Welcome

Dear Delegates,

I would like to extend to you a warm welcome to the 11th Annual Scientific Meeting of the Canadian Pediatric Endocrine Group (CPEG). Our past meetings have provided a wonderful opportunity for the Canadian Pediatric Endocrine community to come together to learn, network and share ideas. The organizing committee has worked hard to craft a program that highlights local Hamilton work and includes presentations by national and international experts, and also provides a forum for our fellows to present their work. We have an exciting program that we hope will meet the educational needs of our nurses, scientists, endocrinologists and trainees.

I would like to thank our sponsors, who make this meeting possible. I would also like to thank those companies who sponsor our CPEG Fellowship Awards and allow us to train endocrinologists for the future. We look forward to the award announcements at this meeting.

I wish you a stimulating and collegial meeting.

Sincerely,

Elizabeth Cummings, M.D., FRCPC
Scientific Chair, CPEG 2017 Scientific Meeting

Bienvenue

Chers délégués,

Je tiens à vous accueillir chaleureusement à la 11ème réunion scientifique annuelle du Groupe canadien d’endocrinologie pédiatrique (GCEP). Nos dernières réunions ont été d’excellentes occasions, pour la communauté canadienne d’endocrinologie pédiatrique, pour se réunir afin d’apprendre, de réseauter et de partager nos idées. Le comité organisateur a travaillé fort pour concevoir un programme qui met en lumière les travaux des gens de Hamilton ainsi que ceux d’experts nationaux et internationaux. Il fournit également un forum pour que nos « fellows » aient l’occasion de présenter leurs travaux. Nous avons un programme captivant qui, nous l’espérons, répondra aux besoins éducatifs du personnel infirmier, des chercheurs, des endocrinologues et des étudiants du domaine de l’endocrinologie.

Je tiens à remercier nos commanditaires, qui rendent cette rencontre possible. Je tiens aussi à les remercier pour le soutien financier qu’ils offrent à notre programme de bourses CPEG; un programme qui nous permet de former les endocrinologues de demain. Nous attendons d’ailleurs avec impatience l’annonce des récipiendaires de cette année lors de ce congrès.

Je vous souhaite une réunion agréable et stimulante.

Bien cordialement,

Elizabeth Cummings, M.D., FRCPC
Scientific Chair, CPEG 2017 Scientific Meeting
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Financial Contributors

The Canadian Pediatric Endocrine Group acknowledges and thanks the following sponsors for their generous support in the form of an unrestricted educational grant:

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![Medtronic](image7)

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![paladin](image9)

![Sanofi Genzyme](image10)
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<th>Year</th>
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<tbody>
<tr>
<td>1992-1993</td>
<td>M. Lawson</td>
</tr>
<tr>
<td>1993-1994</td>
<td>S. Lawrence, M. Lawson, A. Simone</td>
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<tr>
<td>1994-1995</td>
<td>S. Lawrence, S. Taback, A. Simone</td>
</tr>
<tr>
<td>1995-1996</td>
<td>C. Vaz, S. Taback, B. Cummings</td>
</tr>
<tr>
<td>1996-1997</td>
<td>J. Hamilton, E. Sellers, B. Cummings</td>
</tr>
<tr>
<td>1998-1999</td>
<td>J. Curtis, J. Hamilton</td>
</tr>
<tr>
<td>1999-2000</td>
<td>J. Curtis, J. Hamilton</td>
</tr>
<tr>
<td>2000-2001</td>
<td>C. Panagiotopoulos, C. Huang</td>
</tr>
<tr>
<td>2001-2002</td>
<td>C. Panagiotopoulos, S. Stock</td>
</tr>
<tr>
<td>2002-2003</td>
<td>P. Krishnamoorthy, P. Zimakas, R. Meacham</td>
</tr>
<tr>
<td>2003-2004</td>
<td>P. Krishnamoorthy, H. Bui</td>
</tr>
<tr>
<td>2004-2005</td>
<td>M. Nakhla, J. Simoneau-Roy</td>
</tr>
<tr>
<td>2005-2006</td>
<td>M. Nakhla, I. Chapados, M. Jetha</td>
</tr>
<tr>
<td>2006-2007</td>
<td>B. W.icklow, S. Amed</td>
</tr>
</tbody>
</table>

2007-2008: B. W.icklow, T. Pinto, B. Babic, J. Deladoey
2008-2009: A.M. Sbrocchi, P. Olivier, T. Pinto
2010-2011: E. Bassilious, J. Wasserman, Y. Yeshayahu, S. Tsai
2011-2012: M. Millete, J. Wasserman, C. Zuijdik
2012-2013: M. Cohen
2015-2016: L. Chiniara, S. Basak, K. Verbeeten

The CPEG Fellowship Program was and/or is supported by the following:
Eli Lilly, EMDSerono, Hoffmann La Roche, Novo Nordisk, Pfizer, and Sandoz
Program

Please note: 25% of the scientific program will be interactive.

Thursday, February 9, 2017

<table>
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<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>12:00</td>
<td>CPEG Executive Business Meeting (Room 314)</td>
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<tr>
<td>13:00</td>
<td>Welcome &amp; Lunch</td>
</tr>
</tbody>
</table>
| 13:20 | The Diagnosis and Management of Metabolic Bone Diseases in Childhood: An Update for Endocrinologists  
Dr. Leanne Ward |
| 14:30 | Refreshment Break                                         |
| 15:00 | Community Pediatric Endocrine Practice: Life Outside of Academia  
Dr. Karin Winston |
| 16:10 | Conclusion                                                |
| 16:00 | CPEG 2017 Registration Opens (Chedoke A Foyer)           |
| 17:00 | Welcome Reception & Exhibits (Chedoke A)                  |
| 19:00 | Adjourn                                                   |
| 19:00 | Eli Lilly’s Satellite Symposium                           |

Friday, February 10, 2017

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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</table>
| 07:00 | Registration (Chedoke A Foyer)                                          
Breakfast & Exhibits (Chedoke A) |
| 08:00 | Opening Remarks & Welcome (Webster BC)                                  
Dr. Elizabeth Cummings, Ms. Wendy Schwartz, and Dr. Ereny Bassilious |
|       | Poster Highlights                                                        
Each poster presenter will give a 1-minute & 1-slide presentation |
Theme I: Global Health (Webster BC)
Moderator: Dr. Alexandra Ahmet

08:30 Pediatric Endocrinology Education Program for Haiti (PEEP-H) - Example of a Specialty Training Program in Resource-Limited Settings and Opportunities for Health Care Professionals to Get Involved
Dr. Julia von Oettingen

09:00 Access to Medicines in Pediatric Endocrinology and Diabetes: WHO and National Essential Medicines Lists
Dr. Jean-Pierre Chanoine

09:30 Canada: Stuck in the Middle According to UNICEF Child Health Indicators: Real and Potential Impacts on Endocrine Disorders
Dr. Denis Daneman

10:00 Break & Exhibits (Chedoke A)
*Nurses split, see page 7

Theme II: Novel Pathways in Obesity and Energy Balance (Webster BC)
Moderator: Dr. Katherine Morrison

10:30 Physiological and Health Adaptations to Interval Exercise Training
Dr. Martin Gibala

11:15 Novel Pathways Regulating Energy Expenditure: Potential Implications for Treating Obesity and the Metabolic Syndrome
Dr. Gregory Steinberg

12:00 Lunch & Exhibits (Chedoke A)

13:00 Oral Presenter Poster Walks (#1-6) & Global Poster Walks (#1-6) (Chedoke A)

Theme III: Disorders of Sex Development (DSD) (Webster BC)
Moderator: Dr. Rebecca Perry

13:30 New Insights into Molecular Aspects of Gonadal Development
Dr. Barbara Nicol

14:15 Disorders of Sex Development: Recent Clinical Advances
Dr. Diane Wherrett

15:00 Break & Exhibits (Chedoke A)

15:20 *Nurses split, see page 7

15:30 Oral Abstract Presentations (6) (Webster BC)
Moderators: Dr. Karen M cAssey & Dr. Jonathan W asserman

17:00 Adjourn

FRIDAY NIGHT EVENT
Dinner & Entertainment at The Art Gallery of Hamilton (123 King Street West, Hamilton, ON)

18:00 Cocktail Reception & Viewing of Art Gallery

19:00 Dinner & Live Music
**Nursing Program for Friday, February 10 & Saturday, February 11**  
(W ebster A)  
Moderators: M s. Jodi Couture, M s. Barbara Butler

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>10:30</td>
<td>Endocrine Late Effects in Pediatric Cancer Survivors</td>
<td>Eleanor Hendershot</td>
</tr>
<tr>
<td>11:30</td>
<td>Optic Nerve Hypoplasia: Endocrine Issues and Nursing Considerations</td>
<td>Irena Hozjan</td>
</tr>
<tr>
<td>12:00</td>
<td>Lunch and Rejoin CPEG Program</td>
<td></td>
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<tr>
<td>15:20</td>
<td>Testicles, Torsion, Testosterone: Totally Afraid of Needles</td>
<td>Nicole Kirouac</td>
</tr>
<tr>
<td>15:50</td>
<td>Subcutaneous Testosterone Injections: Our Experience</td>
<td>Dr. Anne Marie Sbrocchi</td>
</tr>
<tr>
<td>16:10</td>
<td>Lanreotide Use in a Patient with Hyperinsulinemia</td>
<td>Bailie Tabak, Lori Brnjac</td>
</tr>
<tr>
<td>17:00</td>
<td>Adjourn</td>
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</tr>
<tr>
<td>18:00</td>
<td>FRIDAY NIGHT EVENT</td>
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<td>See page 6 for more information</td>
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**Nursing Program for Saturday, February 11**

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<thead>
<tr>
<th>Time</th>
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<tbody>
<tr>
<td>13:10</td>
<td>CPEN AGM</td>
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<tr>
<td>14:40</td>
<td>Break and Exhibits (Chedoke A)</td>
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<tr>
<td>15:10</td>
<td>Re-join CPEG group</td>
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**Saturday, February 11, 2017**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>07:30</td>
<td>Breakfast (Chedoke A)</td>
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<tr>
<td>08:00</td>
<td>Business Meeting (Webster BC)</td>
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<tr>
<td></td>
<td>Fellowship Awards</td>
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<tr>
<td></td>
<td>Presented by Dr. Celia Rodd</td>
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<tr>
<td>10:00</td>
<td>Break &amp; Exhibits (Chedoke A)</td>
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<tr>
<td>10:40</td>
<td><strong>THEME IV: Hormone Replacement/PCOS (Webster BC)</strong></td>
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<tr>
<td></td>
<td>Moderator: Dr. Jill Hamilton</td>
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<tr>
<td></td>
<td>Hormonal Replacement Therapy in Adolescents and Young Women</td>
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<td></td>
<td>Dr. Sophie Christin-Maitre</td>
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<tr>
<td>11:25</td>
<td>Polycystic Ovary Syndrome (PCOS) in Adolescence</td>
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<td></td>
<td>Dr. Robert L. Rosenfield</td>
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<tr>
<td>12:10</td>
<td>Lunch &amp; Exhibits (Chedoke A)</td>
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<tr>
<td>12:50</td>
<td>Oral Presenter Poster Walks (#7-12) (Chedoke A)</td>
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<tr>
<td>13:10</td>
<td>*Nurses split, see page 7</td>
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<tr>
<td></td>
<td><strong>Oral Abstract Presentations (6) (Webster BC)</strong></td>
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<tr>
<td></td>
<td>Moderators: Dr. Mark Inman &amp; Dr. Melanie Henderson</td>
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<tr>
<td>14:40</td>
<td>Break &amp; Exhibits (Chedoke A Foyer)</td>
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<tr>
<td>15:10</td>
<td>John Bailey Award (Webster BC)</td>
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<tr>
<td></td>
<td>Presented by Dr. Elizabeth Sellers</td>
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<tr>
<td>15:20</td>
<td>Debate: Should screening for celiac disease in asymptomatic patients</td>
</tr>
<tr>
<td></td>
<td>with type 1 diabetes be routinely done? (Webster BC)</td>
</tr>
<tr>
<td></td>
<td>Moderator: Dr. Dan Metzger</td>
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<tr>
<td></td>
<td>Pro: Dr. Farid Mahmud</td>
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<td></td>
<td>Con: Dr. Teresa Pinto</td>
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<tr>
<td>16:20</td>
<td>Closing Remarks &amp; Evaluation</td>
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<tr>
<td>16:30</td>
<td>Adjourn</td>
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<tr>
<td>Time</td>
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<tr>
<td>15:30</td>
<td>Birth Weight, Postnatal Growth, Childhood Adiposity and Risk Factors for Type 2 Diabetes in Children Aged 10-12 Years</td>
</tr>
<tr>
<td>15:45</td>
<td>Diazoxide-Induced Pulmonary Hypertension in an Infant with Congenital Hyperinsulinism – Case Report and Literature Review</td>
</tr>
<tr>
<td>16:00</td>
<td>High Incidence of Early Microvascular Complications in a Cohort of Haitian Children and Adolescents with Diabetes</td>
</tr>
<tr>
<td>16:15</td>
<td>Experiences of a Tertiary Care Centre after Implementation of CALIPER Reference Intervals for Thyroid Function Tests</td>
</tr>
<tr>
<td>16:30</td>
<td>Single Allele PCSK1 Gene Mutation Found in a Child with Early Onset Obesity, Endocrinopathies and Diarrhea</td>
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</tbody>
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**Saturday, February 11**

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Presenter</th>
<th>Abstract #</th>
<th>Page</th>
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</thead>
<tbody>
<tr>
<td>13:10</td>
<td>Children with Idiopathic Isolated Growth Hormone Deficiency Rarely Develop Additional Pituitary Deficiencies</td>
<td>Stephen Zborovski</td>
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</tr>
<tr>
<td>13:25</td>
<td>Age-Dependent Distinctions in Presentation, Treatment and Outcomes of Differentiated Thyroid Carcinoma in Children and Adolescents</td>
<td>Sarah Hampson</td>
<td>8</td>
<td>29</td>
</tr>
<tr>
<td>13:40</td>
<td>A Closer Look at Rickets in Manitoba</td>
<td>Maria-Elena Lautatzis</td>
<td>9</td>
<td>30</td>
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<tr>
<td>13:55</td>
<td>Pseudoacromegaly in the Pediatric Population</td>
<td>Sharmin Hares</td>
<td>10</td>
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</tr>
<tr>
<td>14:10</td>
<td>The Impact of the Social Determinants of Health on Renal Function in Adolescents with Type 1 Diabetes</td>
<td>Laura A.M. Cummings</td>
<td>11</td>
<td>32</td>
</tr>
<tr>
<td>14:25</td>
<td>Primary Amenorrhea due to Müllerian Agenesis in a Girl with Cat Eye Syndrome: Case Report and Review of the Literature</td>
<td>Al Subaihin</td>
<td>12</td>
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### Poster Abstract Listing

<table>
<thead>
<tr>
<th>Title</th>
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<tbody>
<tr>
<td>Two Brothers with Isolated Primary Adrenal Insufficiency</td>
<td>Leah Abitbol</td>
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<tr>
<td>Intermittent Secretory Diarrhea and Profound Hypotension in an Adolescent with a Vasoactive Intestinal Polypeptide Pancreatic Tumor (VIPoma)</td>
<td>Alejandra Acosta-Gualandri</td>
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<tr>
<td>Sirolimus in Treatment of Three Infants with Diffuse Type of Congenital Hyperinsulinism</td>
<td>Ahlam AlOtaibi</td>
<td>3</td>
<td>36</td>
</tr>
<tr>
<td>Interventions Using Pediatric Diabetes Registry Data for Quality Improvement: A Systematic Review</td>
<td>Erica Burry</td>
<td>4</td>
<td>37</td>
</tr>
<tr>
<td>Impact of Neighbourhood-Level Inequity on Paediatric Diabetes Care</td>
<td>Antoine B.M. Clarke</td>
<td>5</td>
<td>38</td>
</tr>
<tr>
<td>A 9-Day Old Boy with Sodium Wasting and Hyperkalemia: Not Always 21-Hydroxylase Deficiency!</td>
<td>Johnny Deladoëy</td>
<td>6</td>
<td>39</td>
</tr>
<tr>
<td>Sub-Q T Is It for Me? Reviewing the Increasing Use of Subcutaneous Testosterone Injections</td>
<td>Brenda Fraser</td>
<td>7</td>
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<tr>
<td>X-Linked Congenital Adrenal Hypoplasia in an Infant Presenting with Cholelithiasis and A Typical Biochemical Results</td>
<td>Robyn LeDrew</td>
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<tr>
<td>A Heterozygous Intragenic Deletion of Exons 3-6 in the Insulin-Like Growth Factor 1 Receptor Gene: A Possible Cause of Postnatal Growth Restriction and Short Stature</td>
<td>Colleen A. Nugent</td>
<td>9</td>
<td>42</td>
</tr>
<tr>
<td>A Rare Case of Hypercalcemia in a TPN-Dependent Child</td>
<td>Julia Sorbara</td>
<td>10</td>
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</tr>
<tr>
<td>Prevalence of Polycystic Ovary Syndrome in Obese Adolescents</td>
<td>Marina Ybarra</td>
<td>11</td>
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</table>

### Global Health Abstract Listing

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<th>Title</th>
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<th>Abstract #</th>
<th>Page</th>
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</thead>
<tbody>
<tr>
<td>Managing Pediatric Cushing’s Disease in a Resource-Limited Setting: A Challenging Case From Haiti</td>
<td>Clorene Cadet</td>
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</tr>
<tr>
<td>Severe Osteogenesis Imperfecta in a Newborn Infant: First Case Report from Haiti</td>
<td>Bianca Meril</td>
<td>2</td>
<td>46</td>
</tr>
<tr>
<td>Clinical Diagnosis of 11-Beta-Hydroxylase Deficiency in a 6 Year-Old Haitian Boy with Sexual Precocity</td>
<td>Tania Ramilus</td>
<td>3</td>
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</tr>
<tr>
<td>MicroResearch: Building Capacity for Health Research in Eastern Africa (EA)</td>
<td>Elizabeth A Cummings</td>
<td>4</td>
<td>48</td>
</tr>
<tr>
<td>Management of Type 1 Diabetes in a Limited Resource Context: A Study of the DREAM Trust Model in Nagpur, Central India</td>
<td>Alexandra Ahmet</td>
<td>5</td>
<td>49</td>
</tr>
<tr>
<td>Access to Medicines in Pediatric Endocrinology and Diabetes in Africa: Insights from the WHO and National Lists of Essential Medicines</td>
<td>Jean-Pierre Chanoine</td>
<td>6</td>
<td>50</td>
</tr>
</tbody>
</table>
Program Organizing and Scientific Committee

Ereny Bassilious  
Barbara Butler  
Jodi Couture  
Elizabeth Cummings  
Danya Fox  
Brenden Hursh  
Nancy Gagne  
Jennifer Galle  
Rose Girgis  
John van der Meulen  
Katherine Morrison  
Jo Nam  
Elizabeth Sellers

Credits

This event has been approved by the Canadian Paediatric Society for a maximum of 12.25 credit hours as an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification program of The Royal College of Physicians and Surgeons of Canada. The specific opinions and content of this event are not necessarily those of the CPS, and are the responsibility of the organizer(s) alone.

Dr. John Bailey Resident Research Award

The John Bailey Award is named after Dr. John D. Bailey. Dr. Bailey graduated from the University of Toronto Medical School in 1949, did his training in pediatrics at the Hospital for Sick Children, Toronto and the University of Manitoba in Winnipeg. By the mid-1950s he was firmly established as a major contributor to pediatric care and education at the Hospital for Sick Children and University of Toronto. His major area of interest was in understanding normal and abnormal growth patterns in childhood and adolescence. He was the first chief of the Endocrine Division at the Hospital for Sick Children and an important contributor to the development of the Canadian national growth hormone treatment program. He was the consummate academic: clinically fastidious, intellectually challenging and constantly learning and sharing.

Below is a list of the recipients of the Dr. John Bailey Resident Research Award:

- 2007 Meranda Nakhla  
- 2008 Meranda Nakhla  
- 2009 David Saleh  
- 2010 Brandy Wicklow  
- 2011 Jonathan Wasserman  
- 2012 Jennifer Harrington  
- 2013 Karine Khatchadourian  
- 2014 Akash Sinha  
- 2015 Rayzel Shulman  
- 2016 Sanjukta Basak
Learning Objectives

The overall learning objective of this meeting is to present the current state of knowledge of topics in pediatric endocrinology and diabetes.

Session Learning Objectives:

Meet the Professor

The Diagnosis and Management of Metabolic Bone Diseases in Childhood: An Update for Endocrinologists
Leanne Ward, MD, FRCPC, Research Chair in Pediatric Bone Health, Associate Professor of Pediatrics, University of Ottawa, Ottawa, ON, Canada
1. Review the pathophysiology, clinical presentations and diagnosis of two pediatric metabolic bone disorders frequently presenting to endocrinologists: osteoporosis and hypophosphatemia
2. Discuss the multi-disciplinary management of osteoporosis and hypophosphatemia of childhood
3. Discuss the clinical trials that are currently underway in Canada to expand the medical tools that will one day be available for the treatment of osteoporosis and hypophosphatemia of childhood

Community Pediatric Endocrine Practice: Life Outside of Academia
Karin Winston, MD, FRCPC, Community Pediatric Endocrinologist; Clinical Assistant Professor, Department of Pediatrics, University of Calgary, Calgary, AB, Canada
1. Compare working as a pediatric endocrinologist in academic and community settings
2. Describe the types of patients appropriate for follow-up in a community practice
3. List some logistical challenges and benefits to working in a community practice

Theme I: Global Health

Pediatric Endocrinology Education Program for Haiti (PEEP-H) - Example of a Specialty Training Program in Resource-Limited Settings and Opportunities for Health Care Professionals to Get Involved
Julia von Oettingen, MD, PhD, MMSc, FRCPC, Pediatric Endocrinologist, Montreal Children's Hospital; Assistant Professor, Department of Pediatrics, McGill University Health Centre, Montreal, QC, Canada
1. Discuss the relevance of subspecialty pediatrics training in resource limited settings.
2. Critique the approach to pediatric endocrine education in low income countries.
3. List reasons for health care professionals to become involved in global health.

Access to Medicines in Pediatric Endocrinology and Diabetes: WHO and National Essential Medicines Lists
Jean-Pierre Chanoine, Clinical Professor, Endocrinology and Diabetes Unit, BC Children's Hospital; University of British Columbia, Vancouver, BC, Canada
1. Understand the WHO and the National Model Lists of Essential Medicines with respect to pediatric endocrinology and diabetes
2. Reflect on the barriers and opportunities around access to medicines in resource-constrained settings.
3. Discuss specific situations where insufficient access to fludrocortisone and hydrocortisone impacts CAH management
Canada: Stuck in the Middle According to UNICEF Child Health Indicators: Real and Potential Impacts on Endocrine Disorders
Denis Daneman, MBCh, FRCP, DSc(Med), Professor of Paediatrics, Chair Emeritus, Department of Paediatrics, University of Toronto; Paediatrician-in-Chief Emeritus, The Hospital for Sick Children, Toronto, ON, Canada

1. Highlight the role of the social determinants of health (SDoH) in maintaining good health and well-being in children
2. Define how the SDoH impact on endocrine disorders of children
3. Determine how these factors can be mitigated in improving outcomes

Theme II: Novel Pathways in Obesity and Energy Balance

Physiological and Health Adaptations to Interval Exercise Training
Martin Gibala, Professor and Chair, Department of Kinesiology, McMaster University, Hamilton, ON, Canada

1. Summarize interval training terminology and protocol design considerations
2. Compare the effects of interval versus traditional endurance training on physiological adaptations linked to improved health
3. Assess the benefits and limitations of interval training protocols that require low time commitment

Novel Pathways Regulating Energy Expenditure: Potential Implications for Treating Obesity and the Metabolic Syndrome
Gregory Steinberg, PhD, Professor and Canada Research Chair in Metabolic Diseases, Division of Endocrinology and Metabolism, Department of Medicine, McMaster University, Hamilton, ON, Canada

1. Discuss factors regulating energy balance
2. Discuss mechanisms regulating energy expenditure
3. Discuss the therapeutic importance of increases in energy expenditure for treating metabolic diseases

Theme III: Disorders of Sex Development (DSD)

New Insights into Molecular Aspects of Gonadal Development
Barbara Nicol, Postdoctoral fellow, Reproductive Developmental Biology Group, National Institute of Environmental Health Sciences (NIEHS/NIH), Research Triangle Park, NC, USA

1. Summarize the process of gonadal differentiation, from the undifferentiated bipotential gonad to an ovary or a testis
2. Describe the molecular mechanisms that regulate gonadal development
3. Apply the knowledge of mouse models to identify potential target genes that are involved in human DSD.

Disorders of Sex Development: Recent Clinical Advances
Diane Wherrett, MD, FRCP, Associate Professor, Department of Paediatrics, University of Toronto, Toronto, ON, Canada

1. Explore challenges in the traditional approach to the diagnosis of disorders of sex development and the impact of new genetic techniques on diagnostic algorithms
2. Assess progress since the DSD Consensus statement in 2006
3. Describe controversies around DSD surgery and international responses
Theme IV: Hormone Replacement/ PCOS

Hormonal Replacement Therapy in Adolescents and Young Women
Sophie Christin-Maitre, M D, PhD, Professor, Head of Endocrine Unit, Hôpital Saint-Antoine, University Pierre and Marie Curie, Paris, France
1. List the different estrogen and progestin molecules
2. Compare contraceptive versus non contraceptive hormonal replacement therapy
3. Plan the follow-up of hormonal replacement therapy

Polycystic Ovary Syndrome (PCOS) in Adolescence
Robert L Rosenfield, M D, Professor Emeritus of Pediatrics and Medicine, The University of Chicago Pritzker School of Medicine, Chicago, IL, USA; Adjunct Professor of Pediatrics, The University of California, San Francisco, San Francisco, CA, USA
1. Understand pathogenesis of PCOS as functional ovarian hyperandrogenism (FOH) and role of obesity in aggravating and mimicking FOH
2. Understand how consensus criteria for PCOS diagnosis in adolescents differ from those in adults and understand the menstrual criteria that indicate abnormal anovulation
3. Understand management principles in adolescent PCOS, and role of insulin-lowering treatments in management

Clinical Debate

Debate: Should screening for celiac disease in asymptomatic patients with type 1 diabetes be routinely done?
Pro: Farid Mahmud, M D, FRCP, The Hospital for Sick Children; Associate Scientist, Sick Kids Research Institute; Associate Professor, University of Toronto, Toronto, ON, Canada
Con: Teresa Pinto, M D, FRCP, Assistant Professor, Division of Pediatric Endocrinology, Department of Pediatrics, Faculty of Medicine, Dalhousie University, Halifax, NS, Canada
1. Describe the epidemiology and pathophysiology of celiac disease in the context of type 1 diabetes
2. Outline controversies in screening approaches to patients with diabetes for celiac disease
3. Discuss potential short and long term implications with regards to treatment in young patients with type 1 diabetes

Nursing Program

Endocrine Late Effects in Pediatric Cancer Survivors
Eleanor Hendershot, M N, BScN, Nurse Practitioner, Oncology, McMaster Children’s Hospital, Hamilton Health Sciences, Hamilton, ON, Canada
1. Recognize the types of endocrine late effects that are seen in pediatric cancer survivors
2. Describe the effects of radiation therapy on pituitary function
3. Discuss risk factors for infertility and premature ovarian failure in pediatric cancer survivors
Biographies

Dr. Jean-Pierre Chanoine
Dr. Chanoine is a pediatrician who graduated from 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.

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 is principal investigator of “Healthy Buddies”, a peer-led curriculum aiming at preventing the development of overweight in elementary school children and initiated the LiGHT project (Living Green, Healthy and Thrifty), a web-based program that emphasizes the beneficial effects of weight management on health, global environment and personal finances.

He is increasingly active in Global Health in the field of Pediatric Endocrinology and Diabetes in resource-constrained settings. Dr Chanoine is presently Secretary General of Global Pediatric Endocrinology and Diabetes (www.globalpedendo.org), an international non-profit organization that aims at promoting Pediatric Endocrine care in low income countries and Chair of the International Relations Council at the Pediatric Endocrine Society.

Dr. Sophie Christin-Maitre
Sophie Christin-Maitre received her medical degree at The University of Paris, France. She trained in endocrinology and reproductive medicine in Paris. She has been a fellow in Reproductive Endocrine Unit at Massachusetts General Hospital, Harvard Medical School, Boston, USA Rochester. She is currently head of the Endocrine Unit, in St Antoine hospital in Paris. She is in charge of a center for rare endocrine diseases. She belongs to the research unit INSERM U933 and she is Professor at the University Pierre and Marie Curie (UMPC) – Paris Sorbonne.

Research Activities Dr. Christin-Maitre’s overall research focus is clinical and translational research relating to female and male reproduction. Her research interests include:

- Primary ovarian insufficiency (POI), essentially finding genes involved in ovarian insufficiency. She is the principal investigator of a French national research project studying families of POI patients.
- Turner syndrome, as a large cohort of adult patients are being followed in the Unit, especially spontaneous pregnancies and aortic evolution in Turner syndrome patients.
- Female contraception and hormonal replacement therapy.
**Dr. Denis Daneman**  
Denis Daneman obtained his MBBCh in 1973, his FRCP(C) in 1981, and his DSc(Med), the University of the Witwatersrand’s highest degree for his thesis entitled “Contributions to type 1 diabetes in children and adolescents.” He has been on the staff at SickKids and UofT since 1981, from 1993-2006 as Head, Division of Endocrinology, 2000-2005 as Associate Chief, Clinical of the SickKids’ Research Institute and from 2006-2016 as Chair of UofT’s Department of Pediatrics and Paediatric-in-Chief at SickKids. He has published well over 200 papers mainly in the field of diabetes in children and youth, co-authored 3 books, one of which, “When a Child has Diabetes”, has served as the major manual for Canadian families with children with recently diagnosed diabetes. He co-chaired the first diabetes clinical practice guidelines in Canada, and continues to be involved in guideline development. Denis has been involved in a number of multicenter international trials, including the DCCT, TRIGR and AdDIT. He has played leadership roles in both national (Canadian Pediatric Endocrine Group, Canadian Diabetes Association) and international organizations (International Society for Pediatric and Adolescent Diabetes, ISPAD). He has received innumerable awards, most recently the 2010 ISPAD Prize, the 2013 Canadian Diabetes Association’s Lifetime Achievement Award and, and the 2015 Canadian Association for Academic Healthcare Centres (CAPHC) Award for Contributions to Child Health. In October 2016 he received an Honorary Fellowship from the Royal College of Paediatrics of Ireland.

**Dr. Martin Gibala**  
Martin Gibala is a professor and chair of McMaster’s Department of Kinesiology. His research on the physiological and health benefits of high-intensity interval training has attracted immense scientific attention and worldwide media coverage. Gibala has authored over 100 peer-reviewed articles, the results of which have been featured by outlets including The New York Times, TIME and NBC News. Penguin Random House will publish his first book, “The One-Minute Workout”, in February, 2017. Gibala has received three awards for teaching excellence from the McMaster Students Union as well as the President’s Award for Excellence in Graduate Student Supervision.

**Ms. Eleanor Hendershot**  
Eleanor Hendershot completed her Master of Nursing in the Acute Care Nurse Practitioner Programs at the University of Toronto in 2003. She is currently working as a Nurse Practitioner at McMaster Children’s Hospital. She has a special interest in pediatric cancers survivors and the late effects of cancer treatment. She was previously the Aftercare Nurse Practitioner at both the Hospital for Sick Children and Princess Margaret Cancer Centre.

Eleanor is also cross-appointed to the Lawrence S. Bloomberg Faculty of Nursing, University of Toronto as an Adjunct lecturer. She has published several book chapters on children and adolescents with solid tumors. She has also published multiple manuscripts on pediatric solid tumors, supportive care and survivorship issues. Eleanor is a member of the Children’s Oncology Group and the nursing representative on the Survivorship and Outcomes committee. Eleanor is involved in multiple research activities, including the co-Principal Investigator of the prospective study involving the outpatient delivery of high-dose methotrexate in patients with Osteosarcoma.
Dr. Farid Mahmud

Farid Mahmud received his medical degree at The University of Alberta, Edmonton. He trained in Paediatric Endocrinology and Metabolism at The Mayo Clinic, Rochester, Minnesota, USA. He is currently Staff Physician in the Division of Endocrinology, Department of Paediatrics, Associate Professor at the University of Toronto and Associate Scientist at The Hospital for Sick Children Research Institute.

Dr. Mahmud’s overall research focus is diabetes, clinical and translational research relating to co-morbid autoimmune conditions, and early evaluation and prevention of related complications. His research interests include:

- Interventions in high risk pediatric groups including type 1 and type 2 diabetes to alter CVD risk. As part of an international, double-blind, randomized control trial, Dr. Mahmud serves as Principal Investigator of the Adolescent Diabetes Cardio-Renal Intervention Trial (AdDIT) Expansion in Canada.
- Assessment of co-morbid autoimmune conditions: impact of celiac disease and type 1 diabetes. Dr. Mahmud has a longstanding interest in celiac disease as an association with type 1 diabetes. He serves as Principal Investigator of a dietary intervention study (Celiac Disease and Diabetes – Dietary Intervention and Evaluation Trial (CD-DIET)).
- Evaluation of social determinants of health on paediatric chronic disease.

Dr. Barbara Nicol

Dr. Barbara Nicol is a post-doctoral fellow in the Reproductive Developmental Biology Group, lead by Dr. Humphrey Yao, at the National Institute of Environmental Health Science (NIEHS/NIH), in North Carolina, USA. She joined Humphrey Yao’s lab in 2012, after completing her PhD in Biology at the University of Rennes, France in 2011. Her research focuses on identifying the molecular mechanisms involved in sex determination and ovarian development using the mouse model.

Dr. Teresa Pinto

Dr. Teresa Pinto is a Pediatric Endocrinologist at the IWK Health Centre and Assistant Professor of Pediatrics at Dalhousie University in Halifax, NS. Born and raised in Montreal, she completed medical training at McGill University with a residency in Pediatrics at Dalhousie University and fellowship training in Endocrinology and Metabolism at the University of Ottawa. She then completed a research fellowship at Auckland University in Auckland, New Zealand. She is expanding her research portfolio in the areas of diabetes and endocrinology with a particular interest in obesity and type 2 diabetes.

Dr. Robert Rosenfield

Dr. Rosenfield has been a “bedside to bench” clinical investigator involved with research into pubertal disorders for nearly 50 years. Since discovering the elevated free testosterone and low sex hormone binding globulin blood levels of hirsute women in 1971, elucidating the role of androgen in normal and abnormal female reproductive endocrinology has been his primary research interest. His group’s development of the gonadotropin-releasing hormone agonist test of pituitary-ovarian function identified the characteristic steroidogenic dysfunction of polycystic ovary syndrome (PCOS), which was instrumental in identifying that the essence of this disorder is functional ovarian hyperandrogenism (FOH). Their discovery that insulin and insulin-like growth factor I up-regulate the thecal androgenic response to luteinizing hormone was a key step in developing their widely accepted hypothesis that steroidogenic dysregulation underlies the ovarian and adrenal dysfunction of FOH. Subsequently, they identified type 5 17ß-hydroxysteroid dehydrogenase as the ovarian testosterone-forming enzyme and then demonstrated a unique transcriptional link between the regulation of this enzyme and adiposity by insulin.
**Dr. Gregory Steinberg**

Dr. Steinberg completed his PhD at the University of Guelph (2002) and postdoctoral fellowship at the University of Melbourne (2007) before establishing his own laboratory at McMaster University where he is currently a Professor in the Department of Medicine and Co-Director of the Metabolism and Childhood Obesity Research Program. Dr. Steinberg’s research uses advanced techniques in biochemistry, molecular biology and physiology in novel animal models and clinical populations, to unravel fundamental mechanisms by which energy sensing, endocrine factors and therapeutics regulate metabolism. Over the last 5 years Dr. Steinberg has discovered how metabolic stressors such as exercise, fasting, aging and commonly used medications for type 2 diabetes elicit their glucose lowering effects. More recently the Steinberg lab has discovered a new way to turn on the body’s metabolic furnace to burn calories and reduce blood sugar levels. His detailed understanding of the mechanisms regulating cellular energy sensing has wide ranging implications for the treatment of many common chronic diseases including obesity, type 2 diabetes, cardiovascular disease and cancer. He has over 130 publications in leading scientific journals such as Nature Medicine and is a member of the Royal Society of Canada College of New Scholars, Artists and Scientists.

**Dr. Julia von Oettingen**

Dr. Julia von Oettingen is a pediatric endocrinologist at the Montreal Children's Hospital and Assistant Professor at McGill University. She obtained her MD (2008) and PhD (2009) degrees from the University of Leipzig medical school in Germany, and a master of medical sciences degree (2015) from Harvard Medical School. She completed her residency in pediatrics at the Massachusetts General Hospital for Children, and her fellowship in pediatric endocrinology at Boston Children’s Hospital, both in Boston, USA. Dr. von Oettingen has been working in Liberia and Haiti to establish pediatric diabetes care, and is a site advisor to the International Diabetes Federation’s Life for a Child program in Liberia and Haiti. She is the founding medical director of a pediatric chronic care center in Haiti, and technical adviser for pediatric endocrinology to Partners in Health. She is a member of the Pediatric Endocrine Society International Relations Council where she leads the Haiti sub-group, including the development of the Pediatric Endocrinology Education Program for Haiti. Julia recently joined the Executive Committee of Global Pediatric Endocrinology Diabetes (GPED). Her clinical and research interests are diabetes and endocrine conditions in non-Caucasian populations, and chronic care delivery in resource limited settings.

**Dr. Leanne Ward**

Dr. Leanne Ward is an Associate Professor of Pediatrics at the University of Ottawa where she has held a Research Chair in Pediatric Bone Health since 2010. She is the Medical Director of the Pediatric Bone Health Clinical and Research Programs at the Children’s Hospital of Eastern Ontario and a pediatric endocrinologist within the Division of Endocrinology and Metabolism. Dr. Ward’s research program is dedicated to the study of bone development and the treatment of bone disorders in children. She has been 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 glucocorticoids on bone health in children with chronic illnesses. She has served as an endocrinology and bone health advisor to numerous national and international organizations on various aspects of skeletal health in children, including the Centres for Disease Control Clinical Care Guidelines for Duchenne Muscular Dystrophy. Dr. Ward has received a number of awards for her work in pediatric bone health, including a Canadian Child Health Clinician Scientist Career Development Award, a Canadian Institutes for Health Research New Investigator Award, a Canadian Child Health Clinician Scientist Career Enhancement Award, and two, five-year Research Chairs in Pediatric Bone Health (University of Ottawa, 2010 and 2015).
Dr. Diane Wherrett
Diane Wherrett received her medical degree at Queen's University in Kingston, Ontario. She trained in Paediatrics and Paediatric Endocrinology at The Hospital for Sick Children, Toronto and did a research fellowship in the immunology of type 1 diabetes at Stanford University. She is currently a Staff Physician in the Division of Endocrinology, Department of Paediatrics, Associate Professor at the University of Toronto and Program Director, Paediatric Endocrinology Training Program at The Hospital for Sick Children. She is the Centre Director of the Canadian site of the NIH multicentre clinical trial group, type 1 Diabetes TrialNet, and a member of the TrialNet Steering Committee. In addition, she is interested in the care of children with disorders of sex development.

Dr. Karin Winston
Karin Winston completed medical school at the University of Calgary and pediatric residency in London, Ontario before returning to Calgary to complete a pediatric endocrine fellowship. In addition to general pediatric endocrinology, her interests to date include obesity and transitioning pediatric patients to adult care. Karin has completed a Master’s degree in Community Health Science. Her thesis focused on work done with a video targeted at improving transition to adult care for patients with type 1 diabetes. It had been her intention to pursue a career in academic pediatric endocrinology but the opportunity for a community practice came at the right time and has been an exciting and rewarding journey.
Disclosure of Conflict of Interest

All speakers and committee members must disclose whether they do or do not have a relationship with a commercial entity such as a pharmaceutical organization, medical device company or a communications firm.

Committee Members

Ereny Bassilious
I have received or expect monetary support (Honoraria, Advisory Boards/ Consulting) from Insulet Canada.

Barbara Butler
I have received or expect monetary support (Honoraria, Advisory Boards/ Consulting) from EMD Serono, where I served on the advisory board in June 2016.

Jodi Couture
I have received or expect monetary support (Honoraria, Advisory Boards/ Consulting) from Saizen.

Elizabeth Cummings
I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by Eli Lilly, Novartis, Pfizer, Sanofi.

Danya Fox
No affiliation

Brenden Hursh
No affiliation

Jennifer Galle
No affiliation

Rose Girgis
No affiliation

John van der Meulen
- I have ownership interest in Gilead Sciences and Amgen Johnson and Johnson.
- I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by OPKO Pharmaceuticals and EMD Serono.
- I have received or expect monetary support (Honoraria, Advisory Boards/ Consulting) from Pfizer and OPKO.

Katherine Morrison
I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by AstraZeneca.

Jo Nam
No affiliation

Elizabeth Sellers
No affiliation
Speakers

Jean-Pierre Chanoine
No affiliation

Sophie Christin-Maitre
No affiliation

Denis Daneman
No affiliation

Martin Gibala
No affiliation

Eleanor Hendershot
No affiliation

Farid Mahmud
- I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by Medtronic.
- I have received or expect monetary support (Honoraria, Advisory Boards/Consulting) from Eli Lilly.

Barbara Nicol
No affiliation

Teresa Pinto
I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by Sanofi and Eli Lilly.

Robert Rosenfield
No affiliation

Gregory Steinberg
- I am on the advisory board of Esperion Therapeutics.
- I have an involvement in research sponsored by or participation in clinical studies concerning the use of the products manufactured by Esperion Therapeutics and Rigel Pharmaceuticals.
- I have received or expect monetary support (Honoraria, Advisory Boards/Consulting) from Esperion Therapeutics and Rigel Pharmaceuticals.
- I have ownership of a patent on tph1, a product referred to in the presentation.

Julia von Oettingen
No affiliation

Leanne Ward
- I have an involvement in research involving zoledronic acid, denosumab and KRN23 sponsored by Novartis, Amgen and Ultragenyx.
- I have received honoraria and consulting fees from Novartis, Amgen and Ultragenyx.
- I intend to make therapeutic recommendations for medications that have not received regulatory approval (i.e. “off-label” use of medications).

Diane Wherrett
No affiliation

Karin Winston
I have received or expect monetary support (Honoraria, Advisory Boards/Consulting) from Eli Lilly and Sandoz.
Oral Abstracts

Oral Abstract 1
Birth Weight, Postnatal Growth, Childhood Adiposity and Risk Factors for Type 2 Diabetes in Children Aged 10-12 Years

ANDREA VAN HULST1,2, GILLES PARADIS1, ANDREA BENEDetti1, MÉLANIE HENDERSON2,3. 1) Department of Epidemiology Biostatistics and Occupational Health, McGill University, Montreal, QC; 2) Centre de recherche du CHU Sainte-Justine, Montreal, QC; 3) Division of Endocrinology and Diabetes, Department of Pediatrics, University of Montreal, Montreal, QC.

Objective:
We examined whether birth weight and postnatal growth during infancy are associated with insulin sensitivity and secretion in children, and assessed potential mediation of associations by childhood adiposity.

Methods:
Data from a longitudinal cohort of 630 Quebec Caucasian children with a parental history of obesity (QUALITY) were used. In a sub-sample of children born at term, weight and length from 0-2 years of age were obtained retrospectively and transformed to sex specific weight-for-length z-scores (n=395). Percentage of body fat was measured by dual-energy x-ray absorptiometry at age 8-10 years. Accelerometry based moderate-to-vigorous physical activity and self-reported daily hours of screen time were measured at age 10-12 years. Insulin sensitivity was measured by the Matsuda insulin sensitivity index (ISI) and insulin secretion was assessed by the ratio of the area under the curve (AUC) of insulin to glucose at 30 min and at 120 min after an oral glucose tolerance test performed at the age of 10-12 years. Multiple linear regressions and path analysis were used.

Results:
Higher birth weight was associated with improved insulin sensitivity: 1 z-score increase in weight-for-length at birth was associated with a 6.9% increase in Matsuda-ISI (95% CI: 2.2; 11.6). This association was independent of childhood adiposity, lifestyle behaviors, and gestational age. Postnatal growth was not directly associated with insulin sensitivity, however faster postnatal growth was positively associated with adiposity at 8-10 years which in turn predicted decreased Matsuda-ISI. Similarly, birth weight-for-length and postnatal growth were associated with insulin secretion only via their effect on adiposity at the age of 8-10 years.

Conclusion:
Our results add to the growing body of evidence regarding the importance of prenatal and postnatal growth for later type 2 diabetes risk factors in children.
Oral Abstract 2
Diazoxide -Induced Pulmonary Hypertension in an Infant with Congenital Hyperinsulinism– Case Report and Literature Review

Paul E. Kahlke¹, Josephine Ho ¹, Erika Vorhies², Carol Huang ¹. ¹) Division of Pediatric Endocrinology, Department of Pediatrics; 2) Division of Pediatric Cardiology, Department of Pediatrics, University of Calgary, Calgary, AB

We present a case of severe pulmonary hypertension (PHTN) in a 6-week-old male treated with diazoxide for congenital hyperinsulinism (CHI). Born in otherwise good health, he was found to have asymptomatic hypoglycemia of 0.9 mmol/ L at two hours of age. CHI was confirmed with an insulin level of 18 pmol/ L when serum glucose was 2.0 mmol/ L. An autosomal dominant ABCC8 R1323H mutation was found on genetic testing. Diazoxide treatment was initiated in the first week of life and he was discharged home on day 19 of life on diazoxide (12 mg/ kg/ d). At 6 weeks of age, he presented with severe respiratory distress and fluid overload requiring PICU admission and non-invasive ventilation. Echocardiogram showed severe PHTN. Suspecting diazoxide-induced PHTN, the medication was withdrawn. PHTN resolved completely over 12 days, both clinically and on echocardiogram. Unsuccessful trials of feed fortification, overnight continuous feeds, nifedipine, and octreotide (up to 20 mg/ kg/ d) were attempted to control hypoglycemia. At 13 weeks of age, the patient was restarted on diazoxide at 5 mg/ kg/ d in addition to hydrochlorothiazide at 3 mg/ kg/ d. Regular clinical and echocardiographic surveillance have shown normoglycemia and no recurrence of PHTN after 4 weeks’ follow-up. Available since 1973, diazoxide is the first line treatment for CHI. A total of 32 cases of diazoxide-associated severe cardiopulmonary adverse events have been reported, including 5 cases reported to the FDA. These cases include 12 PHTN, 8 congestive heart failure, and 12 hypertrophic cardiomyopathy cases. Most cases occurred within 12 weeks of diazoxide initiation at usual doses and resolved within 2 weeks of diazoxide discontinuation. Suggested etiologies of PHTN and congestive heart failure include diazoxide-induced fluid overload and direct cardiopulmonary toxicity. Hypertrophic cardiomyopathy may be due to direct toxicity or underlying hyperinsulinism. Our center recently began routine echocardiographic PHTN screening in addition to providing diuretic prophylaxis to all infants receiving diazoxide. Diazoxide-induced cardiac events are rare but life-threatening. Although some institutions undertake screening and prophylactic measures, lack of research in this area prevents informed decision-making. We propose that collaborative research into the epidemiology of these adverse events is a first step to rational prevention and screening.
Oral Abstract 3
High Incidence of Early Microvascular Complications in a Cohort of Haitian Children and Adolescents with Diabetes

M A R I E - E V E R O B I N S O N 1, E I R I N C A R O L A N 2, M I C H E L E S A I N V I L 3, K E T L Y A L T E N O R 4, V I V I A N E L O R G E A T 5, C H R I S T O P H E R C A R P E N T E R 6, R I C B O N N E L L 7, J U L I A V O N O E T T I N G E N 1. 1) Department of Pediatrics, Division of Endocrinology, McGill University, Montreal, QC, Canada. 2) Department of Pediatrics, Division of Endocrinology, University College Dublin, Dublin 4, Ireland. 3) University of Massachusetts Medical School, Boston, Massachusetts, USA. 4) Kay Mackenson Clinic, Pierre Payen, Haiti. 5) RN, Kay Mackenson Clinic, Pierre Payen, Haiti. 6) Department of Pediatrics, University of California, San Francisco, California, USA. 7) Department of Pediatrics, Division of Emergency Medicine, University of Texas at Austin, Austin, Texas, USA.

Background:
Data on microvascular complications of diabetes in children of African ancestry living in resource-limited settings are limited, and none have been reported from Haiti.

Methods:
Cross-sectional retrospective review of pediatric patients with diabetes referred to a pediatric chronic disease center in Haiti, from 12/01/2012-11/01/2016. Data collection included demographic and anthropometric information, total daily insulin dose (TDD) in IU/kg, timing and result of eye examination by a local ophthalmologist, peripheral neuropathy assessment, point-of-care HbA1c and spot AM urine microalbumin-to-creatinine ratio (Siemens DCA Vantage).

Results:
Of 67 patients (53.7% female, mean age at diagnosis 14.6±3.9 years, mean diabetes duration 3.3±3.0 years, mean HbA1c 9.8±2.0%, mean current insulin requirement 0.49±0.28 IU/kg/day), diabetic retinopathy was diagnosed in 10/57 (17.5%), cataracts in 10/62 (16.1%), microalbuminuria in 8/49 (16.3%), and peripheral neuropathy in 4/47 (8.5%) at a mean age of 19.0±4.3, 19.1±3.3, 19.5±2.5, and 24.8±3.7 years, respectively. Diabetes duration was 4.9±5.4, 3.0±1.5, 4.1±3.5 years and 7.6±6.8 years at the time of diagnosis of retinopathy, cataracts, microalbuminuria and peripheral neuropathy, respectively. At least one diabetic complication was present in 25 (37.7%) patients at a mean age of 19±3.5 years and mean diabetes duration of 3.9±3.6 years. Two patients had both retinopathy and cataracts and one patient had retinopathy and microalbuminuria. A TDD <0.5 IU/kg/day after ≥4 years of diabetes duration was marginally associated with development of any complication (p=0.05). In adjusted regression models, age at complication, diabetes duration, insulin requirement, sex and mean HbA1c did not predict development of any single complication, although in the model predicting any complication, diabetes duration was a significant predictor (p<0.009).

Conclusions:
In this cohort of Haitian children and adolescents with diabetes living in a resource-limited setting, microvascular complications and cataracts occur prematurely and as early as at diagnosis. Metabolic control alone does not explain this phenomenon. Low insulin requirements years after diagnosis, possibly allowing for prolonged undetected hyperglycemia pre-diagnosis, may associate with complication risk. The phenotypes and natural evolution of diabetes in pediatric populations of African ancestry may be distinct and need further investigation. Ophthalmologic evaluation should start at diagnosis and screening guidelines may need to be adapted.
Oral Abstract 4  
Experiences of a Tertiary Care Centre after Implementation of CALIPER Reference Intervals for Thyroid Function Tests

HARPREET GILL, ALEXANDRA AHMET, ELLEN GOLDBLOOM, SARAH LAWRENCE, MATTHEW HENDERSON. Department of Paediatrics, Division of Endocrinology and Department of Laboratory Medicine, Children’s Hospital of Eastern Ontario, Ottawa, ON.

Background:  
In March 2016, the reference intervals (RI) for Thyroid Stimulating Hormone (TSH) and Free Thyroxine (FT4) were updated at the Children’s Hospital of Eastern Ontario (CHEO) based on CALIPER, a national evidence-based initiative aimed at providing paediatric laboratory RI. Adoption of the CALIPER RI led to a marked rise in the number of abnormal TSH and FT4 levels, prompting a systematic review of these RI.

Analysis:  
Two years of historical TSH and FT4 values (n=6813) at CHEO were analyzed to quantify the impact of the RI change. Comparison of previous RI to CALIPER showed an increase in the number of abnormal TSH results from 12.7% to 20.7% and abnormal FT4 results from 11.2% to 19.6%. The majority of the FT4 values flagged as high based on CALIPER RI were not associated with suppressed TSH values. In a retrospective review of positive congenital hypothyroid newborn screen results retrieved through CHEO, 41% of neonates previously classified as unaffected on confirmatory testing would have required repeat laboratory testing based on CALIPER RI. 16% of affected neonates would have been reclassified from compensated to overt hypothyroidism.

RI Modification:  
The RI were systematically re-evaluated. CALIPER reported a single TSH RI for ages 0-12 years on the Beckman-Coulter immunoassay. This led to the use of alternative datasets for finer age-based stratification. The previous CHEO RI were retained for day-of-life 0-3. A Quebec dataset was used for day-of-life 3-25. For 25 days to 12 years, TSH ranges were appropriated from CALIPER data, using the confidence interval outer limits for the upper and lower RI. Specifically, the CALIPER RI of 0.79 (90% CI 0.74-0.91) to 5.85 (90% CI 5.53-6.23) mIU/L was appropriated to 0.74-6.23 mIU/L. For ages 12-18 years, Beckman DxI Adult RI were used. For FT4 RI, CALIPER data was appropriated as described above.

Conclusion:  
Application of CALIPER RI for TSH and FT4 at CHEO resulted in an unexpected increase in abnormal results that were often not clinically congruent. The 90% confidence intervals of the published CALIPER RI and patient data were used to guide modifications to achieve more clinically relevant RI. Ongoing evaluation is required to validate these new RI.
Oral Abstract 5
Single Allele PCSK1 Gene Mutation Found in a Child with Early Onset Obesity, Endocrinopathies and Diarrhea

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We present a three-year-old boy who initially came to medical attention for failure to thrive during the first 15 years of life and stool pattern that fluctuated between periods of constipation and diarrhea. Endoscopy revealed mild villous atrophy and biopsy showed lymphoplasmacytic infiltrates but no other gastroenterological pathology to account for his symptoms. Calorimetry test indicated normal metabolic demands, and metabolic and immunological investigations did not uncover a diagnosis. The patient was subsequently diagnosed with growth hormone deficiency and central hypothyroidism, and hormone replacements were initiated. By age 15, the patient developed hyperphagia, requiring management with food limitation and referral to an early childhood weight management program. Correspondingly, the patient’s BMI Z-score progressed from -3.83 (at 6 month) to 1.76 (at 3 years 3 months). MRI of the brain did not reveal abnormalities in the pituitary gland or hypothalamus. Genetic testing for Prader Willi Syndrome and Russel Silver Syndrome were negative. Given the clinical features, the patient was tested for Proprotein Convertase 1/3 deficiency. Proprotein convertase 1/3 deficiency is a rare monogenetic disorder marked by early childhood obesity, endocrinopathies and malabsorptive diarrhea. It carries an autosomal recessive inheritance through inactivating mutations of the PCSK1 gene. The patient’s blood work did not show an elevated proinsulin levels (<7.5 pmol/L) but this was under a relatively nutritionally-deprived state (glucose 3.7 mmol/L, insulin 1 pmol/L and C-peptide 42 pmol/L). Blood work post glucose load will be completed at the next clinic visit. Interestingly, the patient’s PCSK1 gene sequence analysis showed a heterozygous c.1918A>G (p.T640A) variant. Duplication analysis did not show deletion or duplication in the other allele. Traditionally, a single allelic mutation excludes the diagnosis of Prohormone Convertase 1/3 Deficiency. However, more recent studies have demonstrated that certain single allelic mutations can lead to dominant negative effects where the mutant enzymes inhibit the wild-type enzymes, generating partial phenotypes. While our patient’s mutation is located on a part of the protein that is not known to induce the dominant-negative effect, it raises the possibility of potentially novel and unidentified mechanisms that PCSK1 gene mutations can lead to obesity and endocrinopathies as seen in our patient.
Evaluation of the Effectiveness of a Pediatric Endocrinology Education Program for Haiti (PEEP-H): A Preliminary Report

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Background:
There is currently no pediatric endocrinologist in Haiti and endocrine training is not part of pediatric residency curricula, a problem faced by many resource-limited countries.

Methods:
The Progarme d’Éducation en Endocrinologie Pédiaitrique-Haiti (PEEP-H), supported by the Pediatric Endocrine Society (PES) and the European Society for Pediatric Endocrinology (ESPE), was developed in collaboration with Haiti’s pediatric residency programs, medical schools, professional organizations and the ministry of health, to establish pediatric endocrinology training in Haiti. Initially focusing on two pediatric residency programs, a two-year curriculum is taught during bi-monthly onsite training visits by a rotating body of francophone pediatric endocrinologists. Monthly teleconferences, e-learning and a remote consultation platform supplement the training. Using a prospective cohort study design, we collected participants’ demographic information, and evaluated the impact of PEEP-H by means of pre/post training examinations, and quantitative and qualitative evaluation.

Results:
Four onsite visits were held for 54 trainees between March-October 2016. Residents were in their first, second and third year of training or were pediatricians in 17, 48, 26 and 7%, respectively. Ninety percent had completed medical school in Haiti and 7.5% had previously participated in a pediatric endocrinology rotation. More than 60% evaluated their knowledge in 8 different areas of pediatric endocrinology as insufficient or fair: On a scale of 1 (insufficient) to 5 (excellent), the mean rating was 1.7±0.8. Knowledge in diabetes (2.4±0.9) and hypoglycemia (2.3±0.9) was evaluated significantly higher compared to all other areas (p<0.001). Mean examination scores ranged between 37-45% before and 62-65% after onsite training, with mean percentage increments ranging from 16.6 to 27.8%. Thirty-six Haitian trainees and 11 pediatric endocrinologists from three different countries registered on the consultation platform. Twelve cases were discussed, and 95 messages exchanged. Trainees positively evaluated training and consultation interactions.

Discussion:
Pediatric residents in Haiti subjectively and objectively have insufficient pediatric endocrine knowledge. Knowledge level improves following PEEP-H training, and trainees see benefit in the training modules offered. While interim results are encouraging, long-term evaluation is needed to assess the program’s value and potential as a subspecialty training model for additional specialties and other resource-limited settings.
Oral Abstract 7  
Children with Idiopathic Isolated Growth Hormone Deficiency Rarely Develop Additional Pituitary Deficiencies

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Growth hormone deficiency (GHD) in children can be isolated or present with multiple pituitary hormone deficiencies (MPHD). Children diagnosed with isolated GHD are followed for the development of MPHD with routine screening. Studies have shown that MPHD develops more frequently in patients with isolated GHD due to organic causes than in patients with idiopathic isolated GHD. These data suggest that routine laboratory screening for MPHD in children with idiopathic isolated GHD may not be required. To further address this, we performed a retrospective analysis of all patients diagnosed with idiopathic isolated GHD and treated with growth hormone at our tertiary care children's hospital since 2005. Subjects were excluded if their GHD was the result of an acquired cause or a congenital disorder known to be associated with pituitary abnormalities. Determination of an additional hormone deficiency was made once the treating physician started corresponding hormone replacement. 141 subjects (46 female) were included with 588 total years on GH replacement (mean 50.0 [19.9-131.6] months). MPHD was diagnosed in 6 subjects (4.3%). Central hypothyroidism developed in 4 subjects (2.8%), with diagnosis between 33.4-75.7 months after GH start. Hypogonadotropic hypogonadism was seen in 3 subjects (2.1%), ranging from 22.1-102.7 months after GH start. One subject developed both central hypothyroidism and hypogonadotropic hypogonadism. No subject developed ACTH deficiency or central diabetes insipidus. Investigation of predictive factors revealed that the average length on GH treatment for the MPHD group was 75.4 months compared to 48.9 months in the non-MPHD group (p = 0.01). MPHD was seen in 1/78 (1.3%) subjects with normal hypothalamus-pituitary development on MRI and in 5/33 (15.2%) of those with MRI abnormalities, such as ectopic posterior pituitary or cystic lesion (p = 0.009). There was a trend toward development of MPHD among females (OR 4.4, 95% CI 0.8-25.1) and those with lower peak GH level on stimulation (OR 4.3 for GH <2 ng/ mL, 95% CI 0.7-25.8). Overall, the development of MPHD in this cohort of children with isolated idiopathic GHD was uncommon. This study further questions routine laboratory screening in patients with isolated GHD, particularly in those with a normal MRI.
Oral Abstract 8
Age-Dependent Distinctions in Presentation, Treatment and Outcomes of Differentiated Thyroid Carcinoma in Children and Adolescents

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Thyroid carcinoma is the most common endocrine cancer, and is anticipated to become the second leading cancer site in women by 2030. In children, the incidence of thyroid cancer is also increasing, yet this remains a poorly studied area. The incidence of thyroid cancer in childhood varies with age, with a sharp increase and female predominance emerging around the onset of puberty. This retrospective case series describes the clinical features, treatment and outcomes of nodular thyroid disease and differentiated thyroid cancer (DTC) in children 18 years and under, and compares children under 12 to children ages 12 to 18. The study population included patients at a single tertiary-care hospital who underwent thyroid biopsy or surgery between 1992 and 2012. There was a significantly higher female to male ratio in patients 12-18 years with benign and malignant nodules compared to those under 12. There was no difference across age groups with respect to cytology or histology, size, surgical approach or nodal status. Younger patients had a higher lymph node ratio. Younger patients received a higher cumulative dose of radioactive iodine (99 mCi/m2) versus older patients (72 mCi/m2), although the difference did not achieve significance. Outcomes of patients with malignant disease also differed between the age groups: while a similar proportion achieved a state of “no evidence of disease”, fewer of the younger children remained disease-free. These results suggest that, despite comparable initial disease burden and treatment, younger children have poorer outcomes, and thus may warrant intensification of primary therapy.
Oral Abstract 9
A Closer Look at Rickets in Manitoba

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Introduction:
Vitamin D is essential for adequate bone health and calcium homeostasis. Despite preventative strategies, vitamin D deficient rickets remains a current Canadian problem. A previous national study found the annual Canadian incidence rate of rickets to be 2.9/100,000. A recent study in the province of Quebec found a sharp increase in incidence cumulating in annual incidence of 7.9 per 100,000 live births in 2009. Moreover, there is concern that the true incidence of nutritional rickets is underestimated. The primary objective of this study is to determine the annual incidence of rickets in Manitoba and to determine if this has increased over the past decade. Secondarily, we are interested in determining the age and manifestations of those presenting with severe nutritional vitamin D deficiency.

Methods:
This is a retrospective chart review to determine confirmed cases of vitamin D deficiency rickets at the Children’s Hospital of Winnipeg and its catchment area (Manitoba, NW Ontario and W. Nunavut) from 2003 – 2014. The sources used included Endocrine and hospital charts using ICD-9 and -10 coding, hospital radiology reports, using the word ‘rickets’, and biochemical testing. For the latter, low 25-hydroxy vitamin D tests from 2006-2014 were partnered with chart data to identify cases of nutritional rickets.

Results:
Preliminary results demonstrate 3.8 cases identified per year (~23 cases per 100,000 live births). About 1/3 (14/45) presented early with hypocalcemic seizures, with an average age of presentation of 11.7 weeks. Half (20/45) presented with bony abnormalities seen clinically and confirmed radiologically; (average age 4.5 years). Risk factors for rickets included, but were not limited to a maternal history of type 2 diabetes or gestational diabetes. Additionally, nearly half of affected children were of self-declared First Nations’ heritage. No temporal trend was identified (p > 0.4).

Conclusion:
Nutritional vitamin D deficient rickets remains a problem in our catchment area, especially within certain high-risk groups. Strong preventative strategies are paramount. Besides initiating convenient infant vitamin D supplements (drop format) at birth, clearly improved maternal vitamin D status is essential.
Oral Abstract 10
Pseudoacromegaly in the Pediatric Population

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Introduction:
Pseudoacromegaly is a rare presentation in the pediatric population. We present a case series of two patients displaying excessive growth consistent with pseudoacromegaly and acanthosis nigricans associated with marked hyperinsulinemia. While adult literature focuses primarily on the comorbid metabolic dysregulation, the impact of this condition on excessive growth leads to major psychosocial burden.

Cases:
Both patients, of First Nations descent, presented with excessive growth – patient one (male) at age 3 years 11 months (height 118cm, Z-score +3.75; BMI 28.3, Z-score +5.26) and patient two (female) at 9 years 0 months (height 168.5cm, Z-score 5.15; BMI 34.7, Z-score +2.75). Both patients had normal serial IGF-1 levels and appropriate GH suppression by OGTT with pre-pubertal growth velocities exceeding 9.5cm/year. Fasting insulin (>1100 pmol/ L; normal 43-194) and C-peptide levels were markedly elevated. Patient one had a final adult height of 201cm; patient’s two current height (at age 9y11mo; Tanner 2; bone age 12 years) is 175.8cm; both markedly exceed their mid-parental heights. Patient one’s clinical course was complicated by type 2 diabetes (DM2), hidradenitis suppurativa with skin infections, and infective endocarditis of the aortic valve with post-surgical complications. Patient two has recently developed DM 2. Both patients have suffered significant skin breakdown and infections in the thickness of their acanthosis. Furthermore, each patient desired treatments to blunt their growth.

Discussion:
Pediatric patients with pseudoacromegaly achieve heights well above genetic prediction potentially leading to psychosocial difficulties. Unlike adults with acromegaly, whose linear growth has ceased, the implications in adolescence prompts consideration for therapies to reduce the growth rate. Additionally, the marked hyperinsulinemia/insulin resistance potentiates DM 2 risk and other metabolic disturbances. Insulin receptor defects have been suggested as potential mechanisms, though an underlying genetic defect is rarely found. First Nations background appears to be a risk factor and this heavily applies to our Saskatchewan population. Aside from insulin sensitizing agents, no definitive treatments exist to correct the marked insulin resistance; treatments to reduce further linear growth, such as early pubertal induction or growth plate disruption, are burdensome with comorbidity. Given our population, we expect to see further cases that push us to identify therapeutic options.
Oral Abstract 11

The Impact of the Social Determinants of Health on Renal Function in Adolescents with Type 1 Diabetes

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Background:
The social determinants of health (SDH) are associated with poorer management and outcomes for young patients with type 1 diabetes, including poorer glycemic control and cardiovascular health. This study examined the relationship between SDH and renal function in adolescent T1D patients.

Methods:
The Ontario Marginalization Index (ON-Marg) was used as a neighbourhood-level measure of SDH and linked to participants using de-identified postal codes. Participants (N=199) were stratified into quintiles (most deprived = Q5, least deprived = Q1) across four SDH dimensions: material deprivation, ethnic concentration, residential instability, and dependency. Quintile scores were averaged to determine composite ON-Marg scores. Primary outcomes were estimated glomerular filtration rate (eGFR) and albumin-creatinine excretion ratio (ACR). Secondary outcomes assessed urinary and serum levels of 15 pre-selected inflammatory markers. Patient characteristics, renal parameters and inflammatory markers were compared between patients from the most (Q4/Q5) and least deprived (Q1/Q2) neighbourhoods. Step-wise multiple linear regression was used to develop a model to evaluate SDH and variables of interest.

Results:
Subjects had a mean age of 14.4±1.7 years with duration of diabetes of 7.2±3.1 years. eGFR was significantly higher in patients from neighbourhoods with greater ethnic concentration (r=0.197, p=0.0053) and dependency (r=0.146, p=0.040). There was a highly significant association between eGFR and ON-Marg summary score (r=0.249, p<0.001) which remained when controlling for age, BMI, gender, HbA1c, SBP, and ethnicity in linear regression. Significant associations were not seen with ACR. Levels of 6 out of 15 key urinary inflammatory markers and 5 out of 15 serum markers were higher in patients from neighbourhoods with increased marginalization.

Conclusions:
Measures of SDH were correlated with higher eGFR which may be a marker of early renal risk in T1D. Changes in inflammatory markers were also associated with SDH in patterns similar to those observed in hyperfiltration and diabetic nephropathy. This study highlights the impact of social factors in pediatric diabetes care.
Primary Amenorrhea due to Müllerian Agenesis in a Girl with Cat Eye Syndrome: Case Report and Review of the Literature

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Cat eye syndrome (CES) is a rare chromosomal syndrome with an estimated incidence of 1:50,000 – 1:150,000. The most common underlying chromosomal anomaly found in CES patients is tetrasomy of the proximal region of 22q11 in form of a supernumerary isodicentric chromosome 22 (pter --> q11.2::q11.2 --> pter). The phenotype is characterized by ocular colobomata, pre-auricular ear pits/tags and anal atresia. Other clinical findings reported include congenital cardiac defects and renal anomalies. To our knowledge, only one case of CES with the finding of Müllerian agenesis has been previously reported in the literature. We present a 16-year-old girl who was referred for primary amenorrhea. Physical exam was normal female with Tanner V staging for both breast and pubic hair development. Other findings included bilateral ocular colobomata, facial asymmetry and a pre-auricular skin tag. Biochemical testing showed normal pubertal levels of FSH, LH and estradiol. Pregnancy screening was negative. Pelvic MRI showed absence of the uterus and upper two thirds of the vagina. Chromosomal microarray analysis detected a gain of material from chromosome region 22q11.11-q11.12 resulting in 4 copies of that region. Further analysis with G-Banding confirmed the presence of a supernumerary bisatellited isodicentric marker chromosome. The size of the gain is at least 1,740 KB. The distal breakpoint is proximal to the 22q11.2 microdeletion (velocardiofacial/ DiGeorge) critical region. Although the tetrasomic region in this case is proximal to the velocardiofacial/ Di George critical region, the finding of Müllerian agenesis associated with CES is interesting given multiple case reports of Müllerian agenesis (Mayer-Rokitansky-Küster-Hauser syndrome) in 22q11.2 microdeletion carriers. To date, no gene(s) in the 22q11 region have been implicated in the formation of Müllerian structures. However, accumulating evidence from case reports supports the possibility of a gene, or genes, relevant to Müllerian development at this locus. In conclusion, pelvic imaging to rule out Müllerian agenesis should be part of the clinical work up in patients with CES to facilitate further genetic counseling and medical care.
Poster Abstract 1
Two Brothers with Isolated Primary Adrenal Insufficiency

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A 16 year old male with a two year history of progressive skin hyperpigmentation and gradual hair-thinning presented to hospital twice with nausea, vomiting, weight loss and low mood. Review of systems was otherwise unremarkable, including absence of neurologic symptoms. Blood work showed an elevated ACTH and renin, low morning cortisol and mild hyponatremia. AI was subsequently confirmed with an ACTH stimulation test and the patient was started on hydrocortisone. Due to hyponatremia and hyperreninemia, fludrocortisone was also started for mild mineralocorticoid deficiency. Investigations for an underlying etiology showed negative adrenal antibodies but elevated serum very long-chain fatty acids (VLCFA), consistent with a diagnosis of X-Linked Adrenoleukodystrophy (X-ALD). Genetic testing was sent for ABCD1 gene analysis to confirm the diagnosis. MRI brain looking for evidence of cerebral demyelination was normal. Subsequently, the patient’s 12-year-old brother, who also had a history of hair loss, mild skin hyperpigmentation and no neurologic symptoms, was found to have AI and a VLCFA panel is pending. X-ALD is a peroxisomal disorder caused by a mutation in the ABCD1 gene on the X-chromosome which results in accumulation of VLCFA in a variety of organs. There is no genotype-phenotype correlation and the clinical presentation is broad, ranging from isolated AI to a slowly progressive myelopathy to a devastating cerebral demyelination. X-ALD can present anytime from early childhood to adulthood. Although nearly all males will eventually develop neurologic manifestations, many will present initially with isolated AI, as illustrated by this case. Endocrinologists should be aware of this diagnosis and consider testing for it in males of all ages presenting with AI, even in the absence of neurologic manifestations. Patients should be screened with a VLCFA panel and the diagnosis confirmed by ABCD1 gene analysis. Siblings should be tested, including females who can develop a progressive myelopathy in adulthood (although AI is rare in heterozygous females). Patients with X-ALD require serial MRIs to monitor for evidence of cerebral X-ALD as this may be an indication for stem cell transplantation, the outcomes of which are significantly better in the earliest stages of disease.
Poster Abstract 2

Intermittent Secretory Diarrhea and Profound Hypotension in an Adolescent with a Vasoactive Intestinal Polypeptide Pancreatic Tumor (VIPoma)

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Case presentation:
We present the case of a 13 year-old female referred to Endocrinology during a second hospitalization for secretory diarrhea (>9L/ day) resulting in volume depletion with metabolic acidosis and acute kidney injury (creatinine 414 umol/ L). She was also noted to have hypokalemia (3.0 mmol/ L), and mild hypercalcemia (3.0 mmol/ L) with a normal PTH level of 1.7 pmol/ L. Although initially diagnosed and treated as MRSA enterocolitis during her first admission, a thorough gastrointestinal evaluation for infectious, autoimmune and inflammatory disease was negative during the second presentation 2 weeks later. 24-hour urine collection for catecholamines, metanephrines, and 5-hydroxyindoleacetae were normal. Gastrin and prolactin levels were normal. Notably, the plasma VIP was elevated at 1105 pg/ mol (normal < 75) as was the chromogranin A at 159 ug/ L (normal < less 94). CT and MRI identified a 4.5 cm mass in the pancreatic tail, with no evidence of metastases. F-dopa PET scanning could not be performed because of lack of isotope availability. She experienced profound hypotension and urticaria upon anesthetic induction with rocuronium, not deemed to be anaphylactic (low tryptase level), resulting in 24-hour ICU admission for inotropic support and surgical postponement. While waiting for surgery to be rescheduled, she was admitted for a third episode of secretory diarrhea successfully treated with octreotide 100 ug SQ every 8 hours. Cisatracurium was subsequently used as the anesthetic agent, along with an octreotide infusion of 100 ug/ hour intraoperatively during tumor manipulation to control VIP effects. Histopathology and genetic analysis for MEN1 are pending.

Conclusion:
We report the first Canadian case of an adolescent with a VIPoma presenting with intermittent secretory diarrhea. This case highlights that, in addition to its effects on the gut, VIP has biological effects on the vasculature likely responsible for the profound hypotension seen in this patient, that promptly responded to somatostatin analogs.
Poster Abstract 3
Sirolimus in Treatment of Three Infants with Diffuse Type of Congenital Hyperinsulinism

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Congenital hyperinsulinism which is known as persistent hyperinsulinemia hypoglycemia of infancy is one of the most common causes of recurrent severe hypoglycemia in early infancy. It is characterized by dysregulation of insulin secretion from beta cell of the pancreas in relation to blood glucose level. Worldwide, the incidence of congenital hyperinsulinism is estimated as 1: 50,000 life birth but in Saudi Arabia due to high consanguinity rate, it was reported as common as 1:2675 life birth. The genetic of congenital hyperinsulinemia showed predominant mutation in K ATP channel including ABCC8, KCNJ11 gene with 55% rate among all congenital hyperinsulinism. Among KATP mutation, homozygous mutation in ABCC8 gene was reported as the commonest mutation (81%) in Saudi children from western Saudi region. Different treatment modality was used in the management of congenital hyperinsulinism including diazoxide, octreotide, calcium channel blocker and surgery. The response to the treatment was influenced mainly by the underlying genetic mutation and the histopathology. Recent data was raising regarding the treatment of refractory hyperinsulinism using M TOR inhibitor. The response to M TOR inhibitor that has been reported was euoglycemia, pancreatectomy avoidance and this response has been sustained during 1 year follow up. Case Description: We tried Sirolimus in three infants with diffuse CHI. Diagnosis was confirmed clinically, biochemically and by gene test (mutations involve KCNJ11, ABCC8, KCNJ11 in infants 1, 2, 3, respectively) in which all mutations are in homozygous state. Each infant had received the therapy for about two months with close monitoring to the blood glucose, insulin, c-peptide level and Sirolimus side effects. All the three infants did not respond to the therapy with poor glycemic control, intractable hypoglycemia and non-suppressed insulin and c-peptide level.

Conclusion:
We suggest that Sirolimus in treatment of severe mutation (homozygous) might not be as effective as in treatment of heterozygous or compound heterozygous type of CHI.
Poster Abstract 4
Interventions Using Pediatric Diabetes Registry Data for Quality Improvement: A Systematic Review

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Background:
Quality improvement (QI) interventions that use registry data in adult diabetes care are associated with improved glycemic control, reduced emergency department visits and hospitalizations, and improvement in other quality indicators. The effectiveness of QI interventions that use pediatric diabetes registry data has not been studied. The aim of this project is to conduct a systematic review to characterize QI interventions that use pediatric diabetes registry data and to determine their effect on care processes, organization of care, and patient outcomes.

Methods:
We searched Medline, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials (from inception to October 13, 2016). We also conducted a grey literature search using Google, Google Scholar, the Directory of Open Access Journals, and known diabetes registry websites. We included studies that met both of the following criteria: 1) evaluated the impact of a QI intervention for diabetes management on care processes, organization of care, or patient outcomes and 2) used pediatric (<21 years) diabetes registry data in the intervention or to evaluate outcomes. We included all study designs. Two reviewers independently assessed studies for eligibility, extracted data, and assessed the risk of bias.

Results:
Of the 1213 studies identified, 11 met inclusion criteria. One additional study from the grey literature review was included. After removing duplicates, 985 studies were excluded because they either did not evaluate a QI intervention or use registry data. Four studies were excluded because they did not include pediatric data and two did not evaluate the impact of an intervention on diabetes management. Data extraction is in process and results will be available prior to February 2017.

Discussion:
We identified a small number of studies that used pediatric diabetes registry data as part of a QI intervention. The results of our study will illuminate how pediatric diabetes registry data are being used for QI, and the impact on care processes, organization of care, and patient outcomes. We anticipate these findings will generate new evidence that will support or discourage the development of new registries for QI, and inform optimal use of existing registry data for QI purposes.
Impact of Neighbourhood-Level Inequity on Paediatric Diabetes Care

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Aims:
To evaluate the association between neighbourhood-level inequity and glycaemic control in paediatric subjects with type 1 diabetes using the Neighbourhood Equity Index (NEI).

Methods:
NEI was linked to the clinical data of 519 children with diabetes followed at the Hospital for Sick Children (Toronto, Canada). The NEI is a composite measure of inequity developed using the World Health Organization’s Urban Health Equity Assessment and Response Tool (HEART) that encompasses 15 weighted indicators evaluating economic, social, environmental and lifestyle factors. The geographic distribution of participants was determined using postal codes, and the relationship between Hemoglobin-A1c (HbA1c) and NEI was evaluated using regression and spatial analysis techniques.

Results:
Mean HbA1c of subjects was significantly correlated with NEI (R=-0.24, P<0.0001). Regression analysis demonstrated NEI was a strong predictor of mean HbA1c (P<0.0001), accounting for differences in HbA1c as large as 10% (11 mmol/mol) when controlled for age, sex, diabetes duration, insulin pump therapy, and number of annual clinic visits. Geo-mapping using spatial scan testing revealed the presence of two clusters of low equity neighbourhoods containing 3.22 (P=0.001) and 2.83 (P=0.02) times more subjects with HbA1c ≥ 9.5% (80 mmol/mol) than expected.

Conclusion:
Our findings demonstrated NEI was a strong predictor of HbA1c in our clinic population, providing evidence that a composite, urban-based measure of inequity is well suited for the study of glycaemic control and diabetes-related factors to identify relative inequities in health status on a local level.
Poster Abstract 6  
A 9-Day Old Boy with Sodium Wasting and Hyperkalemia: Not Always 21-Hydroxylase Deficiency!

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Introduction:
Congenital adrenal hyperplasia due to 21hydroxylase deficiency is the commonest, but not the only, cause of salt wasting in neonates.

Case presentation:
This boy is the offspring of first cousins of Lebanese origin and was born weighing 3.680 kg. At 9 days, he was referred because of weight loss. Indeed, he weighed 3.230 kg and he was wasted and dehydrated. The external genitalia were normal but the scrotum was hyperpigmented. After IV rehydration, blood pressure was 75/47 mm Hg. There were no dysmorphic features. Serum sodium was 128 mEq/L and potassium 8.9 mEq/L. Urine sodium was 91 mEq/L. Serum cortisol was 513.9 nmol/L, DHEAS 113 µmol/L and testosterone 3.9 nmol/L. A presumptive diagnosis of 21hydroxylase deficiency was made; the serum cortisol was considered low for the level of stress. Treatment was started with hydrocortisone (20 mg/m2.day), fludrocortisone (0.05, then 0.1 mg die) and NaCl (4 mEq/kg.day). Upon receipt of the normal serum androstenedione (8.1 nmol/L) and 17 OH progesterone (7.2 nmol/L), the diagnosis was revised to primary adrenal insufficiency. At one month of age, the adrenals were small on ultrasound. Serum ACTH and renin were not measured before treatment and were normal and high, respectively, during treatment. A search for the cause of primary adrenal insufficiency was negative: comparative genomic hybridization was normal, as were the sequences of NROB1 and CDKN1C. Finally, exome sequencing of the proband revealed a novel homozygous mutation in CYP11B2 (Asn201Asp, Polyphen score 0.589, possibly damaging). This established the diagnosis or aldosterone synthase deficiency and allowed hydrocortisone to be progressively stopped. At 2 years of age, low dose ACTH stimulation evoked a rise in serum cortisol from 357 to 473 nmol/L.

Conclusion and Teaching Points:
a) Causes other than 21hydroxylase deficiency should be kept in mind in salt wasting newborns.
b) Hyperpigmentation may be difficult to evaluate in dehydrated infants of non-Caucasian ethnicity.
c) Results that do not fit, such as the initial serum cortisol, should not be overlooked.
d) Exome sequencing is a powerful technique for establishing the correct diagnosis in atypical presentations and led to simplifying treatment in this case.
Poster Abstract 7
Sub-Q T Is It for Me? Reviewing the Increasing Use of Subcutaneous Testosterone Injections

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Background:
Through collaboration within the Canadian Pediatric Endocrine Nurses (CPEN) network it has become evident that there are differences in practices in the use of injectable testosterone for hypogonadal and transgender males. Some clinics in Canada offer Testosterone injections subcutaneously following a pilot study conducted at McGill University Health Center in 2006 reporting its safe use and efficacy.

Purpose:
CPEN Nurses across 15 clinical centers in Canada have explored current prescribing, monitoring and teaching practices for injectable testosterone through an online survey. Results of this survey, patient reports and a review of the current literature will inform future best practice as it relates to injectable testosterone in youth.

Description of Topic:
administration was first described in 2006 due to the inconvenience and discomfort of monthly intramuscular dosing. Currently recommended dosing of Depot Testosterone can be divided into weekly or biweekly subcutaneous doses. Due to testosterone’s viscosity, the vial and the syringe are warmed in the patients’ palms or axilla for at least 5 minutes. This allows for easier withdrawal of the medication from the vial, quicker and more comfortable injections. We expect patients will report a preference for subcutaneous administration and may gain independence much earlier in their treatment regime.

Clinical Implications:
For youth who are requiring injectable testosterone, subcutaneous administration can lower the experiences of pain, provide more constant levels of testosterone and allow for easier self-injections. Once initial education has been completed and the patient is independent, fewer injections will need to be given by nurses or other health care providers in clinics, day units and at times pharmacies. This provides for anonymity and privacy for patients who can do the injections in the privacy of their home, thus decreasing the need to answer potentially unwanted questions especially for the transgender youth.
Poster Abstract 8
X-Linked Congenital Adrenal Hypoplasia in an Infant Presenting with Cholelithiasis and Atypical Biochemical Results

ROBYN LEDREW, KARINE KHATCHADOURIAN. Department of Pediatrics, Division of Endocrinology, University of Ottawa, Ottawa, ON

Background:
X-linked congenital adrenal hypoplasia caused by mutation in NR0B1 presents commonly in infancy with symptoms and signs of adrenal insufficiency.

Case:
A male infant born at term to healthy, non-consanguineous parents was admitted to hospital at 4 weeks of age for failure to thrive. On exam he had mild skin hyperpigmentation and normal male genitalia. Mother reported borderline low estriol levels on pre-natal screen. Newborn screening was negative. Investigations revealed: hyponatremia (Na+ 125 mmol/ L), hyperkalemia (K+ 6.4 mmol/ L), unconjugated hyperbilirubinemia and transaminitis. Abdominal ultrasound showed cholelithiasis with non-visualization of adrenal glands. Subsequent investigations included: baseline cortisol 232 nmol/ L, ACTH 94 pmol/ L, renin activity 104.9 (<14 ng/ Ls), ACTH stimulated peak cortisol 323 nmol/ L, 17-OHP 4.2 (3.2-22 nmol/ L), 11-deoxycortisol 99.1 (<2.6 nmol/ L), DHEAS 0.4 (0.1-8.7 umol/ L), and total testosterone 4.2 (0.3-9.9 nmol/ L). At 5.5 weeks of age, he was started on hydrocortisone, fludrocortisone and sodium chloride. Feeding and weight gain improved. Repeat abdominal ultrasound at 8 weeks of age showed cholelithiasis had resolved. Bilateral adrenal glands were visualized but small. By 9 weeks of age, liver enzymes normalized. Molecular testing confirmed he was hemizygous in the NR0B1 gene for a missense mutation (p.Leu262Pro) previously described in two other patients presenting with typical signs of adrenal insufficiency.

Discussion:
This case demonstrates the phenotypic heterogeneity of the condition, even in those with the same genotype. Our case also highlights the following: isolated cortisol deficiency may be a rare cause of neonatal cholestasis, and elevated 11-deoxycortisol level seen usually in 11β-hydroxylase deficiency, could also raise concern for congenital adrenal hypoplasia.
Poster Abstract 9
A Heterozygous Intragenic Deletion of Exons 3-6 in the Insulin-Like Growth Factor 1 Receptor Gene: A Possible Cause of Postnatal Growth Restriction and Short Stature

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Introduction:
Heterozygous microdeletions in chromosome 15q, which encompasses the IGF1R gene (15q26.3), and intragenic deletions in IGF1R are rare causes of intrauterine and postnatal growth deficits. They have also been associated with developmental delay, microcephaly and neuropsychiatric issues. However, the phenotype is highly variable. A few patients with deletions in IGF1R have been shown to have improved growth and normal adult heights when treated with recombinant human growth hormone (hGH) therapy. We present a case of a toddler discovered to have a heterozygous microdeletion in IGF1R.

Case presentation:
Our patient was born at term, from a pregnancy complicated by poorly controlled type 1 diabetes and polysubstance abuse. Her birth weight was 3.9 kg (92%-ile). She was apprehended at birth, and had poor feeding, requiring nasogastric tube feeding for the first six weeks of life. There was no hypoglycemia. At one month of age, her weight was 3.6 kg (14 %-ile), length 50.5 cm (5 %-ile). At 12 months of age, her weight and length were <1%-ile, head circumference 14 %-ile. She was referred to Endocrinology at 16 months of age for poor growth. At that time, she was healthy, developmentally appropriate, but had limited caloric intake. Reported parental heights were: mother 147.3 cm (<1 %-ile), father 162.5 cm (3 %-ile). Physical examination was remarkable only for her small size (weight and length <1%-ile; head circumference 14 %-ile). Baseline investigations included: TSH 4.28 mU/L (normal range 0.3-5.5), free T4 12 pmol/L (normal range 11-22), undetectable tissue transglutaminase antibody, normal chloride sweat test, IGF-1 145 ug/L (normal range 19-160), karyotype 46 XX. Due to ongoing poor growth, she was referred to Medical Genetics at 28 months of age. A chromosomal microarray identified a 149.5 Kb copy loss at chromosome 15q26.3, encompassing exons 3-6 of the IGF1R gene. At 3 years of age, her weight and height remain <1%-ile, BMI 3 %-ile. Her growth velocity is normal.

Conclusion:
The cause of our patient’s growth pattern is not clear, and appears to be unrelated to nutrition, or psychosocial issues. It may be secondary to the IGF1R variant and hGH therapy is being considered.
A Rare Case of Hypercalcemia in a TPN-Dependent Child

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A 7-year-old boy with type III achalasia, enteral feeding intolerance (TPN dependent for 17 months), and cyclical vomiting syndrome was admitted with respiratory distress. There was intermittent emesis and abdominal pain. Hypercalcemia was identified with total calcium (tCa) of 3.15 mmol/L (2.22-2.54) and normal albumin. There was no previously documented hypercalcemia. In the preceding six months, total daily TPN calcium was 17.87 mmol (0.60 mmol/kg/day) and daily phosphate was 23.82 mmol (0.79 mmol/kg/day). Repeat tCa was 2.76 mmol/L and ionized calcium (iCa)1.48 mmol/L (1.22-1.37). Phosphate was 143 mmol/L (1.38-1.94). PTH was low (<5 ng/L) as were 25-OH vitamin D [45 nmol/L (70-250)] and 1,25-OH-vitamin D [20 pmol/L (48-190)]. ALP was 134 U/L (151-342). Renal function was normal. Urinary calcium:creatinine ratio was elevated at 1.70. Vitamin A level was normal. Serum aluminum was elevated at 902 nmol/L (0-293). Renal ultrasound performed four months prior to admission was suggestive of nephrocalcinosis. There were no radiographic findings consistent with rickets. DEXA scan revealed an L1-L4 bone mineral density z-score of 15. PTH related peptide and bone biopsy are pending. Hypercalcemia progressed despite hyperhydration, removal of calcium and vitamin D from TPN, and eventual discontinuation of TPN. Peak hypercalcemia occurred on day 13 of admission with tCa: 3.73 mmol/L and iCa 2.01 mmol/L, Calcitonin (4 u/kg) and zolendronate (0.04mg/kg) were given. tCa and iCa normalized within 72 hours and remained normal upon resumption of calcium-containing TPN (8.7mmol/day, 0.29 mmol/kg/day). Aluminum is a known contaminant of TPN and its accumulation has been associated with metabolic bone disease. Although the specific mechanism remains unclear, aluminum is thought to bind available phosphate, inhibit PTH secretion and vitamin D activation, reduce osteoclast proliferation, and impair calcium uptake by binding to the mineralization front of bones. Hypercalcemic osteomalacia has been described in adults with renal failure exposed to aluminum in dialysis water. Transient, mild hypercalcemia has been observed in adults on long-term TPN with elevated serum aluminum. Significant persistent hypercalcemia with elevated serum aluminum in a TPN-dependent child has not been described. Bone biopsy results should help to further characterize the mechanism of this patient’s hypercalcemia.
Poster Abstract 11
Prevalence of Polycystic Ovary Syndrome in Obese Adolescents

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Background:
Polycystic ovary syndrome (PCOS) in adolescence is a challenging diagnosis and therefore has raised intense discussions. Its prevalence in childbearing age women ranges from 5 to 10%. However, the prevalence in obese adolescents has not yet been reported. Thus, we aimed to assess the prevalence and characteristics of PCOS in a population of obese adolescents followed at a quaternary hospital.

Methods:
We performed a cross-sectional study with 49 postmenarcheal obese adolescents with a mean age of 15.6 years. Anthropometric assessment and review of medical records were performed. Clinical and laboratory hyperandrogenism were evaluated using Ferriman-Gallwey index and serum androgens, respectively. The ovarian morphology was evaluated by supra-pubic pelvic ultrasound.

Results:
The prevalence of PCOS in obese adolescents, according to the Witchel, Oberfield et al. 2015 guideline for PCOS in adolescence, was 18.4%. When assessed by the Rotterdam, the Androgen Excess And PCOS Society and the National Institute of Health criteria, the prevalence of PCOS was 26.4%, 22.4% and 20.4%, respectively. Menstrual irregularity was found in 65.3% of the patients. Clinical hyperandrogenism was observed in 16.3% while 18.4% had total testosterone concentrations above the normal range. Ultrasonography revealed that 18.4% had polycystic ovaries.

Conclusion:
The prevalence of PCOS in obese adolescents is high compared to adult females observed in the literature.
Global Health Abstract 1
Managing Pediatric Cushing’s Disease in a Resource-Limited Setting: A Challenging Case From Haiti

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Background:
There is little precedent for the diagnosis and management of children with clinical signs of hypercortisolism in resource-limited countries.

Case Presentation:
A 15 year-old Haitian boy was evaluated for headaches, visual changes, obesity and visual impairment evolving over the preceding 2 years. Aside from long-standing otorrhea, personal history was non-contributory. Family history was non-contributory. On examination, blood pressure was 150/100 mm Hg (>99th percentile), heart rate 112/minute, respiratory rate 48/minute, temperature 97.4 F. Height was 144 cm (-3.2 SDS), weight 61.4 kg (+0.39 SDS) and body mass index 29.4 kg/m² (+2.44 SDS). There was bilateral supraclavicular fat pads. The face was round, the tonsils enlarged and there was left purulent otorrhea. Testicular volume was 2 cc bilaterally, penile length 5 cm and pubic hair Tanner III. Neither striae nor acne were noted. Visual field testing by confrontation revealed bitemporal hemianopsia. Proximal muscle strength assessment revealed inability to rise from a squatting position. CT scan showed a 3 cm pituitary mass invading adjacent tissues. Biochemistries were normal. Serum TSH and total T4 were normal, while serum cortisol was 95.5 ng/ml at 0800h (reference range 50-230). Gonadal axis was not evaluated given the pre-pubertal testicular volume. Growth hormone stimulation testing was not available in Haiti and was not further pursued given that growth hormone treatment was not considered. Expert neurosurgical and endocrine opinion was sought across North America and the tumor deemed inoperable. Radiation therapy was not available. Anti-hypertensive therapy with hydrochlorothiazide-Enalapril was initiated. Medical supportive treatment with pegvisomant, cabergoline and ketoconazole were discussed with international experts. Only the latter was available in-country and was titrated to a dose of 900 mg PO daily.

Conclusion:
Diagnostic evaluation of rare endocrine diseases in resource-limited countries requires a setting-adapted approach that emphasizes a thorough clinical evaluation and prioritizes actionable investigations. Lack of treatment modalities and subspecialty medical and surgical expertise may lead to insurmountable management challenges. Facilitation of international expert exchange can support local medical teams and assist with alternative management approaches. (345 words)
Global Health Abstract 2
Severe Osteogenesis Imperfecta in a Newborn Infant: First Case Report from Haiti

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Background:
Osteogenesis imperfecta has not previously been reported from Haiti. Genetic investigations are mostly not available in resource-limited settings. Access to pediatric subspecialty consultation was recently established via an e-consultation platform.

Case Description:
A full-term, 2.8 kilogram female infant was born with severe bony deformities involving both upper and lower limbs. Delivery route was via caesarean section due to intracranial calcifications and bony malformations detected on prenatal ultrasound. Obstetric history revealed a G2P2A0 healthy mother. Parents were non-consanguineous, of Haitian descent and without a history of bone disorders. Physical examination at birth showed mild respiratory distress, multiple skull depressions, blue sclerae, shortening and deformities of all limbs and polydactyly of both hands. Investigations showed a normal alkaline phosphatase excluding hypophosphatasia. Plain radiographs revealed multiple rib fractures, bilaterally displaced ulnar and radial fractures, femoral bowing, multiple calluses and severe osteopenia. An echocardiogram showed an ostium secundum atrial septal defect. Pediatric Endocrinology was consulted via a secure stored-and-forward e-consultation platform. The patient was treated with analgesics for comfort. Bisphosphonate treatment was not available. The infant passed away of respiratory insufficiency at 26 days of life.

Discussion:
This represents the first reported case of severe osteogenesis imperfecta in a Haitian infant, clinically most consistent with osteogenesis imperfecta type II. It can be difficult to differentiate osteogenesis imperfecta type II from type III at birth but this should not preclude an attempt to treat with bisphosphonates, a therapy that should be started on clinical grounds. As with other essential medicines, this treatment should be made available in Haiti. Genetic analysis of COL1A1 and COL1A2 gene, the gold standard for the diagnosis of osteogenesis imperfecta, is mostly not available in resource-limited settings, but family counselling regarding future pregnancy can be offered regardless. We suspect that many cases of osteogenesis imperfecta may go unrecognized and/or may be under-reported. Availability of subspecialty endocrine e-consultation and expertise may increase the detection rate of rare pediatric endocrine diseases, empower referring pediatricians and provide management assistance and support even when appropriate medications are not available. (338 words)
Global Health Abstract 3
Clinical Diagnosis of 11-Beta-Hydroxylase Deficiency in a 6 Year-Old Haitian Boy with Sexual Precocity

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Case Presentation:
A 6 year and 11 month-old Haitian boy presented to Mirebalais University Hospital in Haiti with sexual precocity. Pubic hair development had started three years prior and progressed slowly, and gynecomastia had developed over the past month. The child had always been tall, although height had not been recorded previously. Parents had not noticed acne, axillary hair, or a change in the child’s voice. The review of systems was negative and the family history was non-contributory. On physical examination, height was 130 cm (+1.66 SDS), weight 29.3 kg (+1.77 SDS) and blood pressure 156/87 mm Hg (>99th percentile). Breast tissue was Tanner 3, pubic hair Tanner 4, penile length 8 cm, and both gonads measured 2 cc with a hydrocele on the left. Investigations revealed a bone age of 12-13 years. On ultrasound, both gonads measured 19X0.8 cm and had the appearance of normal testes; the left testis was (inguinal?). On a dried blood spot, 17-hydroxyprogesterone was normal (6.1 nmol/ml) and androstenedione was elevated (34.6 nmol/L). Serum testosterone was 4.8 nmol/L (Tanner 3-4 range) and FSH/LH were low at 0.4/0.2 mIU/L. Two months later, repeat serum testosterone was 2.8 nmol/L and estradiol was 183 pmol/L. Diagnostic and Therapeutic Approach: The clinical presentation and diagnostic evaluation were consistent with peripheral isosexual pubertal precocity. The most likely diagnosis was 11-beta hydroxylase deficiency given the time course, high blood pressure and adrenal steroid results obtained on filter paper. A therapeutic trial of nifedipine did not improve blood pressure. A therapeutic trial of prednisone 2 mg/m2.day was initiated, with the goal of lowering blood pressure and with close clinical monitoring of the expected central precocious puberty. A second filter paper specimen was collected for sequencing of CYP11B1 abroad.

Discussion:
This is the first case report of probable 11-beta-hydroxylase deficiency from Haiti. In resource-limited settings, endocrine diagnostic evaluation is often difficult to obtain. Clinicians need to rely on clinical information and therapeutic trials to make a diagnosis. Global partnerships and creative use of diagnostic tools can facilitate diagnostic evaluation.
Global Health Abstract 4
MicroResearch: Building Capacity for Health Research in Eastern Africa (EA)

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Background:
Sub-Saharan African countries have urged grassroots input to improve research capacity (WHO 2008) including community directed research. In East Africa (EA) MicroResearch (MR) is building capacity to support health professionals to design and carry out research aimed at finding local, sustainable solutions for health problems.

Objectives:
To share experiences at 8 years on MR implementation, practices and outcomes.

Methods:
MR training occurred during intensive 2-week workshops (WS) where 20-30 health workers (HW) were introduced to principles of research, community engagement, knowledge translation, & health policy. WS were initially led by Canadian academic pediatricians. Local teachers at each site participated with increasing responsibility for subsequent WS. New teachers are paired with, and coached by, experienced WS teachers in a set, but dynamic curriculum. Small interdisciplinary teams (6-8 HW) self-identified locally relevant research questions and developed proposal outlines during the WS. Post-W S, teams, supported by 2 MR coaches (1 from EA), completed and submitted full proposals for international MR peer review. Following local ethics approval, successful projects were funded (up to $2,000) and implemented. Results were reported and steps taken toward knowledge translation (written report, extended abstract (published in peer-reviewed PubMed journal), policy/practice change) with ongoing involvement of coaches. MR evaluation at 6 years consisted of review of WS participant/proposal data, standardized post WS evaluations and EA MR site data.

Results:
From 2008-June 2016, 27 workshops were conducted at 8 EA sites with 791 participants (47% female); 30% MD, 22% RN or Midwife, and 48% other HW. 68 projects were approved for funding, 21 completed, 23 published or accepted. 4 projects helped change health policy/practice. Projects topics were 36% child health, 33% maternal health, 31% both. Gender equity was fostered by MR: women project leaders (54%), coaches (32%), facilitators, (50%) and judges (44%). Over 90% of participants rated WS as excellent; ~20% noted MR changed culture of inquiry at work.

Conclusion:
MR is building capacity for EA community directed interdisciplinary research at modest cost. MR projects lead to local health care changes, enhance culture of inquiry, and support gender equity.

Supported by International Development Research Council, Canada), Canadian Child Health Clinician Scientist Program, Dalhousie Medical Research Foundation, Canadian Paediatric Society and private donors.
Acknowledgement to Pemba, Senga, Tanzanian Training Centre for International Health, Ifakara, Tanzania; Mwanda, Walter University of Nairobi Institute for Tropical and Infectious Diseases, University of Nairobi, Nairobi, Kenya; Kollmann, Tobias, University of British Columbia, Vancouver, BC.
Objective:
To systematically describe and evaluate the Dream Trust (DT) model in terms of approach to T1D management and factors, both medical and sociodemographic, which influence glycemic control.

Methods:
Cohort study of DT patients diagnosed with T1D before 16 years and followed at DT for $\geq 1$ year. For each participant, a questionnaire was administered, their chart reviewed for retrospective data, and an A1C measurement taken. Univariate and multivariate linear regression were performed to determine factors associated with A1C.

Results:
In total, 102 DT patients completed the interview and chart review. 74 patients completed the full study including A1C measurement. Median age was 16 years (IQR 13, 21), T1D duration 6 years (IQR 3, 9), and 51% were female. Median A1C was 10.4% (IQR 8.8, 11.9). On univariate analysis, lower A1C was associated with a greater number of blood glucose tests per month ($p=0.005$), lower insulin dose per kilogram per day ($p<0.001$), insulin storage in a refrigerator ($p=0.043$), higher maternal education ($p=0.013$), and not holding a Below the Poverty Line Certificate ($p=0.003$). There was no association between A1C and age, sex, caste, or religion. On multivariate regression, A1C was independently associated with insulin dose ($\beta=0.31, p < 0.001$) and holding a Below the Poverty Line Certificate ($\beta=1.38, p=0.004$).

Conclusions:
In T1D patients followed at DT, lower A1C was independently associated with lower insulin dose and not holding a Below the Poverty Line Certificate. DT is a charitable intervention that overcomes status and gender inequalities, but not extreme poverty.
Global Health Abstract 6
Access to Medicines in Pediatric Endocrinology and Diabetes in Africa: Insights from the WHO and National Lists of Essential Medicines

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Background:
Access to essential medicines remains suboptimal in Africa. The World Health Organisation (WHO) maintains two non-binding essential medicine lists (EML) (for children and for adults). Individual countries refer to these lists to prepare national EMLs.

Objective and Hypotheses:
To determine which medicines commonly used in pediatric endocrinology and diabetes are included in the WHO and national EMLs in the WHO African region. We hypothesize that significant differences are present between countries, reflecting at least in part differences in Gross National Income (GNI).

Method:
We compared a master list of medicines with 1 The WHO EML for children and adults and 2. The national EML for countries included in the WHO African region. National EMLs were obtained from the WHO website and GNI data from the World Bank.

Results:
Data from 40 of the 47 countries included in the WHO African region was collected. Four countries (=10%) had separate adult and child EMLs and 33 countries (=83%) were classified as low income. Overall, the WHO EMLs included medicines for contraception, Vitamin D deficiency, Type 1 and Type 2 diabetes and diseases of the adrenals, the thyroid and puberty. Calcitriol, diazoxide, growth hormone and bisphosphonates were not included. In African EM Ls, all countries included at least one glucocorticoid and 96% included a short and/or long acting insulin. In contrast, fludrocortisone was only present in 11 (=25%) and glucagon in 10 (=23%) of the national EM Ls, despite being suggested by WHO. Calcitriol was included by 7% of the countries. Diazoxide was not included in any of the lists. Overall, richer countries had more medicines listed than poorer countries.

Conclusion:
There are significant discrepancies between the content of the WHO and National EM Ls. Future research will determine the extent to which the national EM Ls reflect availability of the medicines in the country.
Pediatric Endocrinology Education Program for Haiti (PEEP-H)

Example of a specialty training program in resource-limited settings and opportunities for health care professionals to get involved

Julia von Oettingen, MD PhD MMSc
CPEG Annual Meeting 2017

Objective

1. Discuss the relevance of pediatric subspecialty training in resource limited settings (RSL).
2. Critique the current approach to pediatric endocrine education in low and middle income countries (LMICs).
3. List reasons for health care professionals to become involved in global health (GH).

Outline

• The need for pediatric endocrine training in RSLs:
  – Burden of pediatric endocrine disease
  – Phenotypes of pediatric endocrine disease
  – Health care delivery gaps
• PEEP-H:
  – Presentation of the program
  – How to get involved

Burden of Disease:
Worldwide T1D Incidence

THE NEED FOR PEDIATRIC ENDOCRINE TRAINING IN RESOURCE-LIMITED SETTINGS

Disclosures

• None
Burden of Disease: Pediatric Endocrine Conditions

- Scarce epidemiologic data
- Small studies from countries with newly trained pediatric endocrinologists
  - Late / more severe presentations
  - Distinct phenotypes
  - Different incidence / prevalence of certain conditions?
- Lack of ascertainment

Pediatric Diabetes Phenotypes

17 year-old girl
Diabetes
Severe cachexia
Bilateral cataracts

17 year-old girl
Diabetes
Chronic diarrhea
Malaise, GI complaints

14 year-old girl
Diabetes
Malaise, GI complaints
Calcified pancreatitis

Pediatric Diabetes Phenotypes

Large skin ulcer in newly diagnosed 22 year-old female

Pediatric Diabetes Phenotypes

Cheiroarthropy
Kwashiorkor
Skin ulcer
Eye complications at diagnosis

Pediatric Endocrine Phenotypes

The common...

Rickets
Thyrotoxicosis
Hypothyroidism
Precocious Puberty
Health Care Delivery Gaps

- Lack of access to diagnosis & treatment
  - Limited / no pediatricians trained in endocrinology
  - Limited / no adequate laboratory and radiology equipment
  - Limited / no access to essential medicines
- Lack of epidemiologic data

Health Care Delivery Gaps

- Lack of public health measures to optimize nutrition
  - Pregnancy complications
  - Low birth weight infants
  - Increased risk of cardiovascular & metabolic disease
- Lack of preventative measures
  - Micronutrient deficiencies
  - Vitamin D deficient rickets
  - Congenital hypothyroidism (newborn screening)
  - National height and weight curves

Health Care Delivery Gaps

- Result:
  - High mortality and morbidity
    - Pediatric Diabetes: 5-year mortality estimated at >50%
  - High risk of life-threatening emergencies
    - Pediatric Diabetes: hypo- and hyperglycemic emergencies
  - Serious complications from poor control
    - Pediatric Diabetes: Blindness, renal failure, poor growth/development
  - Social implications
    - School drop-out, unemployment
    - Social stigma, barriers to finding a marriage partner

The Need

Improve the health care delivery chain:

- Diagnosis
- Treatment
- Long-term care delivery

Health Care Provider Education

“I mean, everybody should have access to medical care. And, you know, it shouldn’t be such a big deal.”
Paul Farmer

RLS subspecialty training examples

- 1 Pediatric Endocrine:
  - Pediatric Endocrinology Training Centre for Africa
- 1 Pediatric specialty and subspecialty:
  - African Pediatric Fellowship Program (no endocrine training)
- Several in vs. out-of-country vs. sandwich fellowship

References:

www.paediatrics.uct.ac.za/scah/apfp/programme/overview; www.paedendoafrica.org;
Kassam F et al., Academic Medicine 2009; Busse H et al., Acad Emerg Med 2013;
Gathuya ZN and Walker IA, Paediatr Anaesth 2009
PETCA:

- **Partnership**
  - University of Nairobi + Aga Khan University
  - 3 Nairobi Hospitals
  - European Society for Paediatric Endocrinology (ESPE)
- **Funding**
  - World Diabetes Foundation (WDF)
- **Program**
  - 18 months → 6 months clinical, 9 months research, 3 months consolidation
  - Faculty → internationally recognized pediatric endocrinologists from Europe who are ESPE members

Odundo et al., Int J Endocrinol 2016

PETCA:

- **Successes:**
  - Establishment of pediatric endocrinology in multiple countries in Africa
  - Clinical Services
  - Research
  - African Society for Pediatric and Adolescent Endocrinology
- **Challenges:**
  - Funding
  - Maintenance of training, supervision, mentorship

Odundo et al., Int J Endocrinol 2016

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PEEP-H

Pediatric Endocrinology Education Program for Haiti

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**PEEP-H Background**

- Poorest country in Western Hemisphere
- Overall health status among lowest in world
- No pediatric endocrinologist
  - Limited education and training at all levels of training
  - Under-diagnosis of endocrine conditions
  - No consultation services
- No newborn screening program

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- Haiti: 10.5 million inhabitants
  - 23,000 km²
  - 30% < 15 y, 95% Black
  - Life expectancy 63 y
  - GDP/capita 1700 $
  - Language: French, Creole

- **PEEP-H**
  - Pediatric Endocrinology Education Program for Haiti
**PEEP-H Background**

**Haiti**
- Poorest country in Western Hemisphere
- Overall health status among lowest in world
- No pediatric endocrinologist
  - Limited education and training at all levels of training
  - Under-diagnosis of endocrine conditions
  - No consultation services
- No newborn screening program

Kessoun F et al., Academic Medicine 2009

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**PEEP-H - Objectives**

- Provide training in pediatric endocrinology for health professionals

1. Formal pediatric endocrinology education program for medical students and pediatric residents
2. Formal remote pediatric endocrine consultation services
3. Continuing medical education
4. Training of 2 pediatric endocrinologists
5. Program evaluation & quality improvement

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**PEEP-H Implementation**

1. Onsite teaching modules
   - 2 year curriculum, visits every 2 months by francophone pediatric endocrinologists

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2. Long distance education
   - 1 video conference per month
   - 1 teleconference lecture or case discussion per month

---

**H-PEEP Implementation**

3. Online platform
   - Reading materials and resources
Physiological and Health Adaptations to Interval Exercise Training

Martin Gibala

Physiological and Health Adaptations to Interval Exercise Training

No conflicts to declare

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Key Points

- Interval training elicits physiological adaptations that are superior to traditional endurance training when total exercise “dose” is matched.
- Interval training is a potent stimulus to elicit physiological adaptations similar to traditional endurance training despite (very) low total work.

What is Interval Training?

Alternating periods of relatively intense exercise and recovery

“Fast and short repetitions with suitable recoveries... are superior to even speed running around the track for the development of endurance.”

— Lauri Pihkala, 1916

High-intensity interval training (HIIT)

Relatively intense but submaximal efforts that elicit ≥80% of HRmax


Sprint interval training (SIT)

Efforts performed in an “all out” manner or at an intensity ≥100% of VO2peak


Simplifying Terminology

VO2peak


“HIIT has more physiological benefits than MICT in patients with lifestyle-induced cardiometabolic disease.”

Is high-intensity interval training more effective on improving cardiometabolic risk and aerobic capacity than other forms of exercise in overweight and obese youth? A meta-analysis

"HIIT could be considered a more effective and time-efficient intervention for improving blood pressure and aerobic capacity levels in obese youth."


"The risk of a cardiovascular event is low after both high-intensity exercise and moderate-intensity exercise."

N = 32 (age ≈ 60 y, BMI ≈ 30); 60 min/session, 5 dwk for 4 months
Continuous or Interval Walking (~66% HRmax) or non-training Control


"Interval walking is superior to energy-matched continuous walking (and) may therefore be a good option when considering which type of training...should be offered in primary care."

"A More Practical HIIT Approach?"

Can you elicit adaptations with reduced time commitment?

10 x 1 min hard efforts (~85-90% HRmax) with 1 min of recovery between

A randomized, controlled trial

Low-volume high-intensity interval training reduces hyperglycemia and increases muscle mitochondrial capacity in patients with type 2 diabetes

Jennison P, Edlin 1, Jonas B, Gilks 1, Michael E, Pasic 1, Christa Gobbi 1, Matt A, Tompso 1, 2, Zohra R, 3, Apaza 1, and Martha J, Gubits 1

n=8 T2D (63 ± 8 y, BMI ≈ 32 ± 6kg/m², HBA1C = 6.9 ± 0.7%)
6 sessions over 2 wk (total of 1 h exercise in a 2 h time commitment)


"HIIT convey benefits to cardiometabolic health which in the cases of insulin resistance and VO2max may be superior to the effect of continuous training."


Mechanisms of Adaptation?


Single-Leg Cycle Training

11 kg counter-weight

20 kg counter-weight

58
Three Minutes of All-Out Intermittent Exercise per Week Increases Skeletal Muscle Oxidative Capacity and Improves Cardiometabolic Health

![Protocol Diagram]

- 1 min of very intense exercise in a 10 min session (~86% \( \text{HR}_{\text{max}} \))
- \( \text{VO}_{\text{peak}} \) increases ~10% in 6 wk

Comparable to:
- 7-cm \( \text{ê} \) in WC
- 5-mm Hg \( \text{ê} \) in SBP
- 1 mmol in \( \text{ê} \) plasma glucose

(Kodama et al., JAMA, 2009)

Twelve Weeks of Sprint Interval Training Improves Indices of Cardiometabolic Health Similar to Traditional Endurance Training despite a Five-Fold Lower Exercise Volume and Time Commitment

![Protocol Table]

<table>
<thead>
<tr>
<th>Protocol</th>
<th>MICT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload</td>
<td>(-600 \text{ W} ) (&quot;all out&quot;)</td>
</tr>
<tr>
<td>Work/session</td>
<td>(-60 \text{ kJ} )</td>
</tr>
</tbody>
</table>

Twelve Weeks of Sprint Interval Training Improves Indices of Cardiometabolic Health Similar to Traditional Endurance Training despite a Five-Fold Lower Exercise Volume and Time Commitment

![VO2peak Graph]

- VO2peak increases ~19% in 6 wk

CS Maximal Activity

Insulin Sensitivity (IVGTT)

High Intensity Interval vs Moderate Intensity Training for Improving Cardiometabolic Health in Overweight or Obese Males: A Randomized Controlled Trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIT Group</th>
<th>MIT Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol</td>
<td>3 x 4 x 20 s</td>
<td>3 x 40 min Cycling</td>
</tr>
<tr>
<td>Frequency</td>
<td>5 Sessions per Week</td>
<td>5 Sessions per Week</td>
</tr>
<tr>
<td>Workload (watts)</td>
<td>65-75% Peak Power, 910 ± 250 W</td>
<td>55-65% VO2peak, 130 ± 13 W</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>170 ± 15 bpm</td>
<td>110 ± 15 bpm</td>
</tr>
<tr>
<td>Workout Time (min)</td>
<td>60 min</td>
<td>60 min</td>
</tr>
</tbody>
</table>

- Cardiorespiratory Fitness ✔
- Insulin Sensitivity (OGTT) ✔
- % Body Fat ✔
- Blood Lipids ✔
"We also found that HIT was well-tolerated in obese/overweight and sedentary men...

The lower time commitment needed to perform HIT may be more appealing and help to improve exercise adherence."

Making SIT More Accessible

~1 MET improvement over 6 wk
10 min session with 1 min intense ex at RPE of ~15 ("hard"), 3x/wk

Take Home Message:
Interval training is a time-efficient strategy to induce physiological remodeling linked to improved health

Interval Training Research: Limitations

• Most studies conducted to date are relatively short-term (up to a couple of months) and involve relatively small numbers of subjects.

• Long-term, large-scale, randomized clinical trials are needed to systematically compare interval and traditional endurance training, with respect to key indicators of health status and disease risk.

• Psycho-social responses to interval training (e.g., enjoyment, motivation, adherence), and in particular how these compare to traditional endurance training, remain to be fully elucidated.
Polycystic Ovary Syndrome (PCOS) in Adolescence.

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Disclosure Statement
• No conflict of interest to disclose
• Off-label use of leuprolide will be discussed

Outline/Objectives
To understand:
I. Pathogenesis of PCOS as functional ovarian hyperandrogenism (FOH)
   • Role of obesity in aggravating and mimicking FOH
II. Consensus criteria for PCOS diagnosis in adolescents differ from those in adults
   • Menstrual criteria that indicate abnormal anovulation
III. Management principles in adolescent PCOS
   • Role of insulin-lowering treatments in management

Etiology of PCOS
PCOS is a complex trait:
• Results from a combination of both heritable & environmental (prenatal & postnatal) factors

Clinical implications:
• These interactions mimic an autosomal dominant trait with variable penetrance
  - PCOS in mothers and sisters (~25%)
  - PCOM in mothers and sisters (~25%)
  - Metabolic syndrome and/or glucose intolerance in fathers (~80%) and mothers (~40%)

Genome-Wide Association Screening (GWAS) Linkage Studies of PCOS
• Widespread linkage to 9q22.32 intronic loci (DENND1A)
• DENND (Differentially Expressed in Normal & Neoplastic Domains) proteins involved in endocytosis & membrane trafficking
  - McAllister JM, et al. PNAS 2014;111:E1519
  - In PCOS theca cells V2 isoform increased
  - In normal theca V2 over-expression stimulates--and

Knowledge gaps:
• 
• 
•

Polycystic Ovary Syndrome (PCOS) in Adolescence.

- Etiology
- Pathophysiology

Pathogenesis of PCOS

- Etiology
- Pathophysiology

- Widespread linkage to 9q22.32 intronic loci (DENND1A)
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Knowledge gaps:

- 
- 
-
Pathophysiology Model:
1. PCOS as FOH

Pathophysiology Model:
2. Insulin-resistant hyper-insulinism

Pathophysiology Model:
2a. Insulin-resistant hyper-insulinism aggravates FOH

Pathophysiology Model:
2b. Hyperinsulinism + hyper-androgenism + FSH prematurely luteinize granulosa cells

Pathophysiology Model:
3a. Androgen excess stimulates LH excess > worsens FOH...

Pathophysiology Model:
3b. LH stimulates estradiol secretion by prematurely luteinized granulosa cells...
**Pathophysiology Model:**

1. LH-stimulated estradiol from prematurely luteinized granulosa cells inhibits FSH

2. **Luteinized Granulosa Cell**
   - **Sex steroid excess**
   - **Anovulation**
   - **PCOM**
   - **INSULIN-RESISTANT HYPERINSULINISM**

3. **Theca Cell**
   - **FUNCTIONAL OVARIAN HYPERANDROGENISM**
   - **Pilosebaceous Unit**
   - **Hirsutism**

4. LH-excess

**Relationship of obesity to PCOS. II.**

- Adipocyte 17β-HSD5 forms testosterone in response to insulin & is upregulated in obesity > androgen excess
- Obesity suppresses LH

**Mechanism:**
- Suppresses pulse amplitude
- Increases clearance of LH & FSH via enhanced sulfonation

- Adipocyte 17β-HSD5 forms testosterone in response to insulin & is upregulated in obesity > androgen excess

**Propose:** Obesity is CAUSE of atypical PCOS (without FOH or FAH)
- Mild testosterone elevation
- DHEAS normal
- LH usually normal
- Ovaries usually normal size

**II. Criteria for Diagnosis of PCOS**

**Background**

Rotterdam criteria yield 4 adult PCOS phenotypes:
- Otherwise unexplained evidence of:
  1. Chronic hyperandrogenism + anovulation + PCOM (**“Classic” criteria**)
  2. Chronic hyperandrogenism + anovulation (**“Essential NIH criteria”**)
  3. Chronic hyperandrogenism + PCOM (**“Ovulatory PCOS”**)
  4. PCOM + anovulation (**Non-hyperandrogenic PCOS**)

In 2013 PES convened an international stakeholder group to address diagnostic criteria in adolescents

**Consensus Criteria for Diagnosing PCOS in Adolescents**

Adolescents require special consideration because:
- Anovulatory cycles are frequent
- Hirsutism is in a developmental phase
- Acne is common
- Testosterone rises during prolonged anovulatory cycles
- Paucity of reliable norms for adolescent androgen levels
- Polycystic ovary morphology (PCOM) is common by adult standards
- The natural history of PCOS diagnosed in adolescence is not well documented
A. Evidence of Oligo-Anovulation

Anovulation is physiologic during adolescence (within age- and stage-specific limits)

In spite of more frequent "anovulatory" cycles, most are asymptomatic; adolescent menstrual cyclicity differs only slightly from adult norms, even in gyn year 1

- Intervals outside 21-45 days abnormal by 3rd gyn year
- Adult norms achieved by gyn yr 4-5
- Most (75%) cycles are 21-45 days even in 1st gyn year
- Cycles > 90 or < 19 days are always abnormal

In adolescents, many more menstrual cycles are regular (21-42 days) than are normal ovulatory

- About half of regular cycles are ovulatory in gyn yr 1
- >75% adolescents have 21-42 day menstrual cycles yr 1
- Discrepancy because most "anovulatory" cycles are asymptomatic (regular) immature ovulatory cycles

Physiology of Asymptomatic Adolescent "Anovulation"

- About 50% of 21-45 day cycles are ovulatory in early adol.
- Half of other 21-45 day cycles are immature ovulatory cycles with varying degrees of luteal insufficiency

Prognosis for Adolescent Menstrual Abnormality Resolving

Adolescent Endocrine Gyn Clinic – symptomatic menstrual bleeding disturbances of diverse cause:

- Ongoing menstrual abnormality for 1-2 yr carries 54%-62%* risk of persistence–indication for evaluation

Worse—But Variable—Prognosis for Hyperandrogenic Adolescent Anovulation

- Testosterone rises during prolonged anovulatory cycles
- About half of oligo-amenorrheic girls are hyperandrogenic
- High testosterone persists in ~ 50% of such girls

B. Clinical Evidence of Hyperandrogenism

**Background: Hirsutism definition in adults**

Ferriman & Gallwey. JCEM, 1961

Hirsutism is defined by an abnormal F-G score (indicates excessive male-pattern hair growth):

- >7 in general population of 18-38 year olds (U.K. & U.S.A.)

**PCOS consensus diagnostic criteria:**

- hirsutism per se is evidence of hyperandrogenism

**Endocrine Society Hirsutism Clinical Practice Guidelines:**

- hirsutism is non-specific evidence of hyperandrogenism

- Half of mild hirsutism (Ferriman-Gallwey score 8-15) is idiopathic, i.e., not associated with hyperandrogenemia

**Criteria for Clinical Evidence of Hyperandrogenism**

**Appropriate Criteria for Adolescent Hirsutism?**

Conclusion: Adult degree of hirsutism seems to be achieved by 2 yr post-menarche

**Criteria for Clinical Evidence of Hyperandrogenism**

**Appropriate Criteria for Adolescent Acne?**

- Conclusion 1: ≥ moderate comedonal acne is common
- Conclusion 2: ≥ moderate inflammatory acne is unusual (risk factor for hyperandrogenemia)


C. Biochemical Evidence of Hyperandrogenism

**Appropriate Criteria for Adolescent Hyperandrogenemia?**

Conclusions:
- Adult testosterone levels achieved peri-menarche
- Adult norms by high specificity assays are appropriate reference range for adolescent androgen levels

D. Polycystic Ovary Morphology (PCOM)

**Background: Adult Consensus Criteria (Rotterdam)**

- Ovarian volume > 10.0cc (by simplified formula), (excluding ovaries with preovulatory follicle, ≥10 mm), or
- Small antral follicle (AF, 2-9 mm) count ≥ 12 per ovary

**Problems with adult consensus criteria emerging:**

- Ovarian volume - falls slightly with age during adult reproductive years
- Variable use of ellipsoid & simplified volume formulae
- AF count higher with recent high-definition equipment
- Exceeds criteria in over one-third young adults
Appropriate Criteria for PCOM in Adolescence?

- "Multifollicular" morphology is normal in adolescents
- AF counts imprecise by abdominal ultrasound
- One-third of normal adolescents meet adult PCOM criteria

Conclusion:

- Uncertainty about appropriate criteria for PCOM in adolescents too great to use PCOM as a diagnostic criterion for adolescents
- Provisionally, PCOM = mean ovarian volume >12.0 cc (or single ovary volume >15.0 cc)

PCOM & Hyperandrogenemia in Normal Volunteers

- Normal adolescent & adult volunteers with normal ovarian morphology (VNOM) & PCOM (VPCOM)
- Free testosterone significantly higher in pooled VPCOM than pooled VNOM
- Volunteers with PCOM are not appropriate for setting androgen reference ranges

Are asymptomatic hyperandrogenemic VPCOM PCOS carriers?

E. Consensus Recommendations Dx Adolesc PCOS

Persistent otherwise unexplained hyperandrogenic anovulation, using age- & stage-adjusted standards

- Uterine bleeding pattern abnormal
  - Abnormal for age/gynecologic age
  - Persistent symptoms for 1-2 yr
- Evidence of hyperandrogenism, preferably biochemical
  - Persistent testosterone elevation above adult norm in reliable reference lab is best evidence
- Moderate-severe hirsutism constitutes clinical evidence of hyperandrogenism
- Moderate-severe inflammatory acne is indication to test for hyperandrogenemia before initiating medical Rx

F. Post-script: Role of Testing for Functional Ovarian Hyperandrogenism (FOH)

Objective: What is the prognosis of FOH?
Background: Hyperandrogenic anovulation often persists
- Hypothesis: persistent cases are due to FOH-PCOS

Adolescent Hyperandrogenism Persistence: Recall

22 Hyperandrogenic adolescents tested for FOH (2000)
Recall after 3.0 yr and >18.0 yr of age

Non-Respondents (7 untraceable / 6 contacted) Respondents (n = 9)

Baseline data:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-Respondents</th>
<th>Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>15.1 ± 2.0 (SD)</td>
<td>15.3 ± 3.0 (SD)</td>
</tr>
<tr>
<td>Gyn age (yr)</td>
<td>3.1 ± 1.6</td>
<td>3.2 ± 3.0</td>
</tr>
<tr>
<td>Body mass index</td>
<td>31.9 ± 9.3</td>
<td>33.3 ± 8.5</td>
</tr>
<tr>
<td>Free testo (pg/ml)</td>
<td>25.8 ± 14.7</td>
<td>31.1 ± 20.2</td>
</tr>
<tr>
<td>OGTT abnormal</td>
<td>2 / 13 (1 IGT)</td>
<td>3 / 9 (IGT)</td>
</tr>
<tr>
<td>FOH diagnosed</td>
<td>8 / 13</td>
<td>8 / 9</td>
</tr>
</tbody>
</table>
Adolescent Hyperandrogenism Follow-up at 18-29 yo

COCs d/ced x ≥ 2mo

FAH Recall (n=1)
- Free testosterone gradually remitted
- DHEAS remained high (213 µg/dl)
- Hirsutism persisted
- Menses normal
- PCOM developed

FOH Recall (n=8)
- Free testosterone elevated in all
- All oligomenorrheic

Adolescent Hyperandrogenism Persistence

Conclusions:
- Data support the hypothesis that PCOS due to FOH persists
- Suggest that testing ovarian androgenic function in adolescents with hyperandrogenism may be of prognostic value
- Caveat: More data needed on prognosis of adolescent PCOS and symptomatically hyperandrogenemic PCOM

III. MANAGEMENT PCOS. Individualized & Symptomatic.

- Hirsutism and acne
  » Combined oral contraceptive (COC) is usual first-line Rx
    - EE2 30 mcg + anti-androgenic progestin
    - EE2 35 mcg + non-androgenic progestin (e.g., norgestimate/Ortho-Cyclen®)
  » If poor response hirs., add spironolactone or laser

- Menstrual irregularity and endometrial hyperplasia
  » COC is most reliable first-line Rx

- Obesity and insulin resistance
  » Behavior modification is first-line Rx
  » Metformin indicated for abnormal glucose tolerance

- Evaluate primary relatives for metabolic synd. & PCOS

Summary: Adolescent PCOS 2015

1. Pathogenesis of PCOS
   - Essence is functional ovarian hyperandrogenism
   - Insulin-resistant hyperinsulinism in half, aggravating
   - Obesity aggravates (and sometimes mimics) PCOS

2. Criteria for the diagnosis of PCOS in adolescence: Persistent, otherwise unexplained hyperandrogenic anovulation, using age- & stage-adjusted standards

3. Management is symptomatic
   - Combined oral contraceptive is best first-line Rx for hyperandrogenic anovulation symptoms
   - Behavioral modification is first-line Rx for metabolic co-morbidities
   - Evaluate family for metabolic syndrome and PCOS

References