14, October 2010 of *Pediatric Diabetes*.

Summary

The 36th annual scientific meeting of the ISPAD was a fantastic forum where the overriding theme was global collaboration to improve outcomes of type 1 diabetes. Dr Danne highlighted our role as members of ISPAD to be part of a community fostering quality in care and research of children and adolescent with diabetes. Also, to take up our role in supporting countries in the early stages of developing diabetes services. There was food for thought for all participants: from allied health professionals to physicians. The individual, family, and community needs were highlighted through the psychosocial and team-based approaches. Finally, the array of basic and clinical science-based research left all those who attended inspired and motivated at the possibilities of therapy, the prevention of complications, and likelihood of a cure. We look forward to the next installment of the ISPAD journey in Miami, USA, 2011.

The Closing Ceremony included local organizer Dr Olga Ramos of Argentina and the transition of the ISPAD Presidency from Dr Thomas Danne to Dr Lynda Fisher. An invitation for next year's ISPAD Conference to be held in Miami, Florida, USA, on 19–22 October 2011 was extended by Dr Alam Delamater who is the local organizer.

References

1. SWEET-Project. Better Control in Pediatric and Adolescent Diabetes: working to create Centres of Reference (available from http://sweet-project.eu/html/en/index_html).
2. Margeirsdottir HD, Larsen JR, Kummernes SJ, Brunborg C, Dahl-Jorgensen K. The establishment of a new national network leads to quality improvement in childhood diabetes: implementation of the ISPAD Guidelines. Pediatr Diabetes 2010; 11: 88–95.
3. El-Osta A, Brasacchio D, Yao D et al. Transient high glucose causes persistent epigenetic changes and altered gene expression during subsequent normoglycemia. J Exp Med 2008: 205: 2409–2417.
4. Danielson KK, Palta M, Allen C, D'Alessio DJ. The association of increased total glycosylated hemoglobin levels with delayed age at menarche in young women with type 1 diabetes. J Clin Endocrinol Metab 2005: 90: 6466–6471.
5. Bruning JC, Gautam D, Burks DJ et al. Role of brain insulin receptor in control of body weight and reproduction. Science 2000: 289: 2122–2125.
6. St James PJ, Younger MD, Hamilton BD, Waisbren SE. Unplanned pregnancies in young women with diabetes. An analysis of psychosocial factors. Diabetes Care 1993: 16: 1572–1578.
7. Gaete X, Vivanco M, Eyzaguirre FC et al. Menstrual cycle irregularities and their relationship with HbA1c and insulin dose in adolescents with type 1 diabetes mellitus. Fertil Steril 2010: 94: 1822–1826.
8. Jawerbaum A, White V. Animal models in diabetes and pregnancy. Endocr Rev 2010: 31: 680–701.
9. Schwarz EB, Sobota M, Charron-Prochownik D. Perceived access to contraception among adolescents with diabetes: barriers to preventing pregnancy complications. Diabetes Educ 2010: 36: 489–494.
10. Martinez-Aguayo A, Araneda JC, Fernandez D, Gleisner A, Perez V, Codner E. Tobacco, alcohol, and illicit drug use in adolescents with diabetes mellitus. Pediatr Diabetes 2007: 8: 265–271.
11. Edge JA, Jakes RW, Roy Y et al. The UK case-control study of cerebral oedema complicating diabetic ketoacidosis in children. Diabetologia 2006: 49: 2002–2009.
12. Jawerbaum A, Gonzalez ET, Sinner D, Pustovrh C, White V, Gimeno MA. Diminished PGE2 content, enhanced PGE2 release and defects in 3H-PGE2 transport in embryos from overtly diabetic rats. Reprod Fertil Dev 2000: 12: 141–147.
13. Lakkakorpi J, Li K, Decker S et al. Expression of the elastin promoter in novel tissue sites in transgenic mouse embryos. Connect Tissue Res 1999: 40: 155–162.
14. Higa R, White V, Martinez N, Kurtz M, Capobianco E, Jawerbaum A. Safflower and olive oil dietary treatments rescue aberrant embryonic arachidonic acid and nitric oxide metabolism and prevent diabetic embryopathy in rats. Mol Hum Reprod 2010: 16: 286–295.
15. Lawrence SE, Cummings EA, Gaboury I, Daneman D. Population-based study of incidence and risk factors for cerebral edema in pediatric diabetic ketoacidosis. J Pediatr 2005: 146: 688–692.
16. Durward A, Ferguson LP, Taylor D, Murdoch IA, Tibby SM. The temporal relationship between glucose-corrected serum sodium and neurological status in severe diabetic ketoacidosis. Arch Dis Child. DOI:10.1136/adc.2009.170530.
17. Al Hanshi S, Shann F. Insulin infused at 0.05 versus 0.1 μ/kg/hr in children admitted to intensive care with diabetic ketoacidosis. Pediatr Crit Care Med 2010.
18. Ludvigsson J. Therapy with GAD in diabetes. Diabetes Metab Res Rev 2009: 25: 307–315.
19. Cheramy M, Skoglund C, Johansson I, Ludvigsson J, Hampe CS, Casas R. GAD-alum treatment in patients with type 1 diabetes and the subsequent effect

on GADA IgG subclass distribution, GAD65 enzyme activity and humoral response. Clin Immunol 2010: 137: 31–40.
20. Limbert C, Seufert J. In vitro (re)programming of human bone marrow stromal cells toward insulin-producing phenotypes. Pediatr Diabetes 2009: 10: 413–419.
21. Weber B, Brink S. ISPAD declaration of KOS. Pediatrics 1994: 94: A26.
22. Hofer SE, Rosenbauer J, Grulich-Henn J, Naeke A, Frohlich-Reiterer E, Holl RW. Smoking and metabolic control in adolescents with type 1 diabetes. J Pediatr 2009: 154: 20–23.e1.
23. Lee P, Greenfield JR, Campbell LV. "Mind the gap" when managing ketoacidosis in type 1 diabetes. Diabetes Care 2008: 31: e58.
24. Robertson K, Adolfsson P, Scheiner G, Hanas R, Riddell MC. Exercise in children and adolescents with diabetes. Pediatr Diabetes 2009: 10 (Suppl. 12): 154–168.
25. Tian Y, Deng YB, Huang YJ, Wang Y. Bone marrow-derived mesenchymal stem cells decrease acute graft-versus-host disease after allogeneic hematopoietic stem cells transplantation. Immunol Invest 2008: 37: 29–42.
26. Van Belle TL, Juntti T, Liao J, von Herrath MG. Pre-existing autoimmunity determines type 1 diabetes outcome after Flt3-ligand treatment. J Autoimmun 2010: 34: 445–452.
27. Bresson D, von Herrath M. Immunotherapy for the prevention and treatment of type 1 diabetes: optimizing the path from bench to bedside. Diabetes Care 2009: 32: 1753–1768.
28. Van Belle T, von Herrath M. Immunosuppression in islet transplantation. J Clin Invest 2008: 118: 1625–1628.
29. Couri CE, Foss MC, Voltarelli JC. Secondary prevention of type 1 diabetes mellitus: stopping immune destruction and promoting beta-cell regeneration. Braz J Med Biol Res 2006: 39: 1271–1280.
30. Haller MJ, Wasserfall CH, McGrail KM et al. Autologous umbilical cord blood transfusion in very young children with type 1 diabetes. Diabetes Care 2009: 32: 2041–2046.
31. Hosler AS, Nayak SG, Radigan AM. Agreement between self-report and birth certificate for gestational diabetes mellitus: New York State PRAMS. Matern Child Health J 2010: 14: 786–789.
32. Swift PG, Skinner TC, de Beaufort CE et al. Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005. Pediatr Diabetes 2010; 11: 271–278.
33. Mauer M, Zinman B, Gardiner R et al. Renal and retinal effects of enalapril and losartan in type 1 diabetes. N Engl J Med 2009: 361: 40–51.
34. de Wit M, Delemarre-van de Waal HA, Pouwer F, Gemke RJ, Snoek FJ. Monitoring health related quality of life in adolescents with diabetes: a review of measures. Arch Dis Child 2007: 92: 434–439.
35. Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. Cochrane Database Syst Rev 2007(4): CD002181.
36. Gunther AL, Liese AD, Bell RA et al. Association between the dietary approaches to hypertension diet and hypertension in youth with diabetes mellitus. Hypertension 2009: 53: 6–12.
37. Karam JH, Grodsky GM, Forsham PH. Coxsackie viruses and diabetes. Lancet 1971: 2: 1209.
38. Fourlanos S, Varney MD, Tait BD et al. The rising incidence of type 1 diabetes is accounted for by cases with lower-risk human leukocyte antigen genotypes. Diabetes Care 2008: 31: 1546–1549.
39. Hober D, Sauter P. Pathogenesis of type 1 diabetes mellitus: interplay between enterovirus and host. Nat Rev Endocrinol 2010: 6: 279–289.
40. Bluestone JA, Herold K, Eisenbarth G. Genetics, pathogenesis and clinical interventions in type 1 diabetes. Nature 2010: 464: 1293–300.