



*NOTE: Meet the Experts and New Perspectives session descriptions coming soon!*

*Free Communications will be abstract presentations that are yet to be selected from the abstract submissions*

## **Thursday 9/14/17**

### **Session 1 (14:15-15:45)**

#### **Topic Symposium: Bone diseases – from bench to clinics**

Speakers of this symposium will highlight how understanding the intricate genetic, cellular and molecular pathophysiologic mechanisms in bone diseases could lead to prospective translational clinical applications.

##### **Somatic mutations that cause skeletal disease**

Matt Warman (USA)

- Elegant clinical and biochemical insights led to the discovery that a somatically arising mutation in *GNAS* is responsible for causing McCune-Albright syndrome. For other non-heritable genetic skeletal disorders, technical advances in massively parallel sequencing and computational advances in sequence data analysis were required to identify causal mutations. Examples include Proteus Syndrome and Klippel-Trenaunay syndrome. This presentation describes general clinical features of non-heritable diseases caused by somatic mutation, methods for discovering or for clinically testing responsible genes, and clinical drug trials for several of these disorders.

##### **Genotype-phenotype correlation in skeletal dysplasias**

Outi Mäkitie (Finland)

- More than 400 different forms of skeletal dysplasias have been described, each with characteristic clinical and radiographic features. With advances in molecular genetics it has become evident that extremely variable phenotypes can be caused by mutations in one gene, the mutation type and location within the gene determining the disease severity. Achondroplasia, hypochondroplasia and thanatophoric dysplasia, a lethal skeletal dysplasia, are all caused by mutations in the *FGFR3* gene. On the other hand, mutations in several different genes may lead to a similar phenotype. In osteogenesis imperfecta most forms are caused by mutations in the genes encoding type I collagen but several other associated genes have also been recognized. Phenotypes overlap but some genotype-phenotype correlations can be recognized. These and their utility in diagnostics will be discussed.

##### **Medical management of orthopedic disorders: manipulation of bone anabolism and catabolism**

Aaron Schindeler (Australia)

- Bone repair outcomes can be influenced by a variety of factors, but the two chief processes are bone formation (anabolism) and bone resorption (catabolism). Bone anabolism can be modulated by local intervention (e.g. bone graft, bone morphogenetic proteins) and by systemic agents (e.g. PTH1-34, anti-SCL antibody).

Alternatively, bone anti-resorptive drugs (e.g. bisphosphonates) can also be employed in an orthopedic setting. The combination of both anabolic and anti-catabolic therapies have yielded synergistic benefits, and have been effective in tackling challenging orthopedic conditions such as tibial pseudarthrosis. Finally, a combined anabolic/anti-catabolic approach may be useful for minimizing fracture risk in pediatric bone fragility disorders, such as osteogenesis imperfecta.

### Controversies: **Metformin treatment for obesity**

**Proposition: Metformin is used as a treatment for obesity. Is it justified?**

- PRO: Shubha Srinivasan (Australia)
- CON: Billy White (United Kingdom)

### Topic Symposium: **Renal and endocrine electrolyte disorders**

This symposium has been planned to focus on the cutting edge knowledge about congenital renal and endocrine electrolyte disorders that are definitely important fields for pediatric endocrinologists.

#### **Bartter & Gitelman Syndromes**

Detlef Bockenhauer (UK)

- Bartter and Gitelman syndromes are at the interface of nephron- and endocrinology due to the elevated levels of renin and aldosterone associated with renal salt wasting. Using clinical cases, the various reasons for hyperaldosteronism will be discussed and how they differ between Bartter and Gitelman syndrome. In addition, the potentially severe systemic consequences of hyperaldosteronism will be discussed.

#### **Pseudohypoaldosteronism**

Eisei Sohara (Japan)

- Mutations in with-no-lysine kinase 1 (WNK1) and WNK4 genes cause pseudohypoaldosteronism type II (PHAII). Moreover, two additional genes responsible for PHAII, Kelch-like 3 (KLHL3) and Cullin 3 (CUL3), have recently been identified. In this talk, we will present the patho-physiological roles of the WNK signaling cascade in PHAII, and novel mechanisms underlying the regulation of WNK signaling by KLHL3 and CUL3.

#### **Familial Hyperaldosteronism**

Evangelia Charmandari (Greece)

- Three familial forms of primary hyperaldosteronism (PA) have been described to date, referred to as FH-I, FH-II, and FH-III. FH-I is attributed to a chimeric CYP11B1/CYP11B2 gene, FH-II is characterized by hyperaldosteronism and bilateral adrenocortical hyperplasia often combined with adenomas, and FH-III is caused by mutations in the KCNJ5 gene encoding the potassium channel Kir 3.4. Early diagnosis and treatment of patients with FH is of fundamental importance because they have significantly higher incidence of stroke, myocardial infarction and atrial fibrillation.

### Topic Symposium: **Diabetes and the Brain**

This symposium will focus on the impact of dysglycemia on the developing brain in type 1 diabetes, exploring mechanisms of injury, the impact on cognitive development and structural and functional changes in the brain associated with dysglycemia.

#### **Aspects of diabetic dysglycemia that are the most injurious to the developing brain**

Fergus Cameron

- The dysglycemia of type 1 diabetes is multifaceted but can be broadly characterized into hypoglycemia, severe hypoglycemia, hyperglycemia, ketoacidosis and glycemically variable. Each of these perturbations has been documented to impact neural activity to varying degrees. These impacts appear to be modified by age and repetition/chronicity of the metabolic insult. Given that all dysglycemic insults may occur in an individual patient it has been difficult to ascribe relative importance to each component and hence prioritize metabolic outcomes in terms of neuroprotection. An exploration of dysglycemic related mechanisms of neural injury will be used to attempt

to elucidate a hierarchy of insults to brain function and outcome in type 1 diabetes in childhood and adolescence.

### **Cognitive development in type 1 diabetes**

Tamara Hershey:

- This talk will review data suggesting that type 1 diabetes can have an impact on aspects of cognitive function during development. The clinical variables most closely associated with any risk and the clinical significance of these effects will be discussed. The talk will also explore the ideas of vulnerability, resilience and compensation during cognitive development and the neurobiological basis of cognitive effects.

### **Neuroanatomical and Neurofunctional Consequences of Type 1 Diabetes in Children**

Allan Reiss

- This presentation will describe findings from a longitudinal, multi-site, multi-modal imaging study of young children with Type 1 diabetes who were followed over three time points. Results from structural, diffusion tensor and functional imaging will be discussed in the context of associations with behavior and cognition. Implications for clinical outcome, functional recovery and brain plasticity will be emphasized.

### **Topic Symposium: Endocrine complications of childhood cancer and its treatment**

The aim of this symposium is to address the medium- and long-term complications of childhood cancer on the endocrine system, particularly pubertal development, the reproductive axis and bone health.

#### **Management of endocrine late effects including fertility preservation.**

Yoko Miyoshi (Japan)

- As the survival rate of pediatric and adolescent patients with cancer has markedly improved, the late effects, especially endocrine disorders are recognized as a critical issue. Gonadal dysfunction, subfertility, and premature ovarian insufficiency are important late effects. The speaker will discuss the results of a nationwide survey on pediatric endocrinologists' experience with childbirth and fertility preservation in childhood cancer survivors in Japan.

#### **Central precocious puberty caused by brain tumors and radiotherapy**

Wassim Chemaitilly (USA)

- Central Precocious Puberty (CPP) may occur secondary to central nervous system (CNS) neoplasms within or near the hypothalamus or subsequent to the exposure of the hypothalamic-pituitary (HP) region to radiotherapy. With a prevalence of 26-29%, CPP is among the most common endocrine dysfunctions in children with a history of a CNS tumor near the HP region. This lecture provides a summary of the most recent knowledge pertaining to CPP as consequence of CNS tumors and their treatments, including data on the long-term growth, reproductive and general health outcomes.

#### **Bone health in childhood cancer survivors**

Sogol Mostoufi-Moab (USA)

- Childhood cancer is associated with numerous risk factors for poor bone acquisition, including the underlying disease, malnutrition, physical inactivity, reduced muscle strength, chemotherapy, radiation exposure, and endocrinopathies. The impact of an abnormal bone accrual may be immediate, resulting in fragility fractures during treatment, or delayed due to suboptimal peak bone mass acquisition. This lecture will focus on threats to skeletal acquisition and bone health in childhood cancer survivors.

### **Topic Symposium: New insights in Disorder of Sex Development (DSD)**

The aim of this symposium is to provide updated basic and clinical strategy using new technology and accumulated clinical data, and to pursue comprehensive approach to the diagnosis and management of DSD.

#### **Disorders of sex development: insights from targeted gene sequencing of a large international patient cohort**

Andrew Sinclair (Australia)

- Currently only 13% of patients receive an accurate genetic DSD diagnosis. Using a Massively Parallel Sequencing targeted DSD gene panel to sequence all 64 known

diagnostic DSD genes and 967 candidate genes, we analyzed the largest international cohort of patients with DSD and found a total of 28 genes implicated in DSD, highlighting the genetic spectrum of this disorder. Sequencing revealed 97 previously unreported DSD gene variants. A likely genetic diagnosis was identified in 43% of patients with 46,XY DSD, a substantial increase over current practice. In patients with 46,XY disorders of androgen synthesis and action the genetic diagnosis rate reached 60%. In many cases, our findings were informative as to the likely cause of the DSD, which will facilitate clinical management. Targeted DSD gene panel represents a cost and time-effective means of improving the genetic diagnostic capability for patients affected by DSD.

#### **Endocrine Evaluation of Suspected XY DSD**

S. Faisal Ahmed (UK)

- Reaching a firm diagnosis in XY DSD is challenging. Rapid advances in diagnostic technology and an improved fundamental understanding of sex and gonadal development is now facilitating the diagnosis of these conditions. There is now a need for clearer guidance on the relative merits of biochemical versus genetic evaluation. In addition, there is a need for greater emphasis on showing that a firm diagnosis for conditions associated with XY DSD is associated with a change in clinical practice that benefits the patient. The standardisation and harmonisation of complex genetic and biochemical analyses and the gathering of patient-centred outcome measures for such rare conditions cannot be performed without relying on international networks and registries.

#### **Differential diagnosis and management – theory and practice**

Chunxiu Gong (China)

- 2006-2016 the DSD bank has registered more than 1200 cases. Include Sex chromosome DSD 126cases ; 46, XY DSD 1018 cases and non-CAH 46, XX DSD 70 cases. Accept gene test about 340 cases. We diagnosed 70 cases HH and AIS 39 cases, and 46 5ARD, 24 rare types CAH 10 NR5A1 related DSD and HSD17B3 2cases.introduce my experience for their diagnosis and management

## **Friday 9/15/17**

### **Session 1 (07:30-08:30)**

#### **Diagnosis and Management of Pseudohypoparathyroidism and Related Conditions**

- **Emily Germain-Lee (USA)**

#### **Meet the Expert: MODY**

- **Siri Atma Greeley (USA)**

#### **Meet the Expert: Prader Willi Syndrome from Birth to Adulthood**

- **Jennifer Miller (USA)**

#### **Meet the Expert: Pediatric cortical adrenal tumors**

- **Margaret de Castro (BRA)**

#### **Free Communication: Puberty**

#### **Free Communication: Bone Min**

#### **Free Communication: Growth IGF**

## Friday 9/15/17

Session 2 (08:45am-09:45am)

### New Perspectives: Microbiome

#### Meet the Expert: Delayed or Absent Puberty

- Yee-Ming Chan (USA)

#### Meet the Expert: Pediatric pheochromocytoma/paraganglioma

- Nalini Shah (IND) (9/15 AM, 9/16 AM)

#### Meet the Expert: Pediatric osteoporosis

- Craig Munns (AUS)

### Free Communication: T2DM and CH2O

### Free Communication: Endo Ethics

### Free Communication: DSD

## Friday 9/15/17

Session 3 (12:45pm-14:15)

### Topic Symposium: **Symposium: New concepts in diagnosis and treatment of CAH**

The aim of this symposium is to introduce the new development in the diagnosis of CAH including newborn screening, hormonal and molecular analysis, as well as the new therapeutic approaches.

#### **A Longitudinal and International Perspective on Neonatal Screening for CAH**

Anna Nordenström (Sweden)

- The general goal of this presentation is to present data on neonatal screening for CAH, in an international perspective. Data on the effects on long term health outcome for the patients, the Swedish experiences, will also be presented.

#### **Pitfall in hormonal and molecular diagnosis in the clinical practice of congenital adrenal hyperplasia**

Berenice Mendonça (Brazil)

- The general aim of this presentation is to present current and upcoming data on hormonal and molecular diagnosis of congenital adrenal hyperplasia for clinical practice.

#### **New treatment approaches to CAH**

Deborah Merke (USA)

- Many of the adverse outcomes in patients with congenital adrenal hyperplasia (CAH) are attributable to suboptimal treatment approaches. This talk will review new therapies being developed that target different aspects of the pathophysiology of CAH.

### Topic Symposium: **Diabetes management in children of resource-limited settings**

- The diabetes management of children of resource-limited settings will take you through the current state of practices in managing various aspects of diabetes in children in settings with less resources. This will be done by experts with firsthand experience in those settings by using the case studies which illustrates the approach to diagnosis, management and the outcomes.

#### **Intensive Insulin Therapy**

Edna Majaliwa (Tanzania)

- Intensive insulin therapy and the new insulin-delivery systems has helped in improving glycemic control. This lecture will explore intensive insulin therapy in resource limited

settings using program descriptions and examples from centers in Sub-Saharan Africa which have been able to use the intensive insulin therapy. We will elaborate on the successes, challenges and outcomes of that therapy in those settings.

### **Glycaemic Control**

Thomas Ngwiri (Kenya)

- Improvements in health-worker training on diabetes have resulted in increased diagnosis and better short term survival for newly diagnosed children. At present only 28% of children and adolescents in one patient cohort in Kenya had reasonable blood glucose control. The next focus of improvement in care will need to be on long term glycaemic control if the debilitating complications of poor control are to be avoided.

### **Neonatal Diabetes management**

Ethel Codner (Chile)

- Advances in the understanding and treatment of neonatal diabetes have allowed treating this young population with oral sulfonylureas. This talk will review the different alternatives to do the molecular study in resource-limited settings and clinical aspects related to the transfer to sulphonylureas.

## **Controversies: Aromatase inhibition to improve stature: do the benefits outweigh risks and costs?**

### **European data**

Matti Hero (FIN)

- Randomized controlled trials with limited numbers of subjects have shown that aromatase inhibitor treatment delays bone maturation and increases predicted adult height in boys with idiopathic short stature and growth hormone deficiency. However, very little adult height data are available. While aromatase inhibitors have been well-tolerated in recent trials, several safety issues remain inadequately studied. In the current presentation, findings from European studies of aromatase inhibitors in pediatric indications are summarized.

### **American data**

Nelly Mauras (USA)

- Estrogen is principally responsible for epiphyseal fusion in puberty in both males and females; hence, suppression of estrogen has been investigated as a mechanism of growth promotion in children with significant short stature and limited height potential that are in puberty. Herein I will present our American experience investigating the pharmacokinetics and pharmacodynamics of aromatase inhibitors in young males (both healthy and with gynecomastia) and the impact of aromatase blockade in growth promotion in males with GH deficiency, testotoxicosis, and, most recently, idiopathic short stature. The latter group was followed to near-adult height and treated with aromatase inhibitors alone, GH alone, or a combination of both. Extensive bone and biochemical data, as well as new quality-of-life results, will be presented.

## **Topic Symposium: Growth hormone safety**

### **How has and how should the safety of rhGH be evaluated over time?**

Les Robison (USA)

- Assessment of the safety of rhGH has been the topic of numerous publications based upon selected research populations as well as post-marketing surveillance efforts. While each report has strengths and limitations, the overwhelming majority have substantial methodological weaknesses that limit interpretation of the data and thus the conclusions that can be drawn. Since some of the disorders treated with rhGH are associated with a higher risk of mortality or other adverse outcomes, it can be challenging to distinguish the impact of rhGH on the risk for adverse events. Methodological approaches applied to other pediatric populations to assess treatment-associated morbidity and mortality will be discussed within the context of how well-characterized cohorts of rhGH-treated patients could inform long-term safety.

### **GH Therapy in Brain Tumor Survivors: Risk of Disease Recurrence and Second Tumors**

Charles Sklar (USA)

- GH and IGF-1 are known to affect tumor growth in vitro and in some animal models; epidemiological studies have shown associations between IGF-1 levels and the development of certain cancers in adults. These data have raised concerns about the use of GH in survivors of pediatric cancers, especially survivors of various brain tumors. In this presentation, we will review the published data on the risks of both recurrence of the primary tumor as well as the risk of developing a second, new tumor in pediatric brain tumor survivors who are treated with GH.

### **Mortality and morbidity after GH therapy in EU SAGhE**

Stefano Cianfarani (Italy)

- The SAGhE (Safety and Appropriateness of Growth Hormone Treatments in Europe) study was initiated in Europe to provide a large-scale international collaborative cohort study of r-hGH-treated patients with long-term follow-up for cancer incidence and mortality.
- SAGhE assembled cohorts of patients treated in childhood with recombinant human growth hormone (r-hGH) in 8 European countries. The cohort consisted of 24,232 patients, most commonly treated for isolated growth failure (53%), Turner syndrome (13%) and growth hormone deficiency linked to neoplasia (12%).
- In patients whose initial diagnosis was “isolated growth failure” (i.e. growth failure without other major disease: isolated growth hormone deficiency, idiopathic short stature, and prenatal growth failure), overall cancer risk was not raised and there were no significantly raised site-specific risks. For patients whose initial diagnosis was not isolated growth failure or cancer, there were significantly raised risks of cancer incidence (SIR 1.4; 95% CI 1.1-1.9) and mortality (SMR 2.2; 95% CI 1.3-3.7) overall, and of bone (SIR 4.1; 95% CI 1.3-12.6) and bladder SIR 27.8 (7.0-111.3) cancer incidence.
- These results do not support a carcinogenic effect of r-hGH in patients without previous risk factors. However, the raised risks of bone and bladder cancers even in patients with initial non-cancer diagnoses, and the rising risk of Hodgkin lymphoma with longer follow-up in such patients, leave possibilities of effects on site-specific cancer causation for which further data are needed.

### **Topic Symposium: Metabolic Syndrome in Early Childhood**

This symposium will aim to define metabolic syndrome in toddlers and young children in order to detect, treat and possibly prevent it early in childhood.

#### **Definition of metabolic syndrome in toddlers and children**

Ram Weiss (Israel)

- The speaker will present the current definitions of the syndrome and their limitations in the younger age group. Strategies to assess metabolic risk in younger children will be also presented along with potential novel biomarkers of CVD risk clustering

#### **Prevention of metabolic syndrome in early childhood**

Wieland Kiess (Germany)

- This presentation will aim to elucidate the evidence and the potential benefits of obesity program and interventions. In addition, it will focus on possible targets of preventive measures in order to improve the rate of success of preventive programs.

#### **Current treatment of metabolic syndrome in children**

Sonia Caprio (USA)

- The general goal of this presentation is to present data on the role of fatty liver in the cardiometabolic dysregulation of obese adolescents. More over, data on the adipo/liver axis changes and inflammation will be presented, as well as potential treatment approaches.

### **Topic Symposium: PUBERTY AND OVARIAN DISORDERS**

The aim of this symposium is to discuss some new aspects of the pathophysiology of puberty and to provide a comprehensive overview of how cancer treatments affect reproductive axis.

#### **RECENT ADVANCEMENT IN THE GENETICS OF CENTRAL PRECOCIOUS PUBERTY**

Ana Claudia Latrónico ( Brasil)

- Central precocious puberty (CPP) results from premature activation of the hypothalamic-pituitary axis. The important role of MKRN3 in human puberty initiation was reinforced by large genome-wide studies. More recently, a complex defect of DLK1 was identified in a multigenerational family with CPP using linkage analysis and whole genomic sequencing, this deletion included the 5'UTR and the first exon of DLK1 including the translational start site. Only family members who inherited the defect from their father have precocious puberty, consistent with the known imprinting of DLK1. These findings suggest a role of genomic imprinting in regulating the timing of human puberty.

#### **NOVEL INSIGHTS IN THE ETIOLOGY OF HYPOGONADOTROPIC HYPOGONADISM**

Ali Kemal Topaloglu ( Turkey )

- Human genetics studies on hypogonadotropic hypogonadism (HH) have contributed enormously to our quest to understand the developmental pattern of the reproductive system. The most outstanding example has been the KNDy concept of the GnRH pulse generator as the source of the rhythmic stimulus driving GnRH release after identifications of the Kisspeptin and Neurokinin B ligand-receptor-encoding gene pair mutations in consanguineous human families with HH. The contemporary molecular genetics techniques such as whole exome/genome sequencing has been promising to identify more HH-associated genes, thus gain further insight into pubertal development

#### **NOVEL INSIGHTS INTO FEMALE REPRODUCTION: PRESERVATION OF FERTILITY IN CANCER PATIENTS**

Teresa Woodduff ( USA )

- Young cancer patients have the added burden that life-preserving cancer treatments, including surgery, chemotherapy, and radiotherapy, may compromise their future fertility. Fertility preservation for females has proved to be a particular challenge because mature female gametes are rare and difficult to acquire. The purpose of this presentation is to provide a comprehensive overview of how cancer treatments affect the female reproductive axis, delineate the diverse fertility preservation options that are currently available or being developed for young women, and describe current measures of ovarian reserve that can be used pre- and post-cancer treatment.

## **Friday 9/15/17**

Session 4 (14:30pm-15:30)

**Free Communication: Bone 2**

**Free Communication: Growth 2**

**Free Communication: DSD Gender 2**

**Free Communication: Obesity 2**

**Yearbook 1**

## **Saturday 9/16/17**

Session 1 (07:30-08:30)

**Free Communication: Endo Care Transition**

**Meet the Expert: Hyperthyroidism in children**

- **Julianne Léger (France)**

**Meet the Expert: Diagnosis and Management of Pseudohypoparathyroidism and Related Conditions**

- **Emily Germain-Lee (USA)**



### Meet the Expert: Diabetes in the Infant

- Thomas Danne (Germany)

### Free Communication: Gender Dysphoria

### Free Communication: Global Health

### Meet the Expert: Pediatric pheochromocytoma/paraganglioma

- Nalini Shah (IND) (9/15 AM, 9/16 AM)

## Saturday 9/16/17

### Session 2 (08:45-09:45)

#### Meet the Expert: Neonatal hypoglycemia

- Khalid Hussain (UK)

#### Meet the Expert: Prader Willi Syndrome from Birth to Adulthood

- Jennifer Miller (USA)

#### Meet the Expert: Exercising safely with T1DM

- Elizabeth Davis (AUS)

#### Meet the Expert: Hypophosphatemic rickets

- Leanne Ward (CAN)

### Free Communication: Quality Improvement

### Free Communication: Thyroid

### Free Communication: NeuroEndo

## Saturday 9/16/17

### Session 3 (13:15-14:45)

#### Topic Symposium: Epigenetics in pediatric endocrine disorders

This symposium will discuss the molecular basis and clinical management of imprinting disorders in humans, focusing mainly on Silver-Russell syndrome and disorders of insulin secretion.

##### **Towards the understanding of imprinting disorders**

Thomas Eggermann, Germany

- Imprinting disorders (IDs) are a group of currently thirteen congenital diseases with common underlying (epi)genetic aetiologies and overlapping clinical features affecting growth, development and metabolism. In the last years it has emerged that IDs are characterized by the same types of mutations and epimutations, i.e. uniparental disomies, copy number variations, epimutations, and point mutations. Each ID is associated with a specific imprinted locus, but the same imprinted region can be involved in different IDs. Additionally, even the same aberrant methylation patterns are observed in different phenotypes. Clinical diagnosis may be difficult. The advances in molecular and clinical diagnosis of IDs help to circumvent these issues, and this talk will explore these advances with their potential impact on patients and their families, with potentially more directed genetic counselling of families and personalized therapeutic approaches.

##### **Diagnosis and Management of Silver-Russell syndrome**

Irene Netchine, France

- The first international guidelines for diagnosis and management of individuals with Silver-Russell Syndrome (SRS), an imprinting disorder affecting pre- and postnatal growth and metabolism, were recently adopted and published. Developments in (epi)genomic technology have rapidly advanced the understanding of the molecular mechanisms underlying SRS. This talk will discuss the expert, multidisciplinary approach required to address management issues in SRS including growth failure, early severe feeding difficulties and later possible rapid weight gain, glycemic dysregulation, dysregulation of insulin secretion, and accelerated puberty.

#### **Epigenetics in neonatal diabetes mellitus and hyperinsulinism,**

Tohru Yorifuji (Japan)

- Disorders of insulin secretion may be due to an underlying disorder of imprinting at two potential loci; namely 6q24 and 11p15. This talk will cover the topics of (1) 6q24-related diabetes as a cause of MODY-mimicker, (2) somatic mosaicism involving the 11p15 imprinted loci as a cause of mutation-negative congenital hyperinsulinism, and (3) a short overview of abnormalities of the 11p15 imprinted loci as a cause of type 2 diabetes.

### **Topic Symposium: Pharmacotherapy for hypothalamic obesity**

#### **New Aspects in hypothalamic regulation of weight**

Sadaf Farooqi (UK)

- By uncovering the fundamental mechanisms that control energy homeostasis, our goal is to identify and validate control points that can be targeted to improve outcomes in obesity associated diseases. Using extensive genetic and clinical data on unique cohorts of individuals at both extremes of the weight distribution (severe obesity and thinness), we are working to map the hypothalamic networks that maintain energy homeostasis. In clinical studies, we characterise the effects of these specific pathways on eating behaviour, energy expenditure and substrate utilisation to learn how these pathways contribute to severe childhood obesity.

#### **Medical therapy for hypothalamic obesity (HyOb)**

Ze'ev Hochberg (Israel)

- HyOb is a complex disease derived from damage to several hypothalamic nuclei that includes leptin resistance and hyperleptinemia, melanocortin deficiency and resistance due to MC4R damage, modulation of POMC and NPY, oxytocin and CRH, finally affecting food intake and weight gain. At the end-organ targets, HyOb leads to enhanced 11 $\beta$ -hydroxysteroid dehydrogenase-1 activity, a decrease in sympathetic tone and increases in vagal tone, resulting in insulin hypersecretion. Attempts to ameliorate only one of these agents have been used for limited periods in a small number of patients with limited success. The complexity of HyOb requires a strategy, probably multi-drug, of simultaneous targeting as many as possible of these mechanisms, adjuncts to behavioral and lifestyle changes.

#### **Surgical therapy for hypothalamic obesity**

Thomas H. Inge (USA)

- Discuss indications and contraindications for weight loss surgery in adolescents
- List surgical procedures that are applicable for adolescents, technical aspects of sleeve gastrectomy, and surgical risks
- Review long term risks and benefits of adolescent bariatric surgery
- Review changes in insulin resistance and insulin secretion after adolescent bariatric surgery
- Compare outcomes of surgical and medical treatment for adolescents with T2D

### **Topic Symposium: Gender dysphoria**

The aim of this session is to explore current concepts of sex differentiation in brain and biological mechanisms that influence the development of gender role and gender identity. In addition, current treatment models and controversies regarding care of transgender youth will be discussed.

## **Epigenetic modification of sex differentiation in brain**

Margaret M McCarthy (USA)

- Sex differences in the brain are established during a critical period of development but endure into adulthood. Using the laboratory rodent we determined that epigenetic modifications to the genome mediated by gonadal steroids direct sex specific programs of gene expression during the critical period. In females, DNA methylation suppresses a cohort of genes required for masculinization of a specific brain region and associated behaviors in adulthood. Steroids from the fetal testis down regulate activity of the DNA methylating enzymes thereby emancipating the cohort of masculinization genes and both establishing and maintaining sex differences in brain and behavior.

## **Sex differences in brain and behavior**

Eric Vilain (USA)

- There are considerable societal debates about gender, and science is often used as arguments by various sides to bolster political opinions. A principal goal of this session to discuss what we know and don't know about the development of gender differences, from cells to behavior. Although there is plenty of evidence that male and female brains develop differently, the underlying biological mechanisms remain poorly understood. The respective influence of hormonal, genetic and epigenetic factors on the development of sex differences, and on gender role and gender identity will be addressed.

## **Clinical management of Transgender Youth**

Peggy Cohen-Kettenis (The Netherlands)

- Although not all adolescents struggling with gender issues need gender affirming medical treatment (hormones and surgery), gender identity clinics increasingly offer this type of treatment. Puberty is suppressed in an early pubertal stage and feminizing or masculinizing hormones are given a few years later. In order to ensure good outcome, appropriate assessment of the gender dysphoria as well as co-existing psychological and social problems by experienced clinicians is crucial. In this presentation, essential components of the most frequently used protocol are described and controversies regarding this approach are discussed.

## **Controversies: Imaging for congenital hypothyroidism**

Congenital hypothyroidism is a common disorder encountered frequently by pediatric endocrinologists around the world. Yet, the optimal evaluation of infants with abnormal newborn screening tests has not been determined. In particular, the routine use of imaging studies remains highly controversial. This session aims to help attendees evaluate the pros and cons of the use of imaging studies in every infant being evaluated for congenital hypothyroidism.

### **Thyroid imaging should be a routine step in the diagnosis and therapeutic planning for congenital hypothyroidism.**

In support--Johnny Deladoëy (Canada)

- Initial newborn screening for congenital hypothyroidism and confirmatory diagnoses are based on blood tests, the interpretation of which varies according to diagnostic thresholds. Thus, the quality control of newborn screening for congenital hypothyroidism is trapped in a closed system of self-validation and self-correlation, with a risk of over-diagnosis. Therefore, establishing the etiology of congenital hypothyroidism through imaging is crucial and cost-effective to assess the efficacy of the newborn screening programs.

### **Thyroid imaging should be a routine step in the diagnosis and therapeutic planning for congenital hypothyroidism.**

In opposition--Stephen Lafranchi (USA)

- Thyroid imaging (ultrasound or radionuclide uptake and scan) in newborns detected with congenital hypothyroidism provides information on anatomy of the gland (and indirectly on etiology), may be useful for genetic counseling, may help guide initial l-thyroxine dosing, and may help predict permanent vs. transient hypothyroidism. But,

should imaging be a “routine step in the diagnosis and therapeutic planning”? This speaker will present arguments that much of this information can be found by other means and/or is not routinely necessary for management of most infants with congenital hypothyroidism.

### Topic Symposium: **Treatment of bone metabolism disorders**

#### **Update on Hypophosphatemic rickets**

Thomas Carpenter (USA)

- The clinical presentation, diagnostic criteria, and medical treatment of XLH will be discussed. The clinical course during childhood and adulthood will be reviewed, including dental disease and enthesopathy. Examples of management dilemmas will be presented, with mention of novel therapeutic strategies.

#### **Update on Osteogenesis Imperfecta**

Frank Rauch (CA)

- Recent advances in sequencing technology have led to the identification of many new genes that are associated with an osteogenesis imperfecta (OI) phenotype. Almost all individuals with a clinical diagnosis of OI have a disease-causing mutation in one of the known OI-associated genes. Anti-resorptive therapy with bisphosphonates is the main treatment option, even though osteoclast inhibition can also be achieved with antibodies against RANKL, an osteoclast protein. Another novel approach to treat osteogenesis imperfecta is to stimulate bone formation through antibody-mediated sclerostin inhibition.

#### **Update on Hypoparathyroidism**

Rachel Gafni (USA)

- Hypoparathyroidism is one of the few endocrine conditions for which hormone replacement therapy is not standard. Subcutaneous PTH appears to effectively correct hypocalcemia of hypoparathyroidism, however, it does not completely restore mineral homeostasis, with variable effects on the skeleton and the kidney observed. Although PTH 1-84 was recently approved for adults with hypoparathyroidism, the lack of long-term safety and efficacy data precludes its routine use, particularly in children, who require decades of treatment. This session will critically review the current data on PTH replacement therapy and discuss evolving therapeutic options.

## **Saturday 9/16/17**

Session 4 (15:15-16:15)

**Free Communication: Type 1 DM**

**New Perspectives: TBD**

**Meet the Expert: MODY**

- **Siri Atma Greeley (USA)**

**Meet the Expert: Pediatric osteoporosis**

- **Craig Munns (AUS)**

**Yearbook 2**

**Free Communication: Obesity lipids**

**Free Communication: Multisys endo dis**

## **Sunday 9/17/17**

Session 1 (07:30-08:30)

#### Meet the Expert: Diabetes in the Infant

- Thomas Danne (Germany)

#### Free Communication: Fetal/Neonate endo

#### Free Communication: Adrenal

#### New Perspectives: CaSR stem cells

#### Meet the Expert: Hypophosphatemic rickets

- Leanne Ward (CAN)

#### Meet the Expert: Delayed or Absent Puberty

- Yee-Ming Chan (USA)

#### Meet the Expert: Hyperthyroidism in children

- Julianne Léger (France)

### Sunday 9/17/17

#### Session 2 (08:45-09:45)

#### Yearbook 3

#### Free Communication: Thyroid 2

#### Free Communication: Type 1 DM2

#### Meet the Expert: Exercising safely with T1DM

- Elizabeth Davis (AUS)

#### Meet the Expert: Pediatric cortical adrenal tumors

- Margaret de Castro (BRA)

#### Meet the Expert: Neonatal hypoglycemia

- Khalid Hussain (UK)

### Sunday 9/17/17

#### Session 3 (10:15-11:45)

#### Topic Symposium: Adult consequences of pediatric endocrine disease

##### Type 1 diabetes

Johnny Ludvigsson (Sweden)

- In spite of modern devices treatment of T1D is heavy for the patients with decreased quality of life, fatigue and increase of suicides. Hypoglycemia unawareness may be a serious problem, and severe hypoglycemia is not a rare cause of death, as well as keto-acidosis. In addition both micro-and macrovascular late complications, contribute to substantially increased mortality. We need to find ways to preserve and if possible improve beta cell function.

##### Disorders of sex development

Olaf Hiort (Germany)

- Sexuality and overall health-related quality of life play a major role in caring for adults with Differences of Sex Development (DSD). Sexual functioning might be impeded due to the given anatomy, surgical interventions or hormonal therapy. Novel approaches require highly specialized interdisciplinary care, including gynecological and urological

management, specialized protocols for hormone therapies or replacements, and overall life-long psychological support.

### **Childhood onset hypopituitarism**

Gudmundur Johansson (Sweden)

- Hypopituitarism is a complex endocrine disorder that in adulthood is associated with metabolic adverse outcome and increased mortality. Childhood onset hypopituitarism and hypopituitary-hypothalamic disorders have a marked excess mortality in comparison with adult-onset patients. This may be related to the difference in the underlying etiology, duration of disease and disruption of care during transition from childhood to adulthood. Un-interrupted care into adulthood, multidisciplinary team management and improved treatment of growth hormone and glucocorticoids deficiency may help to improve outcome of patients with childhood-onset hypopituitarism.

### **Topic Symposium: New insights into growth disorders**

This symposium will explore important recent discoveries in the genetic causes of growth disorders and also the consequences of fetal and early childhood growth on subsequent health.

#### **Insulin and IGF1 receptor signaling**

Susumu Kanzaki (Japan)

- This presentation will review recently identified human mutations in INSR (insulin receptor) and IGF1R (IGF1 receptor). It will focus particularly on heterozygous IGF1R mutations, including the clinical presentation, phenotypic spectrum, diagnostic approach, and treatment.

#### **Genomic aspects**

Andrew Dauber (USA)

- This talk will review recent advances in the field of growth genetics, including coding variants associated with stature found in genome-wide association studies and new genetic causes of growth disorders identified by exome sequencing, such as mutations in PAPP2 and aggrecan. It will also explore the next steps in improving patient care after a novel genetic discovery has been made.

#### **Outcomes after fetal growth restriction**

Verónica Mericq (Chile)

- This presentation will discuss the effect of the intrauterine environment and/or early childhood growth on type 2 diabetes mellitus, cardiovascular disease, hypertension, chronic kidney disease and endothelial and vascular abnormalities. Possible effects on the timing of adrenarche, and puberty will also be explored.

### **Controversies: Is there a role for early surgery in the management of DSD?**

Genital surgery in the context of DSD has been heavily debated in the past decade, both indications and timing. In this session, this topic will be approached from a legal, urological, hormonal and psychological perspective, in order to make the audience familiar with the different arguments and sensitivities surrounding this subject and to provide a broad and nuanced overview. Diverging views that will become apparent during the session will be included in the discussion.

#### **Legal considerations**

Olaf Hiort (Germany)

- In this presentation, recent developments in Germany will be discussed, and an “Expertise Report” by the German Ministry for Family presented. The German law on sex assignment at birth and the implications for patients with DSD conditions will be discussed. Furthermore, the role and legal aspects of parental decisions regarding sex assignment and possible non-reversible interventions for a minor will be discussed.

#### **Urology perspective**

Earl Chang (USA)

- The pros and cons of early surgery in children with DSD will be explained. Technical considerations regarding early versus late surgery will be included in the discussion. The current approach to DSD surgery will be presented from a historical perspective.

## **Psychology perspective**

Amy Wisniewski (USA)

- In this lecture, insights in the psychosocial status of parents of young children with ambiguous genitalia, before and after genitoplasty, will be offered, including the impact of surgical complications on parents' psychosocial status, as well as the difficulty of determining an underlying etiology for some children with 46,XY DSD. Finally, cosmetic outcomes as determined by parents and surgeons, in relation to parents' psychosocial status, will be considered.

### **Panel discussion/Q & A (25 minutes)**

## **Topic Symposium: Thyroid conundrums**

The aim of this session is to explore current understanding of the physiology underlying these common thyroid axis clinical conundrums and how that knowledge can inform treatment decisions.

### **Thyroid axis dysfunction in Down syndrome**

Paul van Trotsenburg

- Down syndrome has been associated with thyroid disease for many decades. Gradually, it has become clear that thyroid autoimmunity is much more prevalent in Down syndrome than in non-Down syndrome individuals, resulting in higher incidences of acquired (subclinical) hypo- and hyperthyroidism already from childhood on. In addition, many Down syndrome neonates have elevated TSH levels suggestive of a mild form of "trisomy 21-induced" congenital thyroid dysfunction. This speaker will present an overview of the current knowledge about thyroid disease in Down syndrome.

### **Non-thyroidal illness syndrome**

Anita Boelen

- The non-thyroidal illness syndrome (NTIS) occurs in a large proportion of hospitalized patients and comprises a variety of alterations in the hypothalamus-pituitary-thyroid (HPT) axis that are observed during illness. Changes in thyroid hormone (TH) metabolism are organ-specific, occur in a time-dependent manner and depend on the severity of illness. At present there is no evidence-based consensus or guideline advocating thyroid hormone treatment of NTIS in the critically ill patients. Underlying mechanisms involved in illness-induced alterations of the HPT-axis and potential treatment strategies will be discussed.

### **Thyroid axis disruption by obesity**

Thomas Reinehr

- Obesity is frequently associated with TSH and fT3 concentrations slightly above the upper normal range. These thyroid hormone alterations in obesity seem rather a consequence than a cause of obesity since weight loss leads to a drop of elevated thyroid hormone levels. This speaker will present the suggested underlying pathways linking obesity to thyroid axis disruption including the role of adipokines and cytokines. Furthermore, the clinical consequences of thyroid hormones alterations in obesity will be discussed, which may explain in part the difficulties to maintain weight loss.

## **Topic Symposium: Technology and diabetes**

This symposium will provide an update on technological advances in the management of diabetes including the use of apps and mobile phones, news on development of the artificial pancreas, smart insulins and novel delivery systems.

### **Use of apps & phones in diabetes management**

Joseph Cafazzo (Canada)

- The ubiquitous mobile phone has created an ecosystem of health apps of which hundreds of diabetes-related apps have emerged. The features of the first wave of these apps are mostly limited to replacing the log book of blood glucose readings and providing some educational material. The next generation apps communicate with BG meters, weight scales, and activity monitors. They now provide deeper insights into data, and most importantly are beginning to be integrated into clinical care. Insights as

to how these apps can elicit positive behaviour change and create more meaningful interactions between patient and provider will be explored.

### **Update on artificial pancreas development**

Roman Hovorka (UK)

- The artificial pancreas combines continuous glucose monitoring with an insulin pump to deliver subcutaneous insulin based on calculations made by adaptive algorithms to accommodate varying and highly-individual insulin needs. The lecture will summarise the recent progress including the description of improved glucose control and reduced risk of hypoglycaemia associated with home use of the artificial pancreas in children, adolescents, and adults.

### **Smart insulins and novel delivery systems**

Zhen Gu (USA)

- A glucose-responsive smart insulin delivery system mimicking the function of pancreatic cells has tremendous potential to improve quality of life and health in diabetes. This talk will discuss ongoing efforts in exploiting novel smart insulin delivery formulations. The speaker will focus on recently developed devices based on a painless microneedle-array patch (“smart insulin patch”) containing glucose-responsive vesicles, which are loaded with insulin and glucose-specific enzyme. The smart patch can effectively regulate blood glucose and avoid the risk of hypoglycemia in a mouse model of type 1 diabetes. Additionally, the speaker will introduce a study applying red blood cells for glucose-responsive insulin delivery.