ISPAD2011

INVITED SPEAKERS

Plenary Session I: Future Directions for Type 1 Diabetes Management

INV01

JDRF's vision, strategy, and priorities for prevention of type 1 diabetes

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The increasing incidence and earlier age of onset of type 1 diabetes (T1D) increase the urgency for its prevention. JDRF is championing the development of population-based approaches for both primary (pre-T1D autoimmunity) and secondary (post-T1D autoimmunity) prevention of childhood-onset T1D.

For primary prevention, JDRF is focusing on the discovery and development of diabetes vaccines for universal infant and childhood immunization. The potential for developing an enteroviral diabetes vaccine is dependent on the enteroviral serotype prevalence and diversity associated with T1D, which is being explored. Multiple beta cell antigen-specific immunoregulatory vaccines are under development and will need to be shown capable of durably and safely preventing the onset or progression of T1D autoimmunity. JDRF is exploring the hypothesis that alteration in the intestinal microbiota in early childhood increases susceptibility to the development of T1D. If correct and the underlying mechanisms were elucidated, scientifically rational vaccine approaches to augment or accelerate microbiome-induced immunoregulation may possibly be developed.

Secondary prevention of childhood-onset T1D will require cost-effective, childhood population-based screening to detect risk of developing T1D. Although screening for T1D-associated auto antibodies is effective, the assays and approaches today are costly. Better biomarkers to stage and predict progression of the disease are also needed. Finally, interventions that preserve functional beta cell mass will be required and may be used individually or in combination to address: islet inflammation, beta cell-specific autoimmunity, beta cell health, stress and survival, and/or glucose intolerance and insulin resistance.

JDRF will partner and leverage its financial and non-financial resources with that of academia, industry, government organizations, payers, and providers for prevention of T1D.

Plenary Session II: Preventing Complications of Diabetes: Screening, Risk Factors, and Interventions

INV02

Macrovascular complications

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The macrovascular complications of childhood onset diabetes include coronary artery disease, cerebral vascular disease and peripheral arterial disease, all of which are increased substantially. This presentation will largely focus on coronary artery disease (CAD) using data from the Pittsburgh epidemiology of diabetes complications (EDC) study and the DCCT/EDIC study. Thirty year mortality has improved dramatically in recent years for childhood onset type 1 diabetes, declining in the US by 40% in the last 10–15 years, leading to life expectancy now being within a few years of that seen in the general population. The incidence of coronary artery disease however is not declining as much as that of other complications, for example renal disease, and the potential reasons for this will be discussed. Risk factors for CAD in type 1 diabetes and potential goals that could be achieved even in childhood will also be presented. The confusing role of glycemic control will also be discussed and reasons for the divergence between the relatively weak associations seen in epidemiologic studies and the very positive results from the DCCT/EDIC Trial will be discussed.

The presentation will also explore new developments in our understanding the pathology of coronary artery disease in type 1 diabetes and in particular the recently recognized role of haptoglobin genotype variation. This recent development gives rise to the possibility of meaningful prevention in a large proportion of patients with type 1 diabetes if positive intervention trials with vitamin E, already seen in those with both type 2 diabetes and the increased risk genotype, can be replicated in a type 1 population.

INV03

Diabetic neuropathy: update on methods for screening and diagnosis

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The diffuse, progressive, and length-dependent injury to peripheral nerves, defined as diabetic sensorimotor polyneuropathy (DSP) but commonly referred to as ''diabetic neuropathy,'' has exceptionally high incidence and is observed in up to half of adults with even short-duration diabetes when evaluated using the gold-standard nerve conduction study tests. It begins with a long subclinical latency period whose identification and management is challenging. At present, under diagnosis is a fundamental issue and the lack of an early biomarker for nerve injury hinders the development of interventions for neuropathy in clinical research. Markers of nerve injury derived from sensory examination testing (such as the monofilament examination), and from quantitative small and large nerve fiber functional testing and morphological measurement appear to be good candidate alternatives to nerve conduction studies for the purpose of screening and diagnosis in clinical practice. Acknowledging that the most relevant question is whether a biomarker can represent incipient nerve injury before the development of clinically recognized diabetic neuropathy, my research group has focused on clinical diagnostic study methodology to determine the concurrent and predictive validity of such markers. The prevailing concept of the natural history of DSP is that the initiating injury to the peripheral nervous system occurs in the small, unmyelinated and thinly myelinated A-delta and C-type nerve fibres, which can be accomplished by the examination of intra-epidermal nerves in skin biopsy samples. As a non-invasive alternative, the small nerve fibres in the subbasal nerve plexus of Bowman's layer of the cornea can be directly visualized reliably and non-invasively by a technique of *in-vivo* corneal confocal microscopy (CCM). In this update, I will review the potential role of CCM as a clinical and research tool for diabetic neuropathy in the context of existing methods for screening and diagnosis.

Plenary Session III: Advances in Obesity

INV04

Advances in obesity: psychosocial issues and lifestyle interventions

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Background: Pediatric obesity has been labeled an epidemic that negatively impacts a number of systems, including metabolic, gastrointestinal, pulmonary, cardiovascular, and skeletal. It also places children at increased risk for a number of psychosocial difficulties.

Objectives: The goals of this presentation are two-fold:
(1) to provide an overview of the psychosocial risks associated with pediatric obesity; and
(2) to review current evidence supporting lifestyle interventions for the treatment of obesity in children and adolescents.

Methods: Original research as well as systematic reviews and meta-analyses were examined.

Results: While pediatric obesity does not uniformly confer risk for increased psychological distress, consistent impairments have been observed in health related quality of life and self-concept, with the heaviest of children at greatest risk. Furthermore, there appear to be important dimensions that serve as mediators of psychological distress, most notably weight related stigma and teasing, as well as body dissatisfaction. There is evidence to suggest that lifestyle interventions are superior to education only controls for the treatment of pediatric obesity, and that comprehensive interventions including behavior modification, dietary change, and leisure time physical activity prescription are most effective. Parental involvement with obesity treatment is clearly indicated.

Conclusion: Pediatric obesity places children and adolescents at risk for a range of negative psychosocial outcomes, including decreased self-concept, impaired quality of life, and weight related stigmatization. While there is considerable evidence to support the efficacy of lifestyle interventions with specific groups of children, fewer studies have been conducted with adolescents, children from ethnic minority backgrounds, and those with severe obesity. Future research directions using innovative and multilevel treatment approaches will be discussed.

Symposium I: VIDIS/ISPAD Symposium

INV05

Enteroviruses and the immune system in type 1 diabetes

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Type 1 diabetes mellitus (T1D) is an autoimmune disorder in which the insulin-producing β-cells in the pancreas are destroyed. Enteroviruses of the human enterovirus B (HEV-B) family, such as coxsackievirus B and echovirus, are associated with the development of T1D. Dendritic cells (DCs) are the major antigen-presenting cells and exert a dual function: they initiate immune responses against pathogens, but also prevent (auto-) immune responses harmful to the host. Multiple DC subsets exist that express a myriad of receptors including the so-called pattern recognition receptors (PRRs). Immune stimulatory signals will unleash the DC's ''immune attack'' program, whereas no- or immune suppressive signals promote the DC's tolerogenic pathway. Their decisive role in immunity and tolerance provides these cells with a crucial role in the pathogenesis of autoimmune diseases like T1D and in the elimination of viruses.

I hypothesize that conditions exist in which the interplay between enteroviruses, enterovirus-infected β-cells, and DC unleash the immune system resulting in β-cell-autoimmunity/T1D in genetically susceptible individuals. I will present data on how human DCs respond to enteroviruses and enterovirus-infected β-cells. We have studied *in vitro* differentiated monocyte-derived DCs as well as primary human myeloid DC subsets isolated freshly from blood (e.g., $BDCA1^+$ mDCs, $BDCA3^+$ mDCs) and found that these are activated upon encountering enterovirus-infected β-cells. The underlying mechanism of how the DCs become activated, as well as whether and how they interact with (autoreactive) T-cells is currently investigated.

We envisage that a detailed understanding of which cells, and how they are involved in initiation of (auto-) immunity, will be instrumental for optimal design of novel T1D intervention strategies.

INV06

What do longitudinal studies tell us about viruses and diabetes?

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Since the 1950's, the incidence of T1D in children has increased world-wide by 3–5%/year. This is consistent with a global gradual increase in exposure to a causative environmental trigger or gradual removal of a protective factor. T1D shows also a distinct seasonal pattern and outbreaks consistent with infectious etiology. The causative environmental agent(s) have been hard to pinpoint due to the long incubation period of T1D. Prospective studies such as DAISY, DIPP, BABYDIAB, MIDIA and TEDDY have attempted identification of triggers of islet autoimmunity and promoters of progression to overt diabetes by following large cohorts of children at high genetic risk of T1D.

Thus far, epidemiological data concerning pre- and post-natal infections appear to be consistent with the ''hygiene hypothesis'', i.e., lower number of symptomatic infections being predictive of autoimmunity and diabetes.

Increased presence of microbial nucleic acids in samples collected prior to the appearance of islet auto antibodies has been reported only by a Finnish study (DIPP) and not confirmed elsewhere. However, DAISY and DIPP have recently shown that detection of enteroviral RNA in blood predicts progression from islet autoimmunity to T1D.

Systematic search for multiple pathogens and next-gen unbiased sequencing of nucleic acids from plasma, saliva, throat, nasal, and stool samples is underway in DAISY, TEDDY, and other studies.

The innate immune system senses microbial pathogens using the Toll-like receptors (TLRs) and helps to mount antiviral response. Preliminary studies showed that incubation of PBMCs from children with pre-diabetic islet autoantimmunity with a TLR7/8 ligand induced exaggerated INF-α expression, compared to controls. Further studies of the role of the INF-α – controlled network are in progress.

Symposium II: Advances in Psychosocial Interventions

INV07

Web-based diabetes education and coping skills training

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Adolescents with Type 1 diabetes (T1D) struggle with psychosocial and metabolic concerns. Adolescence is marked by rapid physical, cognitive, emotional and social changes leading to insulin resistance and lower adherence. Little work has been accomplished in translating psycho-educational interventions into routine care of youth with T1D, despite research showing their efficacy, due to the time and costs involved in busy clinic settings. Also, usual approaches such as clinic-based groups fail to attract large numbers of youth.

Coping Skills Training (CST) was developed with a group format and recently as a web-based approach. The presentation will focus on the development of 2 programs (TEENCOPE™, web-based CST with a graphic novel format & asynchronous discussion boards; Managing Diabetes, web-based diabetes problem-solving educational program) for youth with T1D. TEENCOPE focuses on the skills of social problem solving, social skills training, cognitive behavior modification, assertive communication, and conflict resolution. Managing Diabetes is a web-based age-appropriate diabetes educational program that provides additional information and problem-solving exercises on intensive insulin regimens, carbohydrate counting, sports and sick days, and healthy lifestyles.

Data from a series of studies will be presented on efficacy, satisfaction, and outcomes on A1C, quality of life in youth with type 1 diabetes will be presented. The group-based program was effective in improving A1C and quality of life, but only 50% of teens approached participated, leading to the development of the web-based programs. Recruitment was high at 85% and participation satisfaction with the programs was at 85% in a multi-ethnic group of teens age 10–14 years. Outcome data will be presented on A1C and quality of life. This web-based approach has to potential to be integrated into clinical care with accessibility to busy teens and lower cost than usual approaches to psycho-education.

INV08

Motivational interviewing: an introduction to the core principles and its application in a paediatric diabetes service context

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Motivational interviewing (MI) is a counselling approach which focuses on helping people explore and resolve their ambivalence about behaviour change. MI practice has been gaining ground in adult health services since the early 1980's starting in addictions and then developing in the physical health specialties, particularly in relation to chronic health conditions, a context in which ambivalence about behaviour change is often a significant part of routine consultations. The evidence-base for MI has grown and the ideas have been refined both in the context of counselling relationships but also in connection to other practitioner-patient relationships e.g., nurse, doctor, dietitian. More recently attention has turned to the potential of MI in the paediatric context and the challenges of using it with families with children at differing ages and developmental stages. This paper will provide an introduction to the core principles of MI and details of the studies in which MI has been used in a paediatric diabetes service context. The evidence base related to MI will be described and in the light of this the potential future directions for MI practice in paediatric diabetes will be explored.

INV09

Preconception counseling starting at puberty: providing evidence with ``Reproductive-health Education and Awareness of Diabetes in Youth for Girls'' (READY-Girls) program

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Women with diabetes who have uncontrolled blood glucose prior to and during pregnancy are four times more likely to have an offspring with congenital anomalies than women in the non-diabetic population. Preconception counseling (PC) lowers this risk. The American Diabetes Association (ADA) recommends PC for all diabetic women of child-bearing potential. However, most women don't receive PC and continue to have unplanned pregnancies. Our program of research built the evidence to target PC for teens with diabetes before sexual debut, and in 2009 served as a catalyst for the ADA to specify that PC should be given at all routine clinic visits ''starting at puberty''. We will describe the development and evaluation of our book and DVD, called Reproductive-health Education and Awareness of Diabetes in Youth for Girls (READY-Girls). We examined the long-term (12mons) effects of READY-Girls on intentions and behaviors for family planning and PC in girls with type 1 and 2 diabetes (T1D, T2D). In a multisite RCT with 109 teens [mean age = 15.8 years (13–19years)], 58 were randomized to standard care (CG) and 51 to an intervention group (IG) to receive READY-Girls over 3 clinic-visits (baseline-DVD, 3-mo DVD, 6-mo book). This program demonstrated increased knowledge and enhanced attitudes toward seeking PC, improved use of effective family planning, more frequent initiation of PC discussions with health care providers, and was cost-effective. The program can potentially empower young women to improve their own health and health outcomes of their future offspring.

Symposium III: Which is more Important: A1c or BG Variability?

INV10

Mean blood glucose independent variation in glycated hemoglobin and complications of diabetes

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Conventional understanding suggests that non-enzymatic biochemical formation of HbA1c is directly related to the concentration of the glucose precursor. Ultimately non-enzymatic glycation also leads to the formation of advanced glycation endproducts (AGEs) which have been implicated in the pathogenesis and progression of microvascular complications. However, extensive evidence indicates that in addition to MBG, factors independent of MBG also play a role in determining HbA1c levels. To facilitate study of MBG-independent between-patient differences in HbA1c, we developed a Hemoglobin Glycation Index (HGI) for use in patients with diabetes. HGI = (Patient's observed HbA1c)-(Predicted HbA1c from Patient's MBG). HGI was predictive for risk of retinopathy and nephropathy from patients in the DCCT. HGI has been associated with the extent of skin AGEs in youth with diabetes, while MBG was not. African-American youth with diabetes exhibit higher HGI compared with patients of European heritage. This disparity in HGI may play a role in the disparity of diabetes complications between races. Between-patient, MBG-independent HbA1c differences appear to have a heritable basis. Patients with high HGI may be particularly vulnerable to iatrogenic hypoglycemia when treatment goals are based solely on HbA1c targets. The mechanism/s underlying the MBG-independent component of protein glycation and associated development of complications are poorly understood and do not appear amenable to current diabetes therapies which are aimed at lowering MBG. Elucidation of mechanisms mediating MBG-independent variation in HbA1c may lead to innovative adjunctive therapies for prevention of diabetes complications. HGI is potentially a useful and easily calculated metric for assessing patients with diabetes.

Symposium IV: Behavioral Challenges in Youth with Diabetes

INV11

Depression and type 1 diabetes: screening, intervention, and a call to action

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Objectives: Depression is common, costly, and dangerous. Depression complicates diabetes management and contributes to suboptimal glycemic and quality-of-life outcomes. This presentation will
(1) review the link between depression and pediatric type 1 diabetes,
(2) discuss screening and treatment options, and
(3) challenge the field to make depression and psychosocial screening a higher priority in multidisciplinary diabetes care.
Methods: Data from clinical research are reviewed with a focus on the mechanisms that link depression and type 1 diabetes, including environmental pathways through treatment adherence and potential biologic links. Data are presented on a quality improvement project for implementation of systematic depression screening. Further, data on effective interventions to treat depression, including behavioral and pharmacologic options, are presented. Clinical case examples are used to provide a richer context to these data.
Results: Depression is 2–3 times more common in youth with type 1 diabetes than their peers without diabetes. As much as 25% of adolescents with type 1 diabetes show elevated levels of depression and if left untreated, depression continues in to adulthood. Systematic screening for depression is feasible and can be used to identify youth who would benefit from further psychosocial screening and treatment. Effective interventions include cognitive-behavioral therapy, however, few are adapted to be diabetes-specific. Data are needed on pharmacologic options for youth with type 1 diabetes.
Conclusions: There has been significant progress in the identification of the link between depression and type 1 diabetes. However, there are few systematic psychosocial screening programs, lack of data on diabetes-specific interventions, and few family-focused programs. Efforts are needed to address these areas and prioritize psychosocial screening and treatment in multidisciplinary pediatric diabetes care.

INV12

Updates from SEARCH for diabetes in youth study: quality of life in youth with type 1 diabetes and type 2 diabetes

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The SEARCH for Diabetes in Youth Study has conducted population-based case ascertainment of youth <20 years of age whose diabetes was prevalent in 2001 and 2009 or incident (diagnosed) from 2002 through the present. Youth in the SEARCH study have been recruited from six clinical centers across the United States; have type 1, type 2, and other forms of non-gestational diabetes; and are racially and ethnically diverse. As part of the initial research visit as well the follow-up visits for the 2002–2005 incident cohorts, youth ≥3 years of age have completed the Pediatric Quality of Life Inventory Type 1 Diabetes Module 3.0 (PedsQL-DM) and the PedsQL-Generic Core Scales 4.0 (PedsQL-generic). Youth ≥10 years of age completed the Center for Epidemiologic Studies Depression (CES-D) scale to assess depressive symptomatology. A major goal of diabetes management for youth and their families is for them to be able to manage the daily requirements of their diabetes without a reduction in their health-related quality of life. SEARCH has reported that depression score as well as health-related quality of life are associated with glycemic control, with lower quality of life and more depressive symptomatology being associated with sub-optimal glycemic control. Demographic characteristics (such as having Medicaid or another government-funded insurance), diabetes treatment modalities (such as receiving insulin by injection versus pump), and having other health conditions were all independently associated with lower PedsQL-generic scores among youth with type 1 diabetes. This presentation will review our results to date on the cross-sectional and longitudinal associations between quality of life and depressive symptoms and demographic (e.g., age, gender, race/ethnicity, insurance status) and clinical characteristics (e.g., diabetes type, insulin regimen, glycemic control) among youth from the SEARCH study.

Symposium V: Update on Nutritional Management: To Carb Count or Not to Count, That is the Question

INV13

Carbohydrate management

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Guidance on the amount and type of carbohydrate should be included in the programme of diabetes education. The programme of education should include the individual assessment of the child and family for motivation and psycho-social factors, followed by education and continued support around adjusting food intake, monitoring blood glucose levels and insulin self-adjustment.

Modern carbohydrate counting (CC) is a meal planning approach to enable the adjustment of the meal-time insulin dose to match anticipated carbohydrate consumption. Carbohydrate counting is well accepted as an effective approach, as highlighted by the DCCT, National and International recommendations. Recent interventions stress the importance of using skilled dietitians and diabetes educators for delivery of diabetes education. There is conflict between studies some indicating young people and families can CC accurately, other studies indicating otherwise. Some studies show an increase in errors with time, indicating the necessity for regular review and the maintenance of engagement and motivation. Debate continues about the necessity to count individual grams of carbohydrate versus estimating average portion sizes. Emerging evidence suggests that counting individual grams of carbohydrate is not essential and a small margin of inaccuracy will not affect clinical outcomes. Consistent methods of education for setting the insulin:carbohydrate ratio is important. The regular integration of low glycaemic index (GI) foods into meals and snacks will minimise post-prandial glycaemic excursions and improve long-term glycaemic outcome.

Dietary adherence is one of the biggest challenges to self-care management especially if the education is too prescriptive. Therefore education methods need to be delivered in their simplest form yet still need to achieve good clinical outcomes. Including CC and GI in a full programme of diabetes self-management education should then improve all outcomes.

INV14

Update on nutritional management: to carb count or not to count, that is the question: glycemic index

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Nutritional management for children and adolescents with T1DM is the cornerstone of diabetes management. Dietary recommendations strive for optimal blood glucose control [HbA1c and post-prandial glycemia (PPG)] to reduce the risk of complications and improve quality of life.

Carbohydrate (CHO) is the main dietary factor that influences glycemia, particularly PPG. CHO counting has historically been associated with the diabetes diet since the discovery of insulin, where CHO foods were strictly measured and restricted to prescribed amounts at regimented times. The biggest revolution to the diabetes diet was the glycemic index (GI) when it was discovered that different CHO foods had different effects on blood glucose levels despite having the same CHO content. This called into question the necessity of strictly measuring CHO foods into 10 g or 15 g quantities. Many centres adopted the GI concept, allowing greater flexibility around quantification of CHO without deterioration of diabetes control. Research strongly supports the efficacy of low GI diets.

The development of novel insulins and new technologies (such as CSII) has placed a re-emphasis back to accurate CHO quantification. Advanced CHO counting is where grams of CHO are matched to units of insulin on intensive insulin therapy regimes to allow for greater flexibility around quantity and timing of food intake. Now that insulin dose can be theoretically matched to CHO intake, the relevancy of GI has again been challenged.

A CSII study investigated PPG after consumption of low and high GI meals. The high GI meal had the poorest PPG outcome despite accurate CHO quantification. This supports that CHO quantity alone is not sufficient in achieving PPG targets. GI plays a critical role in modifying PPG effect.

Given the accumulating evidence, it is concluded that CHO quantity and quality (GI) are important considerations to achieve optimal glycemic outcomes and that GI should be an integral component of dietary education.

INV15

Beyond carb counting: attention to the quality of carbohydrates in the T1D diet

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Medical nutrition therapy (MNT) is a fundamental to the management of youth with type 1 diabetes (T1D). Dietary recommendations are similar to those for youth in the general population with an emphasis on optimizing metabolic outcomes, in particular glycemic control. As carbohydrates are the principal determinant of post-prandial glycemic excursions, much attention has focused on carbohydrate estimation in the intensive era of T1D management. The glycemic index, a measure of carbohydrate quality, and protein and fat intakes have also been shown to impact glycemic control in youth with T1D. Perhaps more importantly, international data over the last 15 years have consistently demonstrated poor diet quality for youth and young adults with T1D with suboptimal intakes of whole foods and fiber and excessive intakes of total and saturated fat. Although glycemic control is the major predictor of future complications in T1D, emerging data suggest that suboptimal diet quality may also contribute to overweight and obesity, dyslipidemia, and hypertension increasing the risk of future cardiovascular disease. As such, medical nutrition therapy must provide youth with T1D and their families the knowledge and skills to both estimate carbohydrate content and consume a healthful overall diet. Additional research is required to better understand the determinants of nutritional status in pediatric T1D to inform clinical and research efforts aimed at improving overall dietary quality.

Symposium VI: Vitamin D in Diabetes: Much Ado About Nothing….or Something?

INV16

Bone health in youth with diabetes

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Type 1 (T1) and Type 2 diabetes (T2D) are associated with adverse effects on bone, which may be particularly significant for youth who are actively accruing bone mass. Persons with T1D have decreases in bone mineral density (BMD), whereas BMD can be low, normal, or high in T2D. Both diabetes types are associated with decreases in bone strength, an increased risk of fracture, and worsened fracture healing. Bone turnover analyses suggest that both T1D and T2D are conditions of low bone formation. Recent data in T2D also suggest a complex hormonal cross-talk between adipocytes and bone cells.

Multiple mechanisms underly the adverse bone health effects of diabetes including advanced glycation end-product interference with bone matrix collagen crosslinking, inflammatory cytokine effects, osmotic effects of hyperglycemia on bone formation, reduced bone blood flow due to diabetic microangiopathy, preferential calcium deposition in blood vessels rather than cartilage, and urinary calcium losses with glycosuria. Children with T1D may have delays in pubertal maturation which adversely affect bone accrual. They may also limit milk and substitute phosphoric acid-containing diet colas, which interfere with intestinal calcium absorption. General osteoporosis risk factors, such as vitamin D deficiency, low rates of physical activity, and smoking, are also likely important. T2D treatment with thiazolidinediones may increase fracture risk. Eventually, neuropathy and retinopathy can increase risk of falls and subsequent fracture.

Proactively optimizing childhood bone accrual for long-term skeletal health is important. Studies of relationships between metabolic control and BMD have not consistently demonstrated that improving glycemic control ameliorates skeletal health. Approaches to enhance bone health in children with diabetes therefore should focus on the basics: ensuring adequate calcium intake, optimizing vitamin D, and encouraging regular, weight-bearing physical activity.

Plenary Session IV: ISPAD/JDRF – New Technologies in Diabetes Management

INV17

Closing the loop – benefits and limitations

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Research over the past decade shows that blood glucose control is the most important predictor of diabetes complications. Achieving good blood glucose control dramatically lowers the risk of serious complications, by as much as 75% for some problems. Yet recent studies reveals that even the best-controlled patients spend <50 percent of their day within the normal blood sugar range – especially overnight, when patients are most vulnerable to hypoglycemia.

Our group performed several randomised crossover studies evaluating overnight closed-loop in young subjects with type 1 diabetes. During closed-loop nights (n = 45), sensor glucose values were fed into an MPC, which calculated the insulin infusion rate and the insulin pump was adjusted manually by a research nurse every 15 minutes. During control nights (n = 45), subject's standard insulin pump settings were applied. An analysis of pooled data documented increased time in the target range between 3.9 to 8.0 mmol/l (71% vs. 43%) and reduced time that glucose levels were below 3.9 mmol/l (2.1% vs. 4.1%). Glycaemic variability, as measured by the standard deviation of plasma glucose, was lower during closed-loop compared with conventional pump therapy (1.5 mmol/l vs. 2.1 mmol/l). We conclude that overnight closed-loop may improve glycaemic control and reduce nocturnal hypoglycaemia in both young people and adults with type 1 diabetes. Studies in pregnancies are also promising.

INV18

Feasibility study of automated overnight closed loop control under MD-logic artificial pancreas in type 1 diabetes patients: working towards the DREAM project

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Objective: The overnight period for type 1 diabetic patients is integral to their glycemic control accounting for one third of their day and remains a period of great concern due to nocturnal hypoglycemia. This study aims to establish near-normal overnight glucose control reducing the risk of nocturnal hypoglycemias by using The MD-Logic Artificial Pancreas (MDLAP) which applies fuzzy logic theory algorithm for automated insulin delivery. This in-patient feasibility study is the first step towards the goal of achieving an overnight Closed-Loop MDLAP system in the home setting.

Research design and method: Seven patients with type 1 diabetes [3 adolescents and 4 adults; age 20.6 ± 4.7 years; duration of diabetes 9.6 ± 2.6 years; body mass index (BMI) 24.3 ± 3.9 kg/m^2; glycated hemoglobin (HbA1c) 7.8 ± 0.8%; mean ± standard deviation (SD)] participated in a total of 14 closed-loop overnight sessions. Each participant undertook two closed-loop sessions, one- dinner and the other- dinner following physical activity. The data obtained was compared with matched patients homecare management with subcutaneous insulin pump and continuous glucose monitoring.

Results: The mean (SD) percentage of time spent in the target range (63–140 mg/dl) was 83% (16) and median (interquartile range) was 85% (78–92) for the closed loop vs. 34% (31) and 27% (6–57) in the home care setting respectively. During closed-loop overnight, the mean (SD) percentage of time within range after meals was 92% (9) compared to 73% (16) after physical activity. No hypoglycaemic (<63 mg/dl) events occured during the closed loop sessions.

Conclusion: Closed loop insulin delivery under MDLAP is a feasible and safe solution to overnight glycemic control.

Symposium VII: Current and Future Approaches to Management of Type 2 Diabetes in Youth

INV19

Early complications in youth with type 2 diabetes mellitus

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Historically, type 2 diabetes (T2DM) has been considered a disease of adults. However, over the past several decades the incidence and prevalence of type 2 diabetes in youth (onset <18 years of age) has increased world wide, disproportionally effecting youth of specific ethnic groups. The natural history and true burden of T2DM diagnosed in youth are still largely unknown. Given the relative recent identification of this problem in the pediatric age group, reports are now just emerging of both acute and chronic complications in this population. In adults, serious end-stage complications of T2DM occur within 20 years of diagnosis. Early evidence suggests that complications may occur at an earlier age with a shorter duration of diabetes in youth onset T2DM compared to youth with type 1 diabetes. End stage complications and diabetes related deaths have been reported before 30 years of age in Canadian First Nation young adults who were diagnosed with type 2 diabetes in adolescence. The earlier age of diagnosis raises concerns regarding the burden of disease in these youth who may begin to develop micro- and macro-vascular complications as young adults at the height of their productivity and child bearing years. This would result in significant impact on quality of life for the individual and family and significant economic consequences.
In this lecture, topics of discussion will include:
(1) acute complications,
(2) chronic complications and
(3) the co-morbidities associated with type 2 diabetes of youth onset.

INV20

Psychosocial issues and type 2 diabetes: the TODAY study

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The psychosocial needs of youth with type 1 diabetes have been well documented, but we are only beginning to understand these factors in youth with type 2 diabetes. The TODAY study provided an unparalled opportunity to study the types and severity of psychosocial issues facing youth with type 2 diabetes. The TODAY study tested the relative efficacy of three treatment approaches for type 2 diabetes in youth aged 10 to 17 years:
(1) metformin;
(2) metformin plus rosiglitazone; and
(3) metformin plus an intensive lifestyle intervention.
Psychosocial concerns such as depression, eating disorders, and quality of life were assessed in this cohort using standardized self-report questionnaires at baseline, and then periodically for 2–6 years depending upon time of randomization. A sizeable number of TODAY youth reported psychosocial concerns. For example, nearly 15% of the youth randomized to the TODAY study reported clinically significant symptoms of depression at baseline, and 26% of these youth entered the trial with clinically significant eating disorder symptoms. The treatment team approach utilized by clinics participating in the TODAY study allowed for identification of and response to psychosocial issues as they emerged within the study cohort. Each of the 15 clinical sites for the TODAY study had a psychologist as part of the treatment team. In addition to providing on-site supervision to the interventionist for the lifestyle component of one of the treatment arms, the psychologist was also available to consult with the treatment team as a whole when psychosocial issues were suspected to be affecting adherence to treatment or when critical items such as suicidality were endorsed on the psychosocial measures. TODAY psychosocial assessment procedures, baseline data, and response protocols will be described in this presentation. Recommendations for future directions in the design and implementation of clinical care for youth with type 2 diabetes will be made.

Symposium VIII: Does Neonatal Genetic Screening Enhance Early Detection of T1D?

INV21

Genetic and autoantibody screening for the identification of children at risk for type 1 diabetes

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Genetic screening from cord blood has been applied for the identification of children at increased risk for type 1 diabetes (T1D) for recruitment into prospective observational studies or into intervention trials. Based on HLA genotypes it is possible to identify from the general population in Finland children carrying maximally an absolute risk of 16–20% of progression to clinical T1D before the age of 15 years. This group is, however, very small including 1–2% of the general population. Screening for predisposing non-HLA polymorphisms makes it possible to further increase the absolute risk, but at the same time the risk group shrinks. The current HLA-based screening protocol used in the DIPP study identifies a risk group comprising 9% of newborn Finnish infants. Their average risk of clinical T1D by the age of 15 years is 4–5%, and the identified cohort includes 65–70% of all future T1D patients diagnosed before the age of 15 years. Due to drop-outs from the follow-up, the observational cohort will include about 50% of future T1D patients. The analysis of diabetes-associated auto antibodies from sequential samples helps to identify high-risk subjects from a cohort of children with HLA-conferred disease susceptibility. The risk ofT1D is affected by the number of auto antibodies, their persistence, and age at seroconversion. The combination of specific auto antibodies has also on effect on subsequent risk. Accordingly the combination of ICA and IAA results in young children in a progression rate close to 100% over the next 4 years, while the combination of ICA and GADA is associated with a risk of <20%. So far genetic and immunological screening has been acceptable in the context of research. The recent observation that the combination of initial HLA screening and sequential autoantibody screening and follow-up leads to a conspicuous decrease in the rate of ketoacidosis at diagnosis raises the issue whether screening should be applied more broadly.

INV22

Neonatal genetic screening and longitudinal follow-up allows for early detection of type 1 diabetes and reduced prevalence of diabetic ketoacidosis

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Objective: Young children have an unacceptably high prevalence of diabetic ketoacidosis (DKA) at the clinical diagnosis of type 1 diabetes. The aim of this study was to determine whether knowledge of genetic risk and close follow-up for development of islet auto antibodies through participation in The Environmental Determinants of Diabetes in the Young (TEDDY) study results in lower prevalence of DKA at diabetes onset in children <2 and <5 years compared to population-based incidence studies and registries.

Research design and methods: Symptoms and laboratory data collected on TEDDY participants diagnosed with type 1 diabetes between 2004 and 2010 were compared to data collected during the similar periods from studies and registries in all TEDDY participating countries (US: SEARCH for Diabetes in Youth Study; Sweden: Swediabkids; Finland: Finnish Pediatric Diabetes Register; and Germany: DPV-register).

Results: DKA prevalence in TEDDY participants was significantly lower than in all comparative registries (German DPV register: $P < 0.0001$, Swediabkids: $P = 0.02$, SEARCH: $P < 0.0001$, Finnish register: $P < 0.0001$). The prevalence of DKA in TEDDY children diagnosed <5 years of age was significantly lower compared to SEARCH ($P < 0.0001$) and the German DPV register ($P < 0.0001$) but not to Swediabkids or the Finnish register.

Conclusions: Participation in the TEDDY study is associated with reduced risk of DKA at diagnosis of type 1 diabetes in young children.

INV23

Psychological issues in screening, enrollment and retention in trials

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Screening programs designed to identify persons at risk for type 1 diabetes via genetic and antibody testing are controversial because they typically target children, provide only a crude estimate of type 1 diabetes risk, and offer no means of preventing the disease. The psychological impact of such screening programs include cognitive, emotional, and behavioral sequelae; the available literature has focused primarily on parents – usually mothers – since the target of screening is usually young children. Diabetes risk is a difficult construct to effectively communicate. Many individuals fail to accurately understand risk; inaccurate risk perceptions may increase over time and have been associated with early study withdrawal. Anxiety and worry are common reactions to learning that you or a loved one is at increased risk for type 1 diabetes. For most people, anxiety and worry dissipates with time but some individuals may be particularly vulnerable to prolonged anxiety of depression. Although there is no known means to prevent type 1 diabetes in at-risk individuals, families often report increased surveillance of those at-risk and behavior changes to prevent the disease, potentially threatening the internal validity of the study. There are important differences in the psychological reactions of family members from the general population who have no immediate family members with type 1 diabetes (T1D) and the reactions of family members who have been living with T1D. Compared to general population families, parents of an at-risk child who has a first degree T1D relative are more likely to worry about the at-risk child, to have accurate perceptions of the child's risk for T1D, to join a trial and to stay in the trial, and to engage in behaviors outside of the trial in an effort to prevent the disease. Greater consideration needs to be given to the psychological issues relevant to the population targeted for study.

Plenary Session V: Type 1 Diabetes Prevention and Modulation of Disease Progression

INV24

Findings from NAIMIT: a European project towards a cure for type 1 diabetes

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The goals of a successful therapeutic approach to arrest type 1 diabetes are cessation of beta-cell destruction, reversal of autoimmunity and preservation of surviving beta-cells allowing any natural regenerative potential to be realised. Any such interventions to achieve beta-cell protection and restoration should realise these goals through minimal modulation of the patient́s immune system in order to avoid severe disturbances of immune surveillance mechanisms leading to intolerable side effects.

In NAIMIT, we explore the potential of innovative approaches that operate with a minimal degree of interference in the general functions of the immune system. In order to move the field forward in this respect, we propose a series of studies that represent a novel and integrated approach. Our studies, organised into six scientific work packages, are designed as overlapping and complementary strategies that run the full-length of the journey from bench to bedside, including innovative first-in-man studies that aim to arrest autoimmunity in T1DM with minimal or no immune suppression; rather we aim to harness its extraordinary natural power for regulation, healing and regeneration.

The underlying concept for the therapeutic interventions being explored at the pre-clinical level in NAIMIT is the central role of the immune system in T1DM, but we also recognize the important role that the beta-cell adopts, as a partner actively contributing to its own demise. The concept of a key role for both the immune system and the beta-cell highlights the need for a ''multiple hit'' approach to disease prevention. This will include both modulation and re-education of the immune system, boosting of beta-cell defences against autoimmune damage and arresting the pro-inflammatory dialogue between immune cells and beta-cells. Natural immune modulators (like vitamin D and gut-based interventions) are used in this project. Progress of the project will be presented and can be read at www.naimit.eu.