



CANADIAN PEDIATRIC ENDOCRINE GROUP

2009

Scientific Meeting

Thursday - Saturday

February 26-28, 2009

Fairmont Château Laurier
Ottawa, ON

**CPEG
GCEP**

Canadian Pediatric Endocrine Group
Groupe Canadien d'Endocrinologie Pédiatrique

Welcome

Dear Delegates,

I am delighted to welcome delegates and speakers to the 2009 Scientific Meeting of the Canadian Pediatric Endocrine Group / Groupe Canadien d'Endocrinologie Pédiatrique (CPEG/GCEP) in Ottawa. This meeting is a unique opportunity for our endocrine community of clinicians, nurses and scientists to advance knowledge and network with colleagues.

I would like to thank all those who have assisted in organizing this meeting including the organizing and scientific committee, local planning group and our sponsors. I am confident that you will enjoy both the scientific and social components of the meeting. It has been a privilege to be president of CPEG for the last two years and I wish the group continued success.

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

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Program Organizing and Scientific Committee

Alex Ahmet
Cheril Clarson
Josephine Ho

Robert Barnes
Brenda Fraser
Zubin Punthakee
Diane Wherrett

Jean-Pierre Chanoine
Sarah Lawrence
Wendy Schwarz

Credits

This event is an Accredited Group Learning Activity as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada and approved by the Canadian Paediatric Society. (11.75 hours)

Learning Objectives

Theme I: Bone

How Kids' Bones Get Stronger

Dr. Frank Rauch, Montreal, QC

At the end of the session the participants will have reviewed:

1. the relationship between bone mass and bone strength
2. the mechanical function of bone
3. factors that determine the increase in bone strength during growth

Is a New Recommendation in Order for Vitamin D Supplementation in Newborn Infants?

Dr. Hope Weiler, Montreal, QC

At the end of this session, participants will have reviewed:

1. the current dietary recommendations for vitamin D in infancy
2. canadian data regarding breastfeeding rates and vitamin D supplement usage and vitamin D status
3. emerging new data on how vitamin D intake translates to vitamin D status in young infants

Bone Development in Glucocorticoid-Treated Children with Chronic Illness: Results of the Canadian Steroid-Associated Osteoporosis in the Pediatric Population (STOPP) Research Program

Dr. Leanne Ward, on behalf of the STOPP Consortium, Ottawa, ON

1. to review recent data emerging from the STOPP study as it relates to spine health in the setting of pediatric chronic illness
2. to discuss the timing, pattern and frequency of prevalent and incident vertebral fractures among glucocorticoid-treated children with chronic illness
3. to highlight the relationships between vertebral fractures and relevant clinical indices such as back pain and bone mineral density in children

Theme III: Beta Cell*Preventing Loss of Beta Cells in Type 1 Diabetes – The TrialNet Studies*

Dr. Diane Wherrett, Toronto, ON

1. to understand the major steps in the pathogenesis and prediction of type 1 diabetes
2. to review current trials in prevention of diabetes and intervention to prevent further loss of beta cells after diagnosis and the challenges faced in these trials

Preserving Beta Cell Function

Dr. Robert Sreaton, Ottawa, ON

At the end of this session, participants will have reviewed:

1. the application of functional genomics to identify novel proteins that regulate beta cell function
2. a novel cell signaling pathway involved in glucose-dependent gene regulation
3. the role of Lkb1 in the control of insulin secretion and glucose homeostasis in adult mice

Hyperinsulinism & PET Scanning

Dr. Charles Stanley, Philadelphia, PA

1. to review the causes of hyperinsulinism in neonates and infants
2. to discuss the use of PET scanning in hyperinsulinism

Theme IV: Endocrinology*Thyroid Cancers in Children*

Dr. Gary Francis, Richmond, VA

Following this presentation, the attendee will be able to:

1. list two major changes between the current treatment guidelines in management of thyroid cancer and the anticipated guidelines for 2009.
2. list one reason why we are less enthusiastic about the use of radioactive iodine in low-risk patients.
3. define and use a formula to calculate radioactive iodine doses in children.
4. locate a table containing recommendations for age of prophylactic thyroidectomy in children with a variety of RET mutations.
5. list the two most common symptoms of MEN II during the first year of life.

Female Fertility Preservation

Dr. Seang Lin Tan, Montreal, QC

1. to discuss the advances in fertility options for patients with endocrine disorders, with a particular focus on ovarian tissue and fertilized oocyte preservation

Theme V: Obesity*DEBATE: Obesity Nature vs. Nurture**Robert Lustig, San Francisco, CA*

At the end of this session, participants will have reviewed:

1. the specific genetic, epigenetic, developmental, and environmental inputs to the current obesity epidemic
2. the scope and magnitude by which of these inputs are increasing pediatric obesity
3. the degree to which behavioral interventions can counteract these natural phenomena

*DEBATE: Obesity Nature vs. Nurture**Mark Tremblay, Ottawa, ON*

At the end of this session, participants will have reviewed:

1. the macro- and micro-environmental changes that have occurred over the past few generations and the plausibility that these changes precipitate obesogenic behaviours
2. the research evidence that changes in "nurture" are important, and perhaps dominant, in explaining the pandemic of obesity
3. evidence that the "nature vs nurture" dichotomy is biologically and environmental flawed

*Treatment of Hyperlipidemia in Children**Dr. Brian McCrindle, Toronto, ON*

At the end of this session, participants will have reviewed:

1. the relationship between obesity, lipid abnormalities and cardiovascular disease in children
2. updated guidelines for screening and evaluation
3. the role and impact of lifestyle management
4. updated guidelines for decision-making regarding medications

*Hypothalamic Obesity**Dr. Jill Hamilton, Toronto, ON*

1. to discuss the mechanisms and treatment options for hypothalamic obesity in children and adolescents.

*National Surveillance for Type 2 Diabetes in Canadian Children**Dr. Shazhan Amed, Vancouver, BC*

At the end of this session, participants will have reviewed:

1. the epidemiology of type 2 diabetes in Canadian children < 18 years of age
2. the demographic features, clinical features and existing co-morbidity in Canadian children with newly diagnosed type 2 diabetes
3. treatment practices for pediatric type 2 diabetes by Canadian physicians
4. significant differences between Caucasian and non-Caucasian children and youth with type 2 diabetes

*Ghrelin in Growth & Development**Dr. Jean-Pierre Chanoine, Vancouver, BC*

At the end of this session, participants will have reviewed:

1. the characteristics of acylated and desacylated ghrelin
2. the ontogeny of ghrelin in the perinatal period
3. novel aspects of ghrelin physiology in the neonate

*Identifying Dysglycemia in the Obese Child or Adolescent**Dr. Katherine Morrison, Hamilton, ON*

1. to discuss the epidemiology of glucose intolerance/type 2 diabetes in the pediatric population and the relative pros and cons of screening strategies.

Biographies

Dr. Frank Rauch

Dr. Rauch received his medical degree from the Technical University in Munich (Germany) and trained as a pediatrician at the Children's Hospital of Cologne University, Germany. Following a research fellowship at the Shriners Hospital for Children in Montreal (1997 to 1999), he accepted a position as staff member at that institution. Since that time, his research has focused on children with bone fragility disorders, in particular osteogenesis imperfecta. At present, Dr. Rauch is Associate Professor of Pediatrics at McGill University and Director of Clinical Laboratories at the Shriners Hospital for Children. Dr. Rauch is also Editor of the Journal of Musculoskeletal and Neuronal Interactions. He has published about 115 peer-reviewed publications as well as 25 book chapters and proceedings contributions.

Dr. Hope Weiler

Dr. Hope Weiler is an Associate Professor and Registered Dietitian in the School of Dietetics and Human Nutrition in the Faculty of Agricultural and Environmental Sciences at McGill University. Her educational background includes an undergraduate degree in Applied Human Nutrition from the University of Guelph followed by a Practicum in Clinical Nutrition jointly offered through Chedoke-McMaster Hospitals and McMaster University plus a Doctorate in Medical Sciences, Cell Biology and Metabolism at McMaster University. Dr. Weiler is currently in receipt of a Canada Research Chair at McGill University where her research focus is lipid nutrients, including vitamin D, and their role in bone mineral acquisition in children and maintenance in adulthood.

To date, Dr. Weiler has authored 60 peer-reviewed publications, and secured over 2 million in research funding. Dr. Weiler has served numerous societies, organizations and areas of nutrition. She is incoming director of the Mary Emily Clinical Nutrition Unit of McGill and is a member of the editorial board for Nutrition Research.

Dr. Leanne Ward

Dr. Leanne Ward is an Associate Professor of Pediatrics in the Faculties of Medicine and Surgery at the University of Ottawa where she is the Director of the Pediatric Bone Health Clinical and Research Programs. She has been the recipient of a number of awards for her work in pediatric bone health, including the Canadian Child Health Clinician Scientist Career Development Award (2004), the Canadian Institutes for Health Research New Investigator Award (2004) and the Canadian Child Health Clinician Scientist Career Enhancement Award (2007).

Dr. Ward's research interests span a range of topics in the burgeoning field of pediatric bone health. Her primary focus is on the skeletal effects of chronic childhood illnesses, including children with Crohn's disease for which she holds funding through the Crohn's and Colitis Foundation of America. She is the principal investigator of the "STOPP" research program (STeroid-induced Osteoporosis in the Pediatric Population), a pan-Canadian project funded by the Canadian Institutes of Health Research to evaluate the effect of steroids on bone health in children with leukemia, rheumatic conditions and nephrotic syndrome. The STOPP Consortium, comprised of investigators from 12 tertiary care children's hospitals coast-to-coast, have recently had a manuscript accepted to the Journal of Bone and Mineral Research showing a high vertebral fracture rate in children with leukemia at diagnosis and associated risk factors. She has also maintained an interest in childhood rickets, with a recent publication in Nature Genetics describing a novel form of hypophosphatemic rickets and its pathogenetic basis (Loss of DMP1/DMP1 Causes Rickets and Osteomalacia and Identifies a Role for Osteocytes in Mineral Metabolism Nature Genetics 2006 Nov; 38(11):1310-5), and a publication in the Canadian Medical Association Journal in 2007, describing the incidence of vitamin D deficiency rickets among children living in Canada.

Dr. Dianne Wherrett

Diane Wherrett did her undergraduate studies and medical school at Queen's University in Kingston, Ontario, graduating in 1987. She completed a year of training in internal medicine at the University of Toronto - Wellesley Hospital before realizing that her passion was for pediatrics. She completed her pediatric residency and clinical endocrinology training at the Hospital for Sick Children. She then moved to Stanford University as a Pediatric Scientist Development Program fellow, studying the immunology of type 1 diabetes in the laboratory of Hugh McDavitt. She joined the faculty in the Division of Endocrinology at the Hospital for Sick Children in 1995.

Major areas of clinical focus are care of children with type 1 diabetes and with disorders of sex development. She is a co-author of the section on Care of Children and Adolescents with Type 1 Diabetes in the recently published Canadian Diabetes Association Clinical Practice Guidelines (2008). Her major research effort is as a member of the steering committee of the NIH-sponsored type 1 diabetes prevention study group, TrialNet and PI for the Canadian Clinical Centre. She is also chairing the GAD vaccine in new-onset patients intervention study. She is involved in a study of clinical and psychological outcome in children with disorders of sex development. She recently became director of the endocrinology fellowship at the Hospital for Sick Children.

Dr. Robert Screaton

Dr. Screaton is a Scientist at the Children's Hospital of Eastern Ontario and holds the Canada Research Chair Tier II in Apoptotic Signaling. He is an Assistant Professor in the Department of Pediatrics and is cross-appointed to the Department of Biochemistry, Microbiology and Immunology at the University of Ottawa. He received his undergraduate and graduate training at McGill University in Montreal, Canada (1998). During his post-doctoral work at the Salk Institute in San Diego, USA, he uncovered the signaling components that govern the activity of the cAMP- and calcium-responsive transcriptional coactivators, Transducers of Regulated CREB Activity (TORCs). His current work involves expanding functional genomics approaches into kinomics in order to identify and characterize novel signaling mechanisms relevant to beta cell function and survival. His program involves numerous international collaborations and has fueled the genome-wide cell-based screening initiatives currently employed at CHEO. Dr. Screaton is the recipient of numerous awards, most recently the Ontario Early Researcher Award.

Dr. Charles Stanley

Charles A. Stanley, MD is Professor of Pediatrics at the University of Pennsylvania School of Medicine and a member of the Division of Endocrinology at the Children's Hospital of Philadelphia. He received his BA from Harvard College and MD from the University of Virginia School of Medicine. He has been at CHOP since 1970 as a pediatric resident, fellow in metabolism and endocrinology, and member of the faculty. He served as Chief of the Endocrinology Division from 2001-2008 and is Medical Director of the Core Laboratory for the CTSA (formerly GCRC). His research has focused on disorders of hypoglycemia in children, including genetic defects of fatty acid oxidation and the hepatic glycogenoses. One of his long-standing research interests has been the disorders of hyperinsulinemic hypoglycemia and their genetic basis, diagnosis, and treatment. Recent work includes the description of mutations causing the hyperinsulinism-hyperammonemia syndrome and other forms of hyperinsulinism, mechanisms of amino acid regulation of insulin secretion in mouse models of hyperinsulinism, and the use of ¹⁸F-DOPA for imaging congenital focal hyperinsulinism lesions. This year, Dr. Stanley is serving as president of the Lawson Wilkins Pediatric Endocrine Society.

Dr. Gary Francis

Gary L. Francis, MD, PhD is Professor of Pediatrics and Chair of the Division of Pediatric Endocrinology and Metabolism at Virginia Commonwealth University, Medical College of Virginia in Richmond, VA. Dr. Francis received his MD and PhD in Biochemistry from the University of Florida and took his training in Pediatrics at Yale University and the University of Florida followed by Fellowship training in Pediatric Endocrinology at the University of Oklahoma and the National Institutes of Child Health and Development at the NIH. He devoted the past decade to the study of thyroid cancer in children and has authored over 40 peer-reviewed manuscripts and 10 chapters in this field. He is an elected member of The Endocrine Society, The Lawson Wilkins Pediatric Endocrine Society, The American Thyroid Association and the Children's Oncology Group. He just completed service in January, 2009 on the American Thyroid Association Task Force to develop treatment guidelines for medullary thyroid cancer.

Dr. Seang Lin Tan

Dr. Tan is the James Edmund Dodds Professor and Chairman of the Department of Obstetrics and Gynecology at McGill University. He is also Obstetrician and Gynecologist-in-Chief of the McGill University Health Centre.

Dr. Tan is an internationally recognized infertility expert and a pioneer in the simplification of in-vitro fertilization. He founded the McGill Reproductive Center and led the team that produced the world's first air transport IVF and ICSI pregnancies. His team is the pioneer in Canada in the use of in-vitro maturation of human oocytes for the treatment of infertility and in the use of in-vitro maturation (IVM) and vitrification of oocytes to preserve fertility in young women undergoing cancer treatment. As a result of this groundbreaking work, in 2005, the team was the first in the world to achieve a livebirth from an egg that was matured through IVM, vitrified and then thawed.

Dr. Tan has published 11 books, over 309 original scientific papers and review articles, and he has made over 218 research presentations. He has been on the editorial board of nine medical journals and is regularly invited to speak at national and international scientific meetings.

He is a member of the International Federation of Obstetrics and Gynecology Expert Advisory Panels on Reproductive Medicine and Ultrasound as well as a fellow of the International Academy on Human Reproduction.

He is the Founding President of the International Society of In-Vitro Maturation (ISIVM) and the Global Chinese Association for Reproductive Medicine (GCARM) and the Founding Treasurer of the International Society of In-Vitro Fertilization (ISIVF).

In 1998, he received the Canadian Fertility and Andrology Society – European Society of Human Reproduction and Embryology Exchange Speaker Award and, in 1999, the Resolve Award from the National Infertility Association of the United States for outstanding contribution in the field of ultrasound. Dr. Tan was the John Collins lecturer at the 2001 CFAS meeting. In 2008, he received the Singapore Lecture Gold Medal from the Royal College of Obstetricians and Gynaecologists of the United Kingdom in recognition of his significant scientific contribution to the field of obstetrics and gynecology. He has also been awarded the Howard Eddy Gold Medal by the Royal Australasian College of Surgeons and the MRCOG Gold Medal by the Royal College of Obstetricians and Gynecologists in the United Kingdom.

In 2003, he earned an MBA degree with distinction from the New York University/London School of Economics/HEC Grande Ecole Paris TRIUM Executive MBA Program.

Dr. Robert Lustig

Robert H. Lustig, M.D. is Professor of Clinical Pediatrics, in the Division of Endocrinology at the University of California, San Francisco. Dr. Lustig is a neuroendocrinologist, with basic and clinical training relative to hypothalamic development, anatomy, and function. Dr. Lustig's research focuses on the regulation of energy balance by the central nervous system. He is currently investigating the contribution of nutritional, neural, hormonal, and genetic influences in the expression of the current obesity epidemic both in children and adults. Dr. Lustig graduated from MIT in 1976, and received his M.D. from Cornell University Medical College in 1980. He completed his pediatric residency at St. Louis Children's Hospital in 1983, and his clinical fellowship at UCSF in 1984. From there, he spent six years as a research associate in neuroendocrinology at The Rockefeller University. Dr. Lustig is the current Chairman of the Ad hoc Obesity Task Force of the Lawson Wilkins Pediatric Endocrine Society, a member of the Obesity Task Force of The Endocrine Society, and a member of the Steering Committee of the International Endocrine Alliance to Combat Obesity. He is the author of many articles, chapters, and reviews on childhood obesity.

Dr. Mark Tremblay

Dr. Tremblay has a Bachelor of Commerce degree in Sports Administration and a Bachelor of Physical and Health Education degree from Laurentian University. His graduate training was from the University of Toronto where he obtained his M.Sc. and Ph.D. from the Department of Community Health, Faculty of Medicine with a specialty in exercise science. Dr. Tremblay is the Director of Healthy Active Living and Obesity Research (HALO) at the Children's Hospital of Eastern Ontario Research Institute and Professor of Pediatrics in the Faculty of Medicine, University of Ottawa. Dr. Tremblay is a Fellow of the American College of Sports Medicine, a Fellow of The Obesity Society, former Dean of Kinesiology at the University of Saskatchewan and is currently the Chief Scientific Officer of Active Healthy Kids Canada. Dr. Tremblay was the Scientific Director for the Canadian Health Measures Survey currently being conducted by Statistics Canada and currently Chairs its Expert Advisory Committee. Dr. Tremblay has published extensively in the areas of childhood obesity, physical activity measurement, exercise physiology and exercise endocrinology. Dr. Tremblay's most productive work has resulted from his 20-year marriage to his wife Helen, yielding four wonderful children.

Dr. Brian McCrindle

Dr. Brian McCrindle is a Staff Cardiologist, Director of the Pediatric Lipid Disorders Clinic and Senior Scientist, The Hospital for Sick Children, Toronto. He is a Professor of Pediatrics at the University of Toronto, and holds the CIBC World Markets Children's Miracle Foundation Chair in Child Health Research. He has a long-standing interest in aspects of preventive cardiology and obesity. He is currently the Past Chairperson of the American Heart Association's Atherosclerosis, Hypertension and Obesity in Youth Committee, Council on Cardiovascular Disease in the Young. He is also the Co-Chairperson of the Childhood Obesity Expert Panel working with the AHA and the Clinton Foundation for the Alliance for a Healthier Generation. He is the author of a book, "Get a Healthy Weight for Your Child". His research interests include drug therapy of high risk hyperlipidemia in children and adolescents, and he is the principal author of a scientific statement to this effect published in *Circulation* 2007. He currently leads the CIHR Team in Childhood Obesity Research at the Hospital for Sick Children.

Dr. Jill Hamilton

Jill Hamilton (MD, MSc, FRCPC) is a Pediatric Endocrinologist at the Hospital for Sick Children, Associate Scientist at the Research Institute, and Associate Professor of Paediatrics at University of Toronto. Her clinical research interests are in the area of insulin resistance and pancreatic beta cell function in childhood. She has evaluated mechanisms related to weight gain in children with tumor-induced hypothalamic obesity and risk factors for obesity and type 2 diabetes in babies born to women with gestational diabetes.

Dr. Shazhan Amed

Dr. Amed completed medical school at the University of Calgary (Calgary, Alberta), Pediatric Residency at the University of Manitoba (Winnipeg, Manitoba), and her Endocrinology Fellowship at The Hospital for Sick Children (Toronto, Ontario). She has also completed a Masters of Science in Public Health at the London School of Hygiene and Tropical Medicine (London, England, U.K).

Dr. Amed's academic interests include the epidemiology and prevention of type 2 diabetes in children, innovative models of health service delivery to children with chronic disease, and evaluation of public health initiatives. Dr. Amed recently completed a national surveillance study for non-type 1 diabetes in Canadian children in collaboration with the Canadian Pediatric Surveillance Program. She is also working closely with Child Health BC to develop a provincial pediatric diabetes program in British Columbia. Recognizing the importance of evaluating and reporting the impact of new models of care, she will use existing provincial and national databases to determine if a provincial pediatric model of diabetes care in BC will improve clinical (i.e. diabetes control, reduction of complications) and non-clinical outcomes (i.e. school performance, psychosocial outcomes) in children with diabetes

Dr. Jean-Pierre Chanoine

Dr. Chanoine is a Pediatrician who graduated from the Free University of Brussels, Belgium in 1982. He joined the University of British Columbia in 1998 as Clinical Professor and Head of the Endocrinology and Diabetes Unit at British Columbia's Children's Hospital. Dr Chanoine is Director of the subspecialty care component attached to Shapedown BC, a clinical program addressing the needs of overweight children at BC's Children's Hospital. He is also director of the Pediatric component of the Canadian Obesity Network.

His previous experience includes a fellowship at the University of Massachusetts Medical Center in Worcester, USA; Pediatric Endocrinologist at Hôpital des Enfants Reine Fabiola in Brussels; and Medical Director for Novo Nordisk Belgium.

Dr Chanoine's research is focusing on the role of hormonal and nutritional factors in the development of childhood obesity. The main line of research includes laboratory-based projects aimed at understanding the physiological role of ghrelin, a potent orexigenic peptide, during the fetal and early postnatal period and clinical projects looking at the role of appetite-regulating hormones in the development and treatment of childhood and adolescent obesity. Dr Chanoine is also principal investigator of "Healthy Buddies", a peer-led curriculum aiming at preventing the development of overweight in elementary school children.

Dr. Katherine Morrison

Katherine Morrison is a Pediatric endocrinologist and Associate Professor at McMaster University. Dr. Morrison completed her medical school and pediatric training at the University of Calgary, and her endocrinology training at Stanford University, California.

Her current research interests include obesity and cardiovascular risk factors in children with particular attention to: their early life determinants and optimal treatment strategies for children with lipid disorders and obesity related health consequences. She is active clinically in the Pediatric Lipid and Obesity at Risk Clinics at McMaster Children's Hospital. She was on the steering committee for the development of the recently published Canadian Clinical Practice guideline for the Prevention and Management of Obesity in Adults and Children. Dr. Morrison is supported in her research by the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research.

Dr. Maggie Mamen

Dr. Maggie Mamen is an award-winning clinical psychologist who works with children, adolescents and families in a multidisciplinary private practice in Ottawa. Born and raised in London, England, she moved to Canada in 1971, where she married, undertook her university studies, and gave birth to one child for each of her degrees. Prior to establishing her current practice in 1990, Maggie worked in university, hospital and school board settings. She taught courses on child development and childhood exceptionalities for many years, enjoys giving frequent workshops and seminars for community groups, parents, teachers and other professionals, and has appeared on radio and TV internationally. In addition to The Pampered Child Syndrome, Maggie is the author of *Who's in Charge? A Guide to Family Management*, *Laughter, Love & Limits: Parenting for Life*, and most recently *Understanding Nonverbal Learning Disabilities: A Common-Sense Guide for Parents and Professionals*. She and her husband are the parents of three adults, grandparents of a lovely little girl, and owners of a visually impaired and unashamedly pampered dog.

Chantal Champoux, B.Ed, CCLS

Following the completion of a Bachelor's degree in Psychoeducation at the University of Montreal, Ms Champoux began her career as a Child Life Specialist at the Montreal Children's Hospital, 24 years ago. Initially involved with inpatients on the medical units, Ms Champoux moved onto critical care, ICU, Bone Marrow Transplant and Burn Units, and subsequently began working in Oncology, at the Outpatient clinic. For the past 14 years, Ms Champoux has developed Child Life programs in Ambulatory Care and is currently working in Intensive Ambulatory Care Services, including the Clinical Investigation Unit. Providing preparation and procedural support to children and adolescents, in partnership with their parents and nurses, as well as fostering the use of coping strategies, is part of her daily practice. Ms Champoux is currently involved in educational outreach activities, and this workshop was initially given at the Canadian Paediatric Society's conference, in the summer of 2007.

Julie Bergeron, M.Ed, CCLS

Ms Bergeron has completed a Bachelor's degree in Psychoeducation at the Université du Québec à Trois-Rivières and continued in the same field to achieve a Master's degree at the University of Sherbrooke. During the first 4 years of her career as a Child Life Specialist at the Montreal Children's Hospital, Ms Bergeron developed a recently implemented Child Life program in the Emergency Department. Following this experience of working within a crisis intervention environment, Ms Bergeron has been involved with the inpatient population, on a medical ward, for the past two years. Ms Bergeron is also participating in different educational outreach activities, including the CPS conference workshop, in the summer of 2007.

Thursday, February 26, 2009

- 17:30 Registration Open
- 19:30 Welcome Reception and Exhibits Open
Hord D'œuvres served
- 21:00 Adjourn

Friday, February 27, 2009

- 07:00 Registration Open
- 07:00 Breakfast (Served in the Canadian Room)
- 08:00 Opening Remarks & Welcome
Dr. Sarah Lawrence; Dr. Cheril Clarson and Lina Moisan
- Theme I: Bone
Moderator: Dr. Leanne Ward
- 08:15 How Kids' Bones Get Stronger
Dr. Frank Rauch, Montreal, QC
- 08:45 Is a New Recommendation in Order for Vitamin D
Supplementation in Newborn Infants?
Dr. Hope Weiler, Montreal, QC
- 09:15 Bone Development in Glucocorticoid-Treated Children with Chronic Illness: Results of the
Canadian STeroid-Associated Osteoporosis in the Pediatric Population (STOPP)
Research Program
Dr. Leanne Ward, on behalf of the STOPP Consortium, Ottawa, ON
- 09:45 Refreshment break, exhibits open

**Split rooms, Nurses: to meet in Renaissance Room (please refer to program on pg 15.)

Theme II: Abstracts

Moderators: Dr. Meranda Nakhla and Dr. Sarah Lawrence

- 10:15 Abstracts from CPEG Members and Fellow Presenters
(See page 17 for detailed schedule)
- 12:15 Lunch (Provided in the Canadian Room)
- 13:00 Coffee and Dessert in the Exhibit Area
- 13:45 Fellow's Presentations Cont'd

14:30 Refreshment Break, Exhibits Open

Theme III: Beta Cell

Moderator: Dr. Margaret Lawson

15:00 Preventing Loss of Beta Cells in Type 1 Diabetes – The TrialNet Studies
Dr. Diane Wherrett, Toronto, ON

15:30 Preserving Beta Cell Function
Dr. Robert Sreaton, Ottawa, ON

16:15 Hyperinsulinism & PET Scanning
Dr. Charles Stanley, Philadelphia, PA

17:00 Adjourn

Evening: Dinner

18:30 Reception, in the exhibit area, exhibits open

19:00 Dinner (Served in the Laurier Room)

****Nursing Program:**

10:15 AGM

11:15 Roundtable Discussions

12:15 Lunch (Provided in the Canadian Room)

13:00 Coffee and Dessert in the Exhibit Area

13:30 ParentPower: The Quiet Revolution
Maggie Mamen, Ph.D. Nepean, ON

14:45 Refreshment break, exhibits open

15:15 I SPY WITH MY LITTLE EYE: Distraction Techniques to Empower Nurses and Parents
Julie Bergeron, M. Ed, CAS; Chantal Champoux, B. ED. CCLS

16:15 Adjourn

Saturday, February 28, 2009

- 07:00 Breakfast (Served in the Exhibit Area), exhibits open
- 08:00 Business Meeting
- 10:00 Refreshment Break, exhibits open

Theme IV: Endocrinology

Moderator: Dr. Alexandra Ahmet

- 10:30 Thyroid Cancers in Children
Dr. Gary Francis, Richmond, VA
- 11:15 Female Fertility Preservation
Dr. Seang Lin Tan, Montreal, QC
- 12:00 Lunch (Provided in the Canadian Room)
- 12:30 Coffee and Dessert in the Exhibit Area

Theme V: Obesity

Moderators: Dr. Stasia Hadjiyannakis and Dr. Jill Hamilton

- 13:00 DEBATE: Obesity Nature vs. Nurture
Dr. Robert Lustig, San Francisco, CA
vs. Dr. Mark Tremblay, Ottawa, ON
- 14:15 Treatment of Hyperlipidemia in Children
Dr. Brian McCrindle, Toronto, ON
- 15:00 Refreshment Break, exhibits open
- What is happening in Obesity Research in Canada?
- 15:30 Hypothalamic Obesity
Dr. Jill Hamilton, Toronto, ON
- 15:50 National Surveillance for Type 2 Diabetes in Canadian Children
Dr. Shazhan Amed, Vancouver, BC
- 16:10 Ghrelin in Growth & Development
Dr. Jean-Pierre Chanoine, Vancouver, BC
- 16:30 Identifying Dysglycemia in the Obese Child or Adolescent
Dr. Katherine Morrison, Hamilton, ON
- 16:50 Presentation of Dr. John Bailey Resident Research Award
Presented by Dr. Jean-Pierre Chanoine, Vancouver, BC
- 17:00 Adjourn

Have a safe journey home!

Fellow Presentations Schedule

Friday, February 27, 2009

- 10:15 Dual Thyroid Ectopia and Congenital Hypothyroidism: An Unusual Combination
(*Ellen B. Goldbloom, Margaret L. Lawson, Eoghan E. Laffan, Meranda Nakhla*)
- 10:30 Pleural and Pericardial Effusion in Severe Hypothyroidism in Children
(*Tania Martinez-Soto, Rebecca Trussell, David Stephure, Josephine Ho*)
- 10:45 Sleep Disordered Breathing in Patients with Craniopharyngioma and Hypothalamic Obesity
(*Clodagh S O’Gorman, Judith Simoneau-Roy, Jamie MacFarlane, Ian MacLusky, Denis Daneman, Jill Hamilton*)
- 11:00 Neonatal Diabetes: Four Diverse Cases of a Rare Disease
(*Patricia Olivier, Maria Buithieu, Robert Barnes, Alex Ahmet, Sarah Lawrence*)
- 11:15 Detection of T Cells Reactivity in Auto-Immune Adrenal Deficiency
(*D Rottembourg, F Le Deist, JC Carel, A Lacroix, R Mallone and C Deal*)
- 11:30 Use of Fine Needle Aspiration Biopsy and Outcome in Pediatric Patients Following Surgery
(*Jannette Saavedra, Celine Hout, Yvan Boivin, Guy Van Vliet, Cheri Deal, Nathalie Alos, Dickens Saint-Vil*)
- 11:45 Prediction of Congenital Hypothyroidism (CH) Based on Initial Screening TSH in the Ontario Newborn Screening Program (ONSP)
(*David Saleh, Pranesh Chakraborty, Michael Geraghty, Sarah Lawrence*)
- 12:00 A novel mutation of the Calcium Sensing Receptor gene (CASR): Can one always distinguish between Familial Hypocalciuric Hypercalcaemia (FHH) and Familial Isolated Hyperparathyroidism (FIHP)?
(*M. C. Samaan, D. E. C. Cole, E. Sochett, M.R. Palmert*)
- 13:45 The Short and the Sweaty: A Case of Familial Pheochromocytoma
(*Rayzel Shulman, Jill Hamilton*)
- 14:00 A 19-weeks Fetus with Non-Immune Hypothyroidism and Goiter: Treatment or Observation?
(*Sophie Stoppa-Vaucher, Diane Francoeur, Andrée Grignon, Guy Van Vliet, Johnny Deladoëy*)
- 14:15 Homozygosity Mapping and Identification of the Gene Responsible for Neonatal Diabetes with Intestinal Atresia
(*Nadine Taleb, HuiQi Qu, Patricia Riley, John Mitchell, Constantin Polychronakos*)

Abstracts

Dual Thyroid Ectopia and Congenital Hypothyroidism: An Unusual Combination

Ellen B. Goldbloom, Margaret L. Lawson, Eoghan E. Laffan, Meranda Nakhla
Children's Hospital of Eastern Ontario,
University of Ottawa

Dual thyroid ectopia is an extremely rare entity that is characterized by the simultaneous presence of two separate ectopic foci of thyroid tissue. To date, only 28 cases of dual ectopic thyroid tissue have been reported in the literature. Age of presentation has ranged from 4-71 years, with symptoms varying from none to anterior neck swelling, with or without altered thyroid function. None of the reported cases have been associated with congenital hypothyroidism.

We report a case of an 11-year-old girl with congenital hypothyroidism and dual thyroid ectopia within the sublingual and hyoid regions. Our patient was diagnosed with congenital hypothyroidism through the newborn screening program with a peak TSH of 38 mIU/L at 15 hours of age. Radionuclide scan confirmed a sublingual thyroid gland. TSH normalized with replacement thyroxine. At 11 years of age,

during a routine clinic visit, an asymptomatic anterior midline neck mass was noted. At the time of presentation, she was in early puberty; TSH had recently increased to the high normal range (5.23 mIU/L). Ultrasound of the neck showed two distinct areas of tissue: a discoid-shaped soft tissue mass in the area of the neck swelling that appeared to be thyroid gland and a smaller area of sublingual thyroid tissue. MRI confirmed dual thyroid ectopia in the hyoid and sublingual regions. To our knowledge, this is the first report of congenital hypothyroidism associated with dual thyroid ectopia.

Pleural and Pericardial Effusion in Severe Hypothyroidism in Children

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T3B6A8

Background: Pleural and pericardial effusion a complication of severe hypothyroidism is reported in 10 to 30 % of adults, but is a very rare complication in children. Most cases were associated with Down syndrome. We report two cases of pleural and pericardial effusion in children with severe primary hypothyroidism without Down syndrome.

Case 1: 7 year old girl with a history of congenital hypothyroidism was profoundly hypothyroid due to non compliance. Laboratory tests showed FT4 2.4 pmol/L (8.0-22.0), TSH 160.49 mU/L (0.2-6.0), ALT 135 U/L (1-35). The past medical history was otherwise unremarkable. Her mother was also non compliant with treatment for acquired hypothyroidism. Levothyroxine treatment was restarted at 100 mcg once a day.

One week later, she presented with chest pain and mild respiratory difficulty.

Chest X ray showed a left pleural effusion with mediastinal deviation. ECG was normal. Echocardiogram showed minimal pericardial effusion, normal ventricular function and cardiac structures. She was treated with oxygen and analgesia. No pleurocentesis or pericardiocentesis was performed. The dose of levothyroxine was reduced to 75 mcg once a day. After 3 weeks her laboratory tests were FT4 24.3 pmol/L, TSH 6.9 mU/L. There was complete resolution of pleural and pericardial effusion after 1 month.

Case 2: 4 year 10 month old girl presented with heart failure, renal insufficiency and elevation of liver enzymes [CK 1252 IU/L (20-130), creatinine 82 umol/L (30-70), ALT 300 U/L (1-35)] requiring iv antibiotics and inotropic support. No bacterial or viral causes were identified. The echocardiogram showed moderate pericardial effusion, without tamponade and the chest X ray revealed increased cardiac silhouette without pleural effusion. The past medical history revealed decreased linear growth, long standing constipation, persistent dry skin and decreased energy. Thyroid function assessment showed TSH >750 mU/L (0.2-6.0) consistent with acquired hypothyroidism. Bone age was 3 years. She started levothyroxine 50 mcg daily. The pericardial effusion resolved in 1 month. Thyroid function after 1 month was FT4 19.3 pmol/L and TSH 4.7 mU/L.

Conclusion: This report highlights the importance of suspecting pericardial and pleural effusion in all children with severe hypothyroidism.

Sleep Disordered Breathing in Patients with Craniopharyngioma and Hypothalamic Obesity

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Methods: 31 obese patients were recruited: 16 CP; 15 C. Exclusion criteria included unassociated chronic illness or medications that alter glucose homeostasis. All patients had (i) fasting bloodwork (glucose, ghrelin, PYY, adiponectin, leptin, insulin) and FSIGT (frequent sampling iv glucose tolerance test) with calculation of insulin sensitivity (Si); and (ii) an overnight admission for sleep studies.

Background: Hypothalamic damage, complicated by obesity, temperature and sleep dysregulation, occurs commonly following treatment for pituitary or hypothalamic tumors, including craniopharyngioma (CP). The literature evaluating sleep disordered breathing (SDB) in this population is sparse.

Results: The CP and C groups were similar in age (mean+SD 15.5 ± 4.0 CP and 15.1 ± 2.3 C) and BMI (kg/m²) (35.2 ± 8.0 CP and 33.5 ± 4.9 C). Leptin, PYY and adiponectin concentrations were not different between groups. However, Si was significantly lower in CP than in C (0.15 ± 0.06 v 0.23 ± 0.10, p <0.05).

Table: Results of overnight sleep studies	CP (mean)	C (mean)	p
Sleep onset latency (SOL) (mins)	19.3	31.9	0.03
O2 sats REM sleep (%)	89.0%	94.2 %	<0.001
O2 sats Non-REM sleep (%)	88.4%	94.3%	<0.001
Total sleep time (TST) (mins)	392.6	350.4	0.08
% short wave sleep (SWS) time (mins)	28.3%	23.9%,	0.10
Central apnea index (CAI)	0.99	0.22	0.06
Obstructive apnea-hypopnea index (AHI)	7.5	1.5	0.08

Objective: To compare sleep studies between adolescents with CP and age- and BMI-matched obese controls(C).

Discussion: SDB is significantly more common and severe in patients treated for CP than in BMI- and age-matched obese control patients. Patients with CP had significantly decreased SOL, suggesting that they are “more sleepy” than controls. Based on AHI scores (1.5-5 are mildly abnormal, from 5-10 are moderately severe), the C patients had trend towards mild SDB but CP patients moderately severe SDB. Patients with CP also have decreased Si: factors related to this may contribute to SDB. Further investigation of inflammatory molecules related to Si is warranted. We suggest that sleep studies should become part of the routine care of patients with craniopharyngioma.

Neonatal Diabetes: Four Diverse Cases of a Rare Disease!

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BACKGROUND: Neonatal diabetes (ND) is a rare disease, affecting 1:300,000-400,000 newborns¹. It typically presents in the first 6 months of life and is transient in approximately 50-60% of cases. Transient and permanent ND are usually clinically indistinguishable in the neonate. However, rarely the permanent form occurs in association with other congenital malformations or in specific syndromes such as Wolcott-Rallison and IPEX syndromes. Several genes have been implicated, such as IPF-1,

DISCUSSION: The clinical differentiation of transient and permanent diabetes is not always possible at diagnosis. Two patients in our series, however, had clinical features that could suggest the diagnosis of permanent diabetes: patient 1 had pancreatic agenesis (exocrine pancreatic insufficiency, abdominal imaging) and patient 3 presented with the classic picture of IPEX (diarrhea, rash, hypothyroidism). A mutation of the sulfonylurea receptor was identified in patient 2, who was able to discontinue insulin therapy by 7 months of age and who remains normoglycemic without treatment. Patient 4 has persistent diabetes at 8 months with no known mutations identified on molecular testing.

	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Male	Male	Male	Female
Origin	Caucasian	Congolese	Eastern European	First Nations
Familial history DM	-	-	-	-
Birth weight	1740g (37wks)	2335g (37wks)	2075g (34wks6/7)	2855g (37 wks)
Initial hypoglycemia	Yes	Yes	Yes	-
Hyperglycemia at...	12hrs of life	30hrs of life	9 days of life	29 days of life
DKA	-	-	? (Metabolic acidosis due to diarrhea)	Yes
Malformations	Cardiac and GI malformations	-	-	-
Other diagnoses	Exocrine pancreatic insufficiency Anemia/ leucopenia	Neutropenia Thalassemia	Hypothyroidism Refractory diarrhea Rash Urinary tract infection Multi-organ failure	Sagittal sinus thrombosis Anemia
Genetic testing	No mutation identified	SUR1 mutation +	FOXP3 mutation +	No Mutation Identified
Diagnosis	Pancreatic agenesis	Transient neonatal diabetes	IPEX syndrome	Neonatal diabetes of unknown origin
Therapy	Insulin pump therapy	Insulin stopped at 7 months of age	Deceased 40 days (2e to multi-organ failure) Autopsy refused	T1D insulin regimen continues at 8 months of age. (0.74U/kg/d)

glucokinase, KCNJ11, ABCC8, E1F2AK3, GLIS3, FOXP3 and candidate genes on 6q24. Molecular analysis is important in these children as a subset of neonates with mutations of KCNJ11 and ABCC8 genes have responded to sulfonylurea therapy.

CLINICAL PRESENTATION: Over the past 2 years, 4 patients have been diagnosed with neonatal diabetes at the CHU Sainte-Justine, the MCH and the CHEO:

CONCLUSION: Determination of the etiology of neonatal diabetes can help with both therapy and counselling for families. Close attention to associated features and consideration of a syndrome or congenital anomaly may allow for immediate diagnosis. Most neonates will benefit from early genetic testing which may provide evidence of a sulfonylurea responsive mutation.

*Reference:*1. Polak M, Cavé H: Neonatal diabetes mellitus: a disease linked to multiple mechanisms. Orphanet Journal of Rare Diseases 2007 march; 2(12): 11 pages.

Detection of T Cells Reactivity in Auto –Immune Adrenal Deficiency

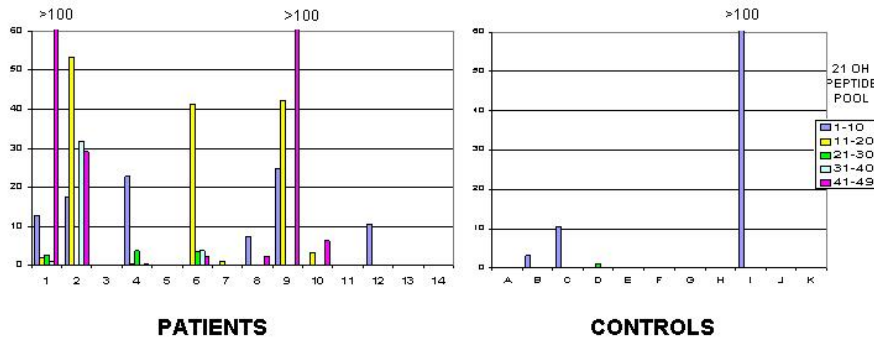
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Auto-immune destruction of the adrenal gland observed in auto-immune primary adrenal insufficiency is assumed to be T cell-mediated but identification of auto-aggressive specific cells has never been established. As in other auto-immune diseases (diabetes, multiple sclerosis) their identification is hindered by their low frequency and the high number of presumed antigenic determinants (epitopes) on the auto-antigen. We used a cytokine enzyme-linked immunosorbent spot (ELISPOT) assay to study directly ex vivo 21-hydroxylase specific memory T cell reactivity from patients with auto-immune adrenal insufficiency and controls. Overlapping 20-aa-long peptides spanning the entire 21-hydroxylase protein were used as antigens to determine IFN- γ production by T cells from peripheral blood mononuclear cells (PBMC).

Our study cohort includes patients with isolated Addison's disease (n=8), APS 2 (n=3) or APECED (n=3) and healthy controls (n=11). In the pediatric patient group (n=10), median time after diagnosis was 30 months. In these assays, 5 pools of 10 adjacent peptides of the 21-hydroxylase protein were used. In responsive patients (9 out of 14), a mean of 2.7 pools per patient were activators, compared to only 1 pool in responsive controls (4 out of 11). Two epitopes were strongly antigenic, in particular one in the C terminal domain and shared among several patients. By adding OKT8 antibody in the PBMC+peptide culture, the IFN- γ response was almost completely abolished in responsive patients, illustrating the identification of a specific CD8 T cell epitope. These results are the first description of T cell reactivity within the context of an epitope mapping study in auto-immune adrenal insufficiency, and support a CD8 T cell-mediated etiopathology.

IFN γ response to 5 pools of 21-hydroxylase peptides

Mean Number of IFN γ SPOTS/ 300 000 PBMC
(NS +3SD subtracted)



Use of Fine Needle Aspiration Biopsy and Outcome in Pediatric Patients Following Surgery

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Thyroid nodules are uncommon and more often malignant in childhood than in adulthood. Fine needle aspiration biopsy (FNAB) can be used to diagnose malignancy or to treat hemorrhagic cysts and abscesses.

Purpose: To determine the outcome in children and adolescents with FNAB suggestive of apparently benign thyroid nodules.

Methodology: In this retrospective study, we reviewed the medical records of patients seen at the CHU Sainte-Justine for a thyroid mass from 2002 to 2007 and for whom FNAB did not show clear evidence of thyroid neoplasia. The following information was retrieved: clinical examination, laboratory tests, thyroid ultrasound, scintigraphy and FNAB.

Results: There were 36 patients (29 females) who presented with either an isolated thyroid mass (n=28) or goiter (n=6). Age at FNAB was 14.1 ± 2.6 yrs (range 7.8-18.2 yrs; median 14.9 yrs). FNAB was performed once in 32 patients, twice in 1 patient and 3 times in 3 patients. Twenty-three patients underwent surgical removal of the mass (partial thyroidectomy (20), total thyroidectomy (2) and cyst removal (1)). Seven patients were found to have papillary cancer after partial thyroidectomy (FNAB: some atypical cells (2), vesicular lesion (1), thyroiditis and vesicular adenoma (1), hemorrhagic cyst (1), inconclusive (1) and colloid and macrophages (1)) while one had metaplastic changes with Hurtle cells. Those 8 patients (22%) underwent surgical completion of thyroidectomy. Median follow-up from FNAB to last visit was 20 months (range 0-72 months) for the 13 patients who did not undergo surgery initially. Two patients have suspicious lesions (partly solid/partly cystic) on ultrasound.

Conclusion: At least one out of five patients with benign findings at FNAB is found to have thyroid carcinoma. Close scrutiny and follow up of pediatric patients with apparently benign thyroid lesions reported by FNAB is recommended.

Prediction of Congenital Hypothyroidism (CH) Based on Initial Screening TSH in the Ontario Newborn Screening Program (ONSP)

David Saleh, MD; Pranesh Chakraborty, MD; Michael Geraghty, MD; Sarah Lawrence, MD

Increasing the TSH-screening cutoff from >17.0 to >20.0 mIU/L decreases the sensitivity of the test from ~100% to 79%. All neonates with an initial screening TSH of >40 mIU/L and 98% of those with >30 mIU/L were later confirmed to have CH.

Background: Since the introduction of thyroid-stimulating hormone (TSH)-based CH screening programs in the 1970's, optimal TSH-screening cutoffs, and the predictive value of various screening TSH levels has been the subject of debate. The principal aim of this study is to examine these values within the ONSP.

TSH Screening Range (mIU/L)	Number of Subjects	Positive Predictive Value (%)
17-19.9	48	31
20-29.9	17	41
30-39.9	4	75
40-49.9	2	100
>50.0	45	100

Methods: The initial screening and follow-up data of 366,658 full term infants born in Ontario, Canada April 1, 2006 to November 30, 2008 were used for the analysis. The screening cut-off used was >17 mIU/L. Confirmed CH cases were based on local endocrinologists' report.

Results: There were a total of 238 positive screening tests (~1/1500 live term births). Follow-up data is available on 116 subjects of which 72 were true positives (~1/2500 live term births). Subjects were further subdivided based on TSH with positive predictive values as indicated in the table below:

Conclusions: The above data supports the notion that a lower initial TSH screening cutoff of at most >17 mIU/L is necessary to detect an acceptable percentage of patients with CH. Thirty one percent in the 17-19.9 mIU/L range were true positives and this group needs to be examined in more detail with extended follow-up data to determine if they have transient or permanent CH. The very high frequency of true positives in term newborns with initial TSH values >30mIU/L suggests that this group should be referred directly to a pediatric endocrinologist in an effort to expedite further assessment and treatment. The abstract presentation will be updated based on data available on currently pending cases.

A novel mutation of the Calcium Sensing Receptor gene (CASR): Can one always distinguish between Familial Hypocalciuric Hypercalcaemia (FHH) and Familial Isolated Hyperparathyroidism (FIHP)?

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We describe a family with hypercalcemia, a novel mutation in the calcium sensing receptor gene [CASR] and features of FHH and FIHP. The proband presented at 36 years with dizziness, and further evaluation revealed hypercalcemia with enlarged parathyroid glands on PET scan. He was diagnosed with primary hyperparathyroidism and underwent 3-gland parathyroidectomy. Histopathology revealed parathyroid hyperplasia; no adenomas were observed. By report, he continued to be hypercalcemic post-operatively.

Concerned about a familial disorder, the primary care physician assessed serum calcium levels in the proband's two sons. Both were found to have hypercalcaemia [3.07 & 3.2 mmol/l, normal 2.19-2.60], with inappropriately normal PTH levels [47 & 51 ng/L, normal 9-55] and low urinary Ca/Cr clearance ratios (0.004 and 0.008, N > 0.01). Both had normal bone mineral densities but the older boy had evidence of nephrocalcinosis on ultrasound. The serum and urinary calcium levels, the normal PTH levels, and BMD data are consistent with FHH; however, the presence of nephrocalcinosis on ultrasound suggests FIHP.

Sequencing of CASR identified a novel, c.1702T>A heterozygous mutation in exon 6, predicting a p.C568S amino acid substitution that would be inactivating.

Previous analysis of a nearby mutation in the same codon in a 57 year old male with hypercalcemia and hyperparathyroidism identified a c.1703A>G (p.C568S) mutation suggesting that the mutation in our cases could lead to FIHP instead of FHH.

Inactivating CASR mutations result in diverse clinical presentations including neonatal severe hyperparathyroidism [NSHPT] when biallelic, and either FHH or Familial Isolated Hyperparathyroidism [FIHP] when a single allele carries a mutation. Both FHH and FIHP are rare conditions that are inherited in an autosomal dominant fashion, but FIHP shows a progressive course. Our cases illustrate the variability in clinical presentations that can result from mutations in a single gene.

The Short and the Sweaty: a Case of Familial Pheochromocytoma

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A 12 yo boy presents to the emergency department with symptoms of tachycardia, hypertension, sweating and flushing, suggestive of pheochromocytoma. Ultrasound and MRI revealed bilateral adrenal masses. Bilateral partial adrenalectomy demonstrated tissue containing multiple nodules of cytomorphologically diverse cells staining strongly positive for chromogranin, consistent with a diagnosis of benign pheochromocytoma.

A 5 year old first cousin presented two weeks later with similar symptoms and was subsequently confirmed to have a right adrenal mass by imaging and pathology. The cousin's 8 year old brother was subsequently diagnosed with a right adrenal pheochromocytoma 3 months later. The 12 year old boy's mother was asymptomatic but had a screening adrenal US given the family history. She was found to have bilateral adrenal masses on US and confirmed on CT.

The boy's parents are first cousins and herald from an island in the Azores in Portugal. Family history is significant for short stature. One of the 12 year old boy's sisters had a history of poor growth and developed antibodies to human cadaveric growth hormone. Genetic testing performed in the 1980's revealed a 3.8 kb band fragment deletion in the growth hormone gene. Her final adult height is 112 cm. Another sister has short stature (final adult height 135 cm) but refused GH therapy because of failure of therapy in her sister. This sister was subsequently diagnosed 7 years ago with bilateral adrenal pheochromocytoma at 9 years of age. There are numerous family members with height < 3rd %ile but no family history of other malignancies associated with the multiple endocrine neoplasia syndromes, nor symptoms to suggest a syndromic form of pheochromocytoma. The question was raised as to whether the two conditions are genetically-linked.

Genetic testing revealed the diagnosis...

A 19-Weeks Fetus with Non-Immune Hypothyroidism and Goiter: Treatment or Observation?

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A 33-year-old G3P1 woman was referred because of the discovery of a goiter in her fetus at 19 weeks of gestation: the fetal thyroid was enlarged (1.9 ml) without signs of tracheo-oesophageal compression (i.e. normal volume of amniotic fluid, normal volume of the lungs). On blood obtained by cordocentesis, TSH, free T4 and Tg values were 90.74 mU/L [1-9], 3.68 pmol [2-7.5], 12.39 µg/L [NA], respectively. Maternal thyroid function was normal (TSH 0.85 mU/L; free T4 8.89 pmol/L) and there were no antibodies against Tg or TPO in maternal plasma. We decided to follow the fetus with echographies q 2 weeks and to treat if signs of tracheo-oesophageal compression (i.e. increased volume of amniotic fluid, neck hyper-extension) developed. At 25 weeks, the volume of the fetal thyroid (4.6 ml) and the amount of amniotic fluid (75th centile) had increased so intra-amniotic (i.a.) L-T4 was initiated at a dose of 200 µg q 2 weeks. Two weeks after the first dose, the thyroid volume (3.3 ml) and the amniotic fluid volume (55th centile) had decreased.

Altogether, i.a. L-T4 was injected three times (25, 27 and 29 weeks). Planned doses after 29 weeks were cancelled because of frequent contractions and stabilization of the fetal goiter. At 38 weeks, the mother spontaneously delivered a boy without any obstetrical and neonatal complications (Apgar 91 95; BW 3205 g; no signs of tracheal compression). Neonatal cord blood revealed TSH 181.14 mU/L [< 30], free T4 10.87 pmol/L [12-19.4]. The goiter was confirmed by echography (7.2 ml [0.83 ml]). At 2 days of life, neonatal screening confirmed hypothyroidism (TSH 20 mU/L [N < 15] and total T4 144 nmol/L [86-230]) and L-T4 50 µg die p.o. was started. In conclusion, i.a. L-T4 decreased the size of a fetal hypothyroid goiter and the associated hydramnios. The benefit-to-risk ratio of i.a. L-T4 needs to be carefully evaluated.

Homozygosity Mapping and Identification of the Gene Responsible for Neonatal Diabetes with Intestinal Atresia

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Background and cases: Recently we described a syndrome comprising neonatal diabetes with absent pancreatic islets and intestinal atresia resulting in early death of infants, born to unaffected parents, that we have observed in two families (two and three affected children) and five sporadic cases. The parents of two probands were cousins, which suggests a new autosomal recessive syndrome resulting from mutations in a gene necessary for the development of the endocrine pancreas and intestine.

Methodology: Recessive mutations in probands of consanguineous families are expected to map to stretches of the genome for which the probands are homozygous by descent (HBD) for a segment of the common ancestral chromosome. In the two consanguineous probands, we used the Illumina Hap550 array that genotypes 550,000 common single nucleotide polymorphisms (SNP's) over the whole genome to determine homozygous chromosomal segments. Two of the probands, born to consanguineous Pakistani families, had overlapping HBD in three segments, totaling 25 Mb. We initially sequenced three genes and a micro-RNA, in a segment of identity-by-descent in the two families, without finding a mutation.

We then sequenced a transcription factor gene temporarily named gene X, that is downregulated in the neurogenin (NGN3) knockout and maps to the HBD region of interest. NGN3 knockouts have absent islets but a functional exocrine pancreas, similar to our cases (NGN3 itself was excluded by homozygosity mapping). Three different potentially disease-causing mutations in three probands were identified: a non-synonymous Serine to Proline mutation in exon 6, an out-of-frame deletion in exon 7 and a disrupted donor splice site in exon 2 caused by a point mutation.

Conclusion: Gene X, whose exact function is yet to be characterized, might not only be a novel gene necessary for pancreatic islet development but potentially contribute to β -cell replacement therapies for diabetes from embryonal or somatic non-endocrine precursors.

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**The next CPEG Scientific Meeting will be held in Calgary
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