CPEG 2008 Scientific Meeting

Vancouver, B.C.
April 3-5, 2008

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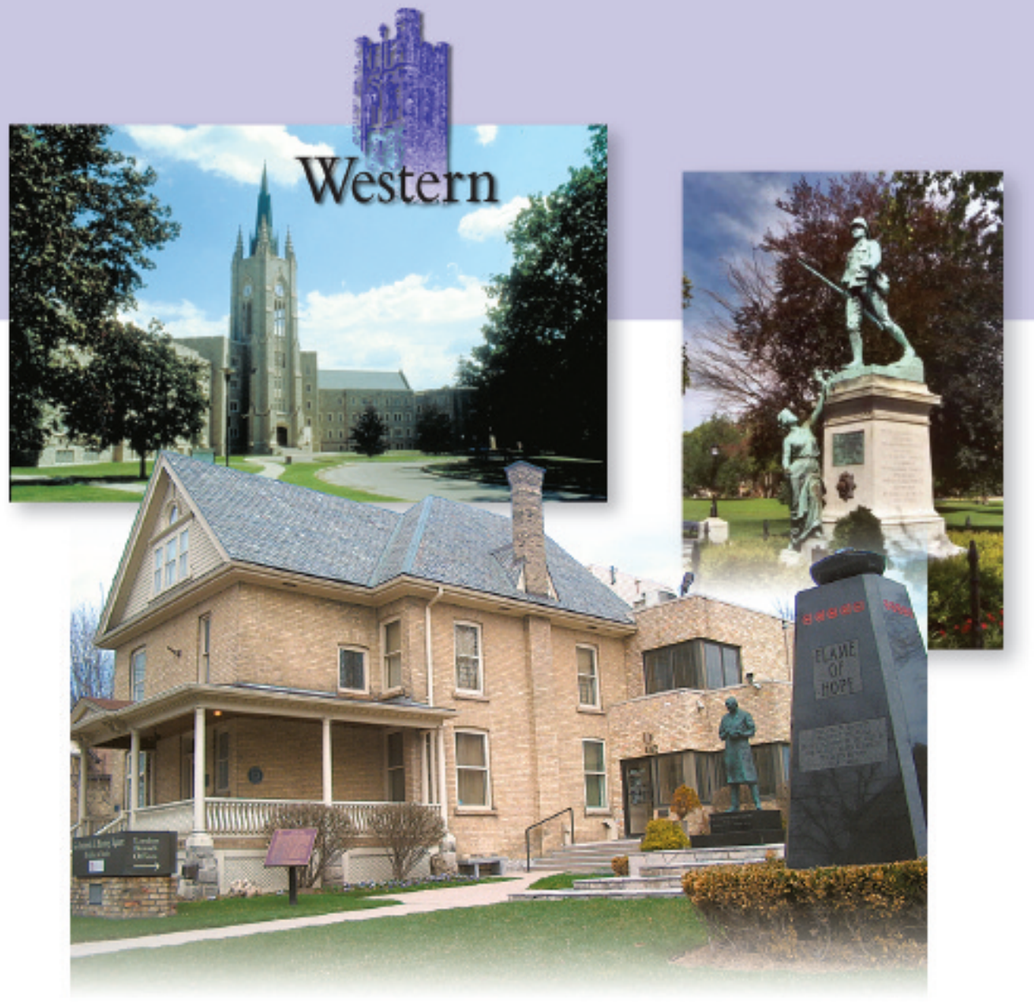

CPEG GCEP CANADIAN PEDIATRIC ENDOCRINE GROUP

2007 Scientific Meeting

London, Ontario — APRIL 19 - 21, 2007

NOTES

Dear Delegates,

It is a great pleasure to welcome you to the first independent meeting of the Canadian Pediatric Endocrine Group / Groupe canadien d'endocrinologie pédiatrique (CPEG/GCEP), held in London, Ontario. Canadian Pediatric Endocrinologists have met regularly before, but within the framework of much larger groups, such as the annual meeting of the Canadian Diabetes Association / Canadian Society of Endocrinology and Metabolism (CDA/CSEM), or of groups with a narrower mandate, such as the Canadian Growth Hormone Advisory Committee.

CPEG was established in 1996 as a section of the CSEM. Its members met at the annual CDA/CSEM Conference and as a satellite group of the annual meeting of the investigators who were involved in the randomized study of growth hormone supplementation to adult height in Turner Syndrome. In 2006 CPEG established itself as an independent association and decided to organize an annual independent meeting, starting in 2007.

Many tasks derived from this historical decision and many individuals have worked tirelessly over the past year to raise funds and to develop an exciting scientific and social program for this first meeting. It is impossible for me to name them all here, but I am very grateful for their enthusiasm and generosity. I am also grateful to our sponsors for their supportive participation.

It has been a privilege to be the president of CPEG for the past two years. I trust you will enjoy both the scientific and social aspects of our first independent meeting. I am also confident that CPEG will continue to thrive in the future!

Guy Van Vliet, M.D.
President, CPEG, 2005-2007

Welcome

As incoming president of CPEG I am delighted to welcome you to London for the first independent meeting of the Canadian Pediatric Endocrine Group / Groupe canadien d'endocrinologie pédiatrique (CPEG/GCEP).

We are very proud of London's vibrant research community which spans both pediatric and adult endocrinology as well as basic science. We hope that the relaxed atmosphere of this meeting promotes collegial interaction and collaboration between fellows in training, clinicians and scientists. I am confident that you will also enjoy the social program which includes a trip to historic Banting House and live entertainment orchestrated by CHWO (Children's Hospital of Western Ontario) Endocrine Section.

Cheril Clarson, FRCP(C)
President, CPEG, 2007-2009

Program Organizing and Scientific Committee

Robert Barnes
Jean-Pierre Chanoine
Cheril Clarson
Jill Hamilton
Guy Van Vliet
Diane Wherrett

Local Organizing and Entertainment Committee

Cheril Clarson
Farid Mahmud
Robby Stein

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Luteoma of Pregnancy:

A rare cause of intraLuteoma of Pregnancy: A rare cause of intra-uterine virilization

Dror Koltin, Rachel Spitzer, Diane Wherrett

Born at 35 wk gestation, the patient presented at four days of age with clitoromegaly. The pregnancy was induced by IVF treatment, and complicated by PIH and GDM.

The patient was born vaginally, with an uneventful perinatal course. On physical examination, normal BP, clitoris – 1.5 cm, ruggated labia with some fusion, gonads – not palpated. Pelvic U/S: midline normal appearing uterus, ovaries – not demonstrated, normal appearing adrenal gland. Blood work: normal electrolytes and glucose, 17(OH)-progesterone, DHEAS, androstenedione –all normal, Karyotype-XX.

On day 6 of life, the patient's mother was met by the team for the first time. The mother had severe acne that started during the pregnancy. She also reported increased hirsuitism, deepening of her voice, and when specifically asked, clitoral enlargement. On pelvic ultrasound, a luteoma of pregnancy was observed. This is a rare benign tumor-like ovarian mass, that can be hormonally active, secreting androgens, and causing virilization of both mother and fetus. To date, less than 200 cases have been described in the literature. The lesion was subsequently removed. The mother is currently well, with all of her symptoms resolved. Because of prolonged exposure to androgens in utero, the baby has a urogenital sinus, and will need surgical repair.

The first case of bariatric surgery in a 14-year-old boy with hypothalamic obesity at the Sainte-Justine Hospital: major weight loss but significant short term complications

Diane Rottembourg[1], Ana-Maria Carceller[2], Diane Vadeboncoeur[3], Pierre Y Garneau[4], Guy Van Vliet[1], Céline Huot[1] and Nathalie Alos[1].

Endocrinology[1], Pediatrics[2] and Psychology[3] Services, Hôpital Sainte-Justine and Department of Surgery4, Hôpital Sacré-Coeur, Université de Montréal.

The outcome of adolescents undergoing bariatric surgery should be reported in detail, as surgery is being contemplated in an increasing number of pediatric cases of morbid obesity. Adolescents with hypothalamic obesity after surgery for craniopharyngioma are particularly challenging. We report our first experience with bariatric surgery in such a patient.

In 1995, this then four-year-old boy underwent surgical removal of a hypothalamic craniopharyngioma. Postoperative pan-hypopituitarism required hormone replacement therapy. Despite educational efforts about diet and physical activity and active participation in a weight reducing clinical trial, a major satiety disorder led to relentless weight gain, with BMI increasing from 20 to 47 kg/m2 over a ten-year period. At 15 years, dyslipidemia, hepatic steatosis and hyperinsulinism without glucose intolerance were documented, and walking perimeter was incompatible with normal school and social life. Under such circumstances, bariatric surgery was contemplated by the family and the indications and contraindications were explored with a surgeon with experience in adults. In January 2006, the patient underwent gastric bypass (biliopancreatic derivation with duodenal switch) successfully. Weight decreased by 40 kg in 10 months (BMI now 33 kg/m2), quality of life and exercise tolerance improved and the diarrhoea due to induced malabsorption was well tolerated. The metabolic disorders improved, no vitamin deficiencies were noted except a low vitamin E level, and bone mineral density remained unchanged one year post-surgery. Nevertheless, severe post-operative co-morbidities occurred: four months post-surgery, an unexplained bradycardia required the implantation of a pace-maker. Twelve months after the bypass, an inflammatory intestinal stenosis at the biliopancreatic distal anastomosis was diagnosed and required several surgeries, multiple transfusions, and a two-month hospitalization. Conclusion: Our clinical experience with this patient underlines the need for fully informed consent, for multidisciplinary pre-operative evaluation and for well-coordinated long-term surgical, medical and psychological follow-up of pediatric bariatric surgery

Biographies

Robert A. Hegele

Dr. Robert Hegele received his MD (Honours) in 1981 from the University of Toronto, with speciality training in Internal Medicine and certification in Endocrinology and Metabolism. After post-doctoral research fellowships at Rockefeller University (New York) and Howard Hughes Medical Institute (Salt Lake City), he joined the University of Toronto. In 1997 he joined Robarts Research Institute, becoming Professor of Medicine and Biochemistry at the University of Western Ontario (London, Canada). He holds the E.S Vinet Canada Research Chair in Human Genetics and the Jacob Wolfe Chair in Functional Genomics at the Schulich School of Medicine, University of Western Ontario.

He directs a tertiary referral lipid clinic. His laboratory studies atherosclerosis and metabolic disorders in Canadian sub-populations, and has discovered the molecular genetic basis of 10 human diseases, including hepatic lipase deficiency, Oji-Cree type 2 diabetes and 3 forms of partial lipodystrophy. He has published more than 270 original scientific articles and 60 reviews and book chapters.

In 2001, he was elected to the American Society for Clinical Investigation and his studies of monogenic insulin resistance were judged a “Top 10 Scientific Advance” by the American Heart Association. He has received the Joe Doupe Award from the Royal College of Physicians and Surgeons (Canada), the Canadian Diabetes Association Top Scientist Award, the Haynes and Moen Award from the Genetic Society of Canada and the American Heart Association’s JM Hoeg Award for Basic Science and Clinical Research.

Cheri L. Deal

Dr. Cheri Deal obtained her B.Sc. in Cell, Molecular and Developmental Biology, and her Ph.D. in Experimental Medicine (funded by the Medical Research Council of Canada) from McGill University, Montreal. She then went on to pursue an M.D. degree at the Université de Montréal, followed by a residency in Pediatrics at both the Montreal Children’s Hospital (McGill) and Ste-Justine Hospital (Université de Montréal). After an additional year in Clinical Endocrinology at the Montreal Children’s Hospital under the direction of Dr. Harvey Guyda, she obtained a Medical Research Council Scholarship to pursue a research fellowship in the laboratory of Dr. Ron Rosenfeld, at Stanford University.

Dr. Deal has been on staff with the Endocrine Service at Ste-Justine Hospital (Centre Hospitalier Universitaire Mère-Enfant) since 1992. She is an Associate Professor (tenured) with the Department of Pediatrics and an Associate Member of the Department of Biochemistry at the Université de Montréal. She is also an Associate Member of the Faculty of Medicine (Division of Experimental Medicine) of McGill University.

An F.R.S.Q. Research Scholar since 1996, the major focus of her laboratory has been the genetic and epigenetic regulation of IGF2, for which she received the LWPES Clinical Scholar award in 1994. Her more recent work includes the contribution of polymorphisms in IGFBP3 and IGFI to normal biological variation, as well as the role of various members of the GH-IGF axis in carcinogenesis, within the context of pre-pubertal obesity, and as a target for clinical intervention in children with Turner Syndrome. She has also contributed to the elucidation of the molecular defects associated with a wide range of rare pediatric endocrine disorders, as well as participated in clinical studies aimed at ameliorating outcomes in endocrine diseases such as congenital hypothyroidism and APECED, and has over 70 publications in peer-reviewed journals.

Constantin Polychronakos

Dr. Constantin Polychronakos is Professor in the Department of Pediatrics at the McGill University Health Centre and Director of the Division of Endocrinology at the Montreal Children's Hospital, with cross-appointments in Experimental Medicine and Human Genetics at McGill. Doctor Polychronakos has a long-standing interest in the molecular genetics of diabetes. He discovered expression of insulin in the thymus as the mechanism through which insulin gene variants affect risk to type 1 diabetes and, more recently, was corresponding author in a report of a genome-wide association study that revealed novel susceptibility loci for type 2 diabetes and served as proof of principle for the use of this approach in all complex diseases. He is currently preparing publication of similar results for type 1 diabetes.

Tsutomu Ogata

Dr. Tsutomu Ogata graduated from Keio University School of Medicine, Tokyo, Japan, where he later took a clinical fellowship in pediatrics. In 1985, he worked as a pediatrician at General Ohta Hospital, and moved on in 1989 as a Research Fellow at the Laboratory of Human Molecular Genetics at the Imperial Cancer Research Fund in London. In 1992, he became the director of Pediatrics at Tokyo Electric Power Company Hospital. Since 2002, he has been the director of the Department of Endocrinology and Metabolism at the National Research Institute for Child Health and Development, Tokyo, Japan. He is also visiting Professor of several universities. His main research interests include growth failure, sex determination and reproduction, congenital malformation syndrome, and epigenetic disorders. He is now acting as both a scientist and clinician.

Steven Chernausek

Dr. Steven Chernausek recently became Director of the Children's Medical Research Institute Diabetes and Metabolic Research Center at the University of Oklahoma Health Sciences Center and is the Edith Kinney Gaylord Professor of Pediatrics at the University of Oklahoma College of Medicine. Prior to that he was Professor of Pediatrics in the University of Cincinnati College of Medicine and Associate Director of Pediatric Endocrinology at Cincinnati Children's Hospital Medical Center. He attended medical school and trained as a resident in pediatrics at the University of Minnesota. He was a pediatric endocrine fellow at the University of North Carolina at Chapel Hill where he was introduced to the somatomedins (IGFs).

Following fellowship, Dr. Chernausek moved to Cincinnati Children's Hospital Medical Center and continued studies of human growth with specific reference to the actions of IGF-I. His resume lists more than 90 publications and includes the first description of IGF resistance due to IGF receptor gene defect and the results of clinical trials of rhIGF-I and rhGH in a variety of disorders. He has served on the editorial boards of Endocrinology and Journal of Clinical Endocrinology and Metabolism and on the Sub-board of Endocrinology for the American Board of Pediatrics.

Ambiguous genitalia: an ambiguous case…

Céline Girardin[1], Céline Huot[1], Françoise Rypens[2], Anne-Marie Houle[3], Pierre Brochu[4], Robert Wilson[5], Maria New5, Guy Van Vliet[1]

Departments of Pediatrics1, Medical Imaging[2], Surgery[3], Pathology[4], Hôpital Sainte-Justine and Université de Montréal, and Adrenal Steroid Disorders Program[5], Mount Sinai School of medicine, New York

A neonate born at 39 weeks to non-consanguineous parents presented with ambiguous genitalia: genital tubercle 2.0 x 1.4 cm, labioscrotal folds partially fused and no palpable gonads. The karyotype was 46 XX. The ultrasound revealed the presence of a uterus while the left gonad was not found; in the right inguinal region, a gonad was seen with structures compatible with either a testicle or an ovotestis. However, on day 3 plasma steroids were (nmol/L): 17-OHP 143.4, T 4.2, ¢4AD 10.3, DHEAS 9900 and congenital adrenal hyperplasia (CAH) was diagnosed. The sex of rearing was female and treatment with hydrocortisone and 5 alpha fludrocortisone was started. At surgery for a right inguinal hernia at age 2 months, a small biopsy of the right gonad revealed ovarian tissue with no evidence of testicular tissue; on the left, a normal infantile ovary was seen; the uterus was normal and there were two Fallopian tubes.

Complete sequencing of *CYP21B* and *CYP11B1*was later performed for the purpose of genetic counseling, but no mutation was found. Under replacement therapy, 17OHP never exceeded 0.7 nmol/L, which also made CAH unlikely. Given the ultrasound aspect of the right gonad, hCG (3000 U/m2) was given IM qod for 3 doses and plasma T was 2.86 nmol/L 3 days after the last dose, confirming the presence of Leydig cells. A tentative diagnosis of true hermaphroditism was then made and hydrocortisone and fludrocortisone were stopped without problems.

In this case, the initial plasma steroid levels were given more weight than the ultrasound aspect of the right gonad and led to an erroneous diagnosis of CAH which was only reconsidered after mutation analysis. Because of the risks of masculinization at puberty and of gonadal tumor formation, the testicular tissue will need to be removed but with preservation of ovarian tissue for fertility.

The Harry Houdini of the Adrenal Gland - Pseudohypoaldosteronism - Type 1

Dr. Teresa Pinto, Dr. Margaret Lawson
Children's Hospital of Eastern Ontario

Introduction: Pseudohypoaldosteronism Type 1 (PHA1) is a rare genetic disease that is characterized by salt wasting, dehydration and failure to thrive in the newborn. Two different forms exist: the recessively inherited form which has a generalized presentation and the dominantly inherited form, which has isolated renal resistance to aldosterone. Recognizing the presenting signs and identifying the key differences between it and congenital adrenal hyperplasia (CAH) are crucial to making the correct diagnosis and instituting appropriate therapy.

Case: S.A. presented to the emergency department at 2 weeks of age with marked failure to thrive, poor feeding and lethargy. He had been born of an uncomplicated pregnancy to Lebanese parents who were first cousins. He was found to have marked hyponatremia (Na 115 mmol/L) and hyperkalemia (K 8.5 mmol/L). A cardiac arrhythmia was noted, likely secondary to the electrolyte imbalance. The patient's hyperkalemia was treated and he was started on hydrocortisone and florinef with the presumptive diagnosis of CAH. Subsequent examination by endocrinology concluded that he was not hyperpigmented and had normal male genitalia. 17-OHP was normal (5.7 nmol/L) and serum aldosterone was >3300 pmol/L. The clinical diagnosis of PHA1 was made. Genetic testing was sent, the results of which will be discussed.

This presentation will review the clinical and biochemical presentation of PHA1. A review of the genetics of the disease will be presented as well as the molecular mechanism of the disease. Finally, treatment and prognosis will be discussed.

David E. Sandberg

Dr. David Sandberg is Associate Professor of Pediatrics and Director of the Division of Child Behavioral Health at the University of Michigan. He recently relocated from the University at Buffalo to Ann Arbor to lead this new division comprising developmental and behavioral pediatrics, pediatric psychology, and adolescent medicine. The division has a broad clinical, research and education portfolio.

Dr. Sandberg received his doctorate from Concordia University in Montreal and completed postdoctoral fellowships at the University of Miami and the College of Physicians & Surgeons of Columbia University/New York State Psychiatric Institute. Dr. Sandberg's research program flows from his clinical service to youths with endocrine disorders and their families. He explored psychosocial aspects of short stature and assumptions underlying growth hormone therapy. His current focus involves the psychological development of children born with disorders of sex development (ie, intersexuality).

Dr. Sandberg serves on the editorial board of the Journal of Pediatric Psychology, and is associate editor of Growth, Genetics and Hormones. He is a member of several national advisory boards of family support and patient advocacy organizations. As an invited participant to the International Consensus Conference on Intersex, he contributed to a recently published consensus statement on clinical management.

David Phillips

Dr. David Phillips is Professor of Endocrine and Metabolic Programming at the University of Southampton, UK, and a consultant physician at Southampton University Hospitals NHS Trust. He is also an adjunct Professor at the Department of Physiology, University of Toronto. He was educated at the Universities of Cambridge and London and is uniquely qualified as an endocrinologist (currently practising endocrinology and diabetes), clinical researcher and epidemiologist. He was appointed to his current post in 1991 and his research programme has focussed on the mechanisms of fetal programming. These studies have involved detailed studies of clinical physiology in human cohorts of men, women and children for whose early growth and development was recorded in detail. Many initial observations concerning the relationship between early growth and programming of major hormonal axes have been made by his group. The current research is directed at elucidating how environmental factors in early life affect the stress response and the way this is linked with adult disease. His work is supported by programme grants from the Medical Research Council and the National Institutes of Health.

Dr. Phillips group collaborates extensively with research groups in Europe (notably Finland, the Dutch Hunger Winter investigators in Holland, and the East Flanders Prospective Twin Study in Belgium), the Caribbean (The Tropical Metabolism Research Unit in Jamaica) and India. He frequently gives invited or plenary lectures at major international conferences including the Endocrine Society, The American Diabetes Association, the Berzelius Symposium, The International Twin Congress and The International Society for Psychoneuroendocrinology.

David Hill

Dr. David Hill is the Scientific Director of the Lawson Health Research Institute, Integrated Vice President, Research for London Health Sciences Centre and St. Joseph's Health Care London, and a Professor in the Departments of Medicine, Pediatrics and Physiology at The University of Western Ontario. Dr. Hill received his B.Sc. from the University of Nottingham and a D.Phil. from the University of Oxford in 1978. Dr. Hill is involved in national health research advocacy as Past Chair of both Research Canada and the National Board of Directors of the Canadian Diabetes Association (CDA).

He has published over 200 research papers and his research centres on the generation of new insulin producing beta cells in the pancreas as a strategy for the reversal of diabetes.

Laurie L. Baggio

Dr. Laurie Baggio received her Ph.D. in the Department of Laboratory Medicine and Pathobiology at the University of Toronto in 2001. She is currently a Research Associate in the laboratory of Dr. Daniel J. Drucker in the Banting and Best Diabetes Centre at the University of Toronto. A major focus of the Drucker laboratory is the study of the peptide hormone glucagon-like peptide-1 (GLP-1). GLP-1 is of clinical relevance as it lowers elevated blood glucose levels in both type I and type II diabetic patients and stimulates the growth and development of insulin-producing pancreatic ,-cells. Consequently, there has been considerable interest in the use of GLP-1 and related analogs as therapeutic agents for the treatment of diabetes. Dr. Baggio's research is centered on examining the physiologic effects of GLP-1 and related molecules on blood glucose regulation, cardiovascular function and other physiological parameters.

Katherine Morrison

Dr. Katherine Morrison is a Pediatric endocrinologist and Assistant Professor at McMaster University. Her current research interests include obesity and cardiovascular risk factors in children with particular attention to: their early life determinants, the measurement of early atherosclerosis in children and optimal treatment strategies for children with obesity related health consequences. She is active clinically in the Pediatric Lipid and Obesity at Risk Clinics at McMaster Children's Hospital. Dr. Morrison is supported in her work by the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research.

Learning Objectives

At the end of the program participants should be able to:

- Understand current state of knowledge of genetics of lipid disorders and diabetes
- Identify risks and benefits of growth hormone therapy in idiopathic short stature and small for gestational age children
- Link fetal programming to future development of vascular and metabolic disease, including diabetes
- Describe clinical practice guidelines for prevention and treatment of

Coma with Diffuse White Matter Hemorrhages in Diabetic Ketoacidosis

Farid H. Mahmud, MD[1], David A. Ramsay, MD[2], Simon S. Levin, MD[3], Ram N. Singh[4], MBBS, Trevor Kotylak, MD[5] and Douglas D. Fraser, MD, PhD[4].

[1]Paediatric Endocrinology, [2]Department of Pathology, [3]Paediatric Neurology [4]Paediatric Critical Care Medicine, [5]Department of Radiology, Children's Hospital of Western Ontario, London, Ontario, Canada.

Background: Since the initial descriptions linking cerebral edema (CE) with DKA, numerous published reports coupled with advances in neuroimaging have refined our understanding that the neurologic complications of DKA should be described using the broader term "intracerebral complications". Other intracerebral complications that occur with DKA include hemorrhage and arterial and venous thrombus formation, which have been estimated at 10% of cases based on clinical series.

Objective: Case Series: We report two adolescent patients with DKA, presenting with coma and diffuse white matter hemorrhages in the absence of either CE or cerebrovascular accident (CVA). These two cases illustrate a novel clinical and neuropathologic description of diffuse white matter hemorrhages in DKA.

Results: Two atypical cases of new onset DKA with coma and diffuse white matter hemorrhages in the absence of radiologic or pathologic evidence of CE or CVA. Both cases were profoundly acidotic and had greatly elevated serum ketones. One patient died and a post mortem examination of the brain was performed. The other patient underwent a diagnostic brain biopsy and experienced a protracted recovery with lingering neuropsychological deficits. These cases describe acute neurologic dysfunction with neuropathologic evidence of diffuse white matter injury which we propose is secondary to cytotoxic factors related to metabolic abnormalities and the systemic inflammatory response.

Conclusion: These cases provide further clinical and neuropathologic insight into the cerebral dysfunction present in children with severe DKA.

Prevalence of asymptomatic vertebral fractures in a high-risk pediatric population

Meranda Nakhla, Rosie Scuccimarri, Michel Azouz, Nazih Shenouda, Ciaran Duffy, Karen Duffy, Gaelle Chedeville, Sarah Campillo, Celia Rodd

Departments of Pediatrics and Radiology, McGill University and University of Ottawa, Canada

We set out to determine the prevalence and risk factors of asymptomatic vertebral fractures in our cohort of children with chronic inflammatory rheumatologic disorders. After completing a questionnaire assessing calcium and vitamin D intake, family bone health, and other risk factors, subjects recruited to the study underwent standard thoracic and lumbar spine radiographs and lumbar spine dual-energy x-ray absorptiometry (DXA).Charts were reviewed for rheumatologic diagnosis, duration of illness and cumulative glucocorticoid and methotrexate exposure. Spine radiographs were reviewed by a pediatric bone radiologist for Genant scoring.

Of the104 children approached, 94 agreed to participate (90%). Their mean age at diagnosis was 7.02 y (SD 4.49) and duration of illness was 5.0 y (SD 3.9) at the time of enrolment. There were 24 boys and 70 girls. Eight boys and 8 girls were noted to have fractures, with an average age of 7.0 y (SD 3.9). Five had a diagnosis of JIA (1 OligoE, 2 Poly, 2 Psoriatic/Poly course and 5 Systemic), 4 had connective tissue diseases, and 2 had vasculitis. These 16 children had a total of 34 fractures, on average 2 per child, of which 80% had a Genant score of 1 (mild) and the remainder was moderate. Upper thoracic region fractures (T5-8) accounted for 54% of all fractures, while those in the lumbar region accounted for 24%. Over half of the fractures were asymptomatic (56%), and 68% were not apparently associated with trauma.

In terms of risk factors, average calcium and vitamin D intake satisfied RDI/AI, and those with and without vertebral fractures did not differ in dietary intake, age at diagnosis, cumulative methotrexate dose, or bone mineral density. They did differ in long-term glucocorticoid exposure, with a cumulative prednisone dose of 404 vs.143 mg/kg, respectively ($p< 0.03$). To better examine the role of risk factors, multivariate Poisson regression was used to relate fracture number and age, duration of disease, gender, bone density, and cumulative exposure to glucocorticoids and methotrexate (mg/kg). Positive relationships were identified for the following predictors: male gender (OR 4.0, $p<0.001$), duration of disease (each year increasing fracture risk by 13%, $p< 0.03$), and cumulative glucocorticoid dose (each 100 mg/kg prednisone associated with a 13% increase in fracture risk, $p=0.003$). The relationship between the same predictors and bone mineral density was examined by multivariate linear regression, with only cumulative steroid dose associated with reduced bone mass ($p=0.005$).

THURSDAY, APRIL 19, 2007

17:00-19:00	Registration
19:00-21:00	Welcome Reception / Exhibits open

FRIDAY, APRIL 20, 2007

07:00-8.30	Breakfast
08:00	Exhibits open

THEME: **GENETICS**
MODERATOR: **DR. CHERIL CLARSON**

09:00	Welcome and Fellowship Announcements – Dr. Guy Van Vliet
09:10	Dr. Robert Hegele, London, Canada *Genetic disorders of lipid and lipoprotein metabolism*
10:00	Nutrition Break / Exhibits
10:20	Dr. Cheri Deal, Montreal, Canada *APECED as a model for evaluating genetic susceptibility of diabetes*
11:10	Dr. Constantin Polychronakos, Montreal, Canada Genetics of Diabetes
12:00 – 13:00	Lunch / Exhibits

THEME: GROWTH
MODERATOR: DR. ROBERT STEIN

13:00	Serono Canada sponsored speaker: Dr Tom Ogata, Tokyo, Japan *Idiopathic Short Stature: A Shrinking Black Box*
13:50	Dr. Steven Chernausek, Cincinnati, USA *Treatment of the Short Child Born SGA*
14:40	Nutrition Break / Exhibits
15:00	Dr. David Sandberg, Ann Arbor, USA *Growth Hormone Therapy for Short Stature: Added Inches Versus Quality of Life as the Measure of Treatment Success*
16:00 – 18:00	CPEG Annual General Meeting
18:30	Buses leave the Hilton for Banting House ***(sponsored by Novo-Nordisk)***
19.30	Buses leave Banting House for the Hilton
20:00	Dinner at the Hilton Entertainment

SATURDAY, APRIL 21, 2007

07:00 – 08:30	Breakfast
08:00	Exhibits open

THEME: FETAL PROGRAMMING
MODERATOR: DR. FARID MAHMUD

09:00	Dr. David Phillips, Southampton, UK *Fetal programming of vascular and metabolic disease: the neuroendocrine connection*
09:50	Dr. David Hill, London, Canada *Programming of the Endocrine Pancreas*
10:40	Nutrition Break / Exhibits

Insulin-Like Growth Factor-Binding Protein-1 (IGFBP-1): Correlation between Serum Levels and Factors of the Metabolic Syndrome in Short Children Born Small for Gestational Age (SGA)

D.C.M. van der Kaay[1,2]; A.C.S. Hokken-Koelega[1]; C.L. Deal[2]

[1] Department of Paediatrics, Division of Endocrinology, Erasmus University Medical Centre / Sophia Children's Hospital and Dutch Growth Foundation, Rotterdam, The Netherlands

[2] Endocrine Service, Sainte-Justine Hospital Research Center, University of Montreal, Montreal, Quebec, Canada

Background

Being born SGA has long-term consequences for postnatal growth and development. Epidemiological studies showed that 'the metabolic syndrome' (a combination of insulin resistance, hypertension, dyslipidemia and obesity) is associated with low birth weight. IGFBP-1 is the only acute regulator of insulin-like growth factor I (IGF-1) bioavailability, and production of IGFBP-1 in the liver is rapidly suppressed by insulin, thereby forming a link between glucose metabolism and the IGF axis. Reduced IGFBP-1 levels are considered to reflect insulin resistance and cardiovascular risk in adults, women with polycystic ovary syndrome and prepubertal obese children.

Objectives

To determine serum IGFBP-1 levels within a large SGA cohort and evaluate the associations between serum IGFBP-1 levels and components of the metabolic syndrome.

Results

Results are expressed as median (range).

	Prepubertal		Pubertal	
	Girls (n=24)	Boys (n=29)	Girls (n=24)	Boys (n=19)
Gestational age (weeks)	39 (35.6; 40)	38 (35.5; 39.8)	38 (36; 40)	38 (36.8; 39.8)
Birth length (SDS)	-2.1 (-2.8; -1.6)	-2.3 (-3.2; -1.8)	-2.8 (-3.3; -2.1)	-2.5 (-3.3; -2.1)
Birth weight (SDS)	-1.8 (-2.3; -1.3)	-1.8 (-2.8; -0.8)	-2.1 (-2.6; -1.4)	-1.9 (-2.3; -1.6)
Current age (years)	10.1 (9.7; 11.0)	10.1 (9.1; 11.2)	12.1 (11.2; 12.7)[b]	13.0 (12.6; 14.2)[a,b]
Current height (SDS)	-3.0 (-3.6; -2.8)	-2.9 (-3.2; -2.6)	-2.8 (-3.4; -2.4)	-2.7 (-3.5; -2.3)
IGFBP-1 (ng/ml)	**107 (97; 126)**	**134 (107; 175)[a]**	**58.5 (46.5; 91.3)[b]**	**85.0 (60.8; 108.8)[b]**
IGF-1 SDS	-1.5 (-2.3; -1.0)	-1.6 (-2.3; -0.9)	-0.7 (-1.6; 0.4)[b]	-1.0 (-2.0; 0.2)
IGFBP-3 SDS	-1.2 (-1.6; -0.8)	-1.4 (-1.6; -0.6)	-0.9 (-1.5; -0.6)	-1.0 (-1.5; -0.6)
Insulin (pmol/l)	16 (14; 24)	21.5 (16.8; 28.5)[a]	39 (22; 49)[b]	67 (43; 105)[a,b]
Systolic bloodpressure (SBP) SDS	1.1 (0.7; 1.5)	1.3 (0.5; 2.0)	1.6 (0.9; 3.0)[b]	1.1 (0.7; 1.7)
Diastolic bloodpressure SDS	0.1 (-0.2; 0.6)	0.3 (-0.4; 1.0)	0.3 (-0.1; 1.1)	-0.02 (-0.3; 0.5)[a]
Fat SDS	-0.9 (-1.4; -0.3)	-1.7 (-2.6; -0.6)[a]	-0.4 (-1.3; 0.07)	-0.4 (-1.4; 0.5)[b]
Lean SDS	-0.8 (-1.6; -0.4)	-1.2 (-2.2; -0.8)	-1.0 (-1.3; -0.5)	-0.6 (-1.4; -0.1)[b]
Total cholesterol levels (mmol/l) (N: 2.8-5.4)	tbd	tbd	3.9 (3.8; 4.6)	4.2 (3.7; 4.6)
HDL-cholesterol levels (mmol/l) (N: 0.8-1.9)	tbd	tbd	1.3 (1.1; 1.5)	1.5 (1.4; 1.7)[a]
LDL-cholesterol levels (mmol/l) (N: 1.3-3.4)	tbd	tbd	2.2 (1.9; 2.5)	2.4 (1.7; 2.8)[a]
Triglyceride levels (mmol/l) (N: 0.3-1.1)	tbd	tbd	0.9 (0.7; 1.2)	0.6 (0.5; 0.7)

[a] girls vs boys: P values 0.04 - < 0.001 [b] prepubertal vs pubertal: P values 0.03 - < 0.001 tbp: to be determined

In prepubertal children, IGFBP-1 levels were significantly inversely correlated with fasting insulin levels, IGF-1 SDS, lean SDS, fat SDS and sex. After adjusting for sex, IGFBP-1 levels were significantly inversely correlated with fasting insulin levels and IGF-1 in boys.
In pubertal children, IGFBP-1 levels were significantly inversely correlated with fasting insulin levels, IGF-1 SDS, lean SDS, triglyceride levels, SBP SDS and sex. After adjusting for sex, IGFBP-1 levels were significantly inversely correlated with fasting insulin levels, IGF-1 SDS and lean SDS in boys and with SBP SDS in girls. All P-values were between 0.05 and < 0.001.

Conclusions

IGFBP-1 levels were significantly lower in pubertal children, compared to prepubertal children born SGA, likely due to a decreased insulin sensitivity associated with puberty. Even in lean SGA children, whereas fat SDS was significantly lower than zero in all children except for pubertal girls (P=0.09), the known inverse correlation between IGFBP-1 levels and indices of body-fat is preserved. We hypothesize that this decrease in IGFBP-1levels may contribute to the development of the metabolic syndrome.

Simultaneous Epimutations at Both 11p15.5 Imprinted Domains in Absence of UPD in the Affected Twin of a Female Monozygotic Pair Discordant for Beckwith-Wiedemann Syndrome

Catherine E. Hamelin[1,2], Jean Paquette[2], Chris Wake[3], Patricia Crock[3], Cheri Deal[1,2,4].

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Beckwith-Wiedemann syndrome (BWS) is a congenital condition involving pre- and post-natal macrosomia, macroglossia, anterior abdominal wall defects and predisposition to embryonal neoplasia. Although genetic abnormalities such as paternal uniparental disomy (UPD) and rare maternal mutations in *CDKN1C* have been described in sporadic cases, they are more frequently the consequence of aberrant methylation at the 11p15.5 differentially-methylated regions *H19*DMR and KvDMR1. Disruption of normal imprinting profile at either of these loci is associated with biallelic *IGF2* expression, the *sine qua non* of overgrowth in BWS, whereas abnormal methylation at KvDMR1 causes loss of *CDKN1C* (cyclin-dependant kinase inhibitor) activity, known to be associated with omphalocele. The incidence of female monozygotic twins discordant for BWS is increased and, imprinting defects at KvDMR1 have been reported. We have investigated female monozygotic twins discordant for BWS; physical findings in the affected twin included a 28% birth weight differential, omphalocele, ear lobe creases, macroglossia, visceromegaly and hyperinsulinemic hypoglycemia. Monozygosity was confirmed (average certainty=99.99%). No evidence of 11p15.5 chromosomal rearrangements, UPD and *CDKN1C* mutations was observed. Using bisulfite sequencing, we found hypermethylation at *H19*DMR in the affected twin only (93% (14/15) of methylated clones compared to 42% (5/12) in the non-affected twin (p=0.0085)). Her methylation profile at KvDMR1 showed almost complete hypomethylation at both CpGs investigated with methyl-sensitive restriction enzymes. The non-affected twin presented a methylation profile intermediate to that of her twin and her mother. In conclusion, this is the first case where an epigenetic alteration at *H19*DMR is found in female monozygotic twins discordant for BWS and, where a KvDMR1 defect coexists in the absence of UPD. This is similar to the more widespread 11p15.5 defects seen in sporadic singleton BWS, and may be due to defects in methylation maintenance enzyme(s). *H19*DMR hypermethylation and KvDMR1 hypomethylation are relevant for long term follow-up in BWS subjects since *IGF2* and *CDKN1C*/*KCNQ1OT1* LOI have been associated with higher risk of tumorogenesis.

THEME:	**NEW ADVANCES IN "DIABESITY"**
11:00	Dr. Laurie Baggio, Toronto, Canada *Targeting the Incretin Axis for the Treatment of Type 2 Diabetes*
11:50	Dr. Kathy Morrison , Hamilton, Canada *Canadian Clinical Practice Guidelines for the Prevention and Treatment of Obesity: The Childhood Perspective*
12:40 – 14:00	Lunch / Exhibits
THEME: **MODERATOR:**	**FELLOW PRESENTATIONS / FREE COMMUNICATIONS** **DR DIANNE WHERRETT**
14:00 – 15:15	Presentations
15:15	Nutrition Break
15:30 – 17:00	Presentations
17:00	Presentation of Dr. John Bailey Resident Research Award and Concluding Remarks – Dr. Cheril Clarson

Abstracts

Pseudodominant inheritance of congenital thyroid dyshormonogenesis from *TPO* mutations in a non-consanguineous family: clinical, genetic and *in silico* studies.

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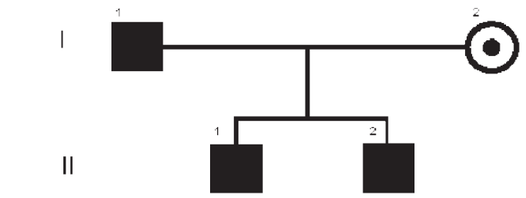
Most cases of congenital thyroid dyshormonogenesis (CTDH), which follows a recessive mode of inheritance, are due to mutations in the *thyroid peroxidase* gene (*TPO*). We report the genetic mechanism underlying the apparently dominant inheritance of CTDH in a non-consanguineous family of French Canadian origine. Two brothers identified by newborn TSH screening had severe hypothyroidism and a large thyroid gland with increased ^{99m}Tc uptake. The mother was clinically and biochemically euthyroid, but the father had also been diagnosed with CTHD as a newborn. The biochemical and genetic information is shown on the pedigree. Because of the dominant transmission of hypothyroidism with a gland *in situ*, we first sequenced the coding exons of the *PAX8* gene directly from genomic DNA, but only polymorphisms were found. We next hypothesized that the euthyroid mother could be a carrier of a *TPO* mutation. Indeed, sequencing analysis of the TPO gene revealed, that both probands had inherited a deletion from their mother (nt 1496 del C). From their father, one brother had inherited a missense mutation (Q660E) and the other an insertion (nt 1955 ins T).

In conclusion, we report the first pedigree presenting with pseudodominant CTDH due to compound heterozygous *TPO* mutations. Although CTDH generally follows a recessive mode of inheritance, the high frequency of carriers of *TPO* mutations in the general population may lead to pseudodominant inheritance. Wild-type and Q660E TPO are currently modelized *in silico*.*(232 words)*



Screening:				
age	3 days	2 days	2 days	
TSH (mU/L)	646	232	453	
TT4 (nmol/L)	5	50	23	
Diagnosis				
age	33 days	6 days	3 days	24 years
TSH (mU/L)	873	417.3	556.8	1.18
TT4 (nmol/L)	10			
FT4 (pmol/L)		11.1	3.1	9.66
Tg (µg/L)		1264	1246.4	
TPO mutations:	A / B	A/C	B / C	C / WT

WT: wild-type
A : nt 1948 C>G (Q660E)
B : nt 1955 ins T
C : nt 1496 del C

Vitamin D- dependent Rickets, type II: A novel homozygous mutation in exon 10 of the vitamin D receptor gene and response to thiazide diuretics."

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The steroid hormone 1, 25-dihydroxyvitamin D [1, 25(OH)2D] regulates a number of biological processes including calcium homeostasis, cellular differentiation, and immune function. The activity of 1, 25(OH)2D is mediated by the vitamin D receptor (VDR), a member of the steroid-thyroid-retinoid receptor superfamily of ligand activated transcription factors. Vitamin D-dependent rickets type II, is a rare recessive genetic disorder caused by inactivating mutations in the VDR. Patients with this disorder present with early-onset rickets, hypocalcemia, secondary hyperparathyroidism and short stature. Patients have significantly elevated serum levels of 1, 25(OH)2D indicative of their resistance to the hormone. In addition, some patients exhibit total body alopecia (50% of cases) together with dermal cysts. We present a case of a 5-year old girl of Filipino descent, with consanguineous parents, who presented with failure to thrive and radiographic evidence of rickets. The laboratory investigations showed a low total calcium level, low phosphate, elevated alkaline phosphatase, elevated PTH, normal 25-hydroxyvitamin D and elevated 1,25(OH)2D. She also presented with alopecia on the physical exam, which has not been reported on patients with mutations that disrupt the ligand binding or coactivator binding domains. *VDR* sequencing demonstrated a homozygous mutation in the last codon (amino acid 341) of exon 10 that changes CAG (Proline) to TAG (Stop) resulting in interruption of the ligand binding domain. This mutation has not been reported previously. Minimal clinical and biochemical responses to calcium supplementation and pharmacologic doses of 1, 25(OH)2D3 were seen and hypophosphatemia and hypercalciuria were prominent. With the introduction of thiazide diuretics to improve renal retention of calcium, biochemical normalization of serum calcium, phosphate, PTH and near normalization of alkaline phosphatase were seen. This was accompanied by significant radiographic improvement and an increased growth velocity of 7.6 cm/year. These observations suggest an alternative treatment regimen for VDDRII.