February 14-17, 2017

4th Annual

CANADIAN NATIONAL PERINATAL RESEARCH MEETING

Montebello, Quebec

Co-Hosted by :

McMaster University

Children's Health Research Institute

Schulich Medicine & Dentistry

Western

WELCOME DELEGATES

Welcome to the 4th Annual Canadian National Perinatal Research Meeting (CNPRM). We are delighted that you have all decided to join us for exciting and novel science and great fun at the Fairmont Montebello, Quebec!

As you may know, although the CNPRM is only in its fourth year, Canadian perinatal researchers have been meeting yearly for nearly 40 years as Western and Eastern groups, and in February 2014 we came together to form a Canadian National meeting that was held in Banff. It was so successful that this new national annual format was adopted for the 2015 (Montebello) and 2016 (Banff) meetings and has formed the basis for the 2017 meeting as well.

The 2017 meeting has achieved record numbers of registrants and trainees, which is evidence of Canada's vibrant and growing perinatal research community, and our immense contribution to perinatal research and our role in the global effort of supporting and maintaining maternal and child health and policy. This year we have 384 registered delegates and 275 submitted abstracts (65 oral and 210 poster trainee presentations - A big thank you to all the members of the Thematic Committees who judged the submission). We also have three world-class international Plenary speakers, and for this year's scientific program, we have added a few new themes to the program, increasing the number of these concurrent sessions to 12 in 2017. As in previous years, the meeting in 2017 will host two evening poster sessions; as well, for the first time this year, eight special interest workshop sessions will be included, with topics ranging from how to secure that first faculty position to topics such as neonatal feeding and improving neonatal care with the help of veteran parents. There will also be several topical group meetings, and the conference will conclude with a banquet dinner.

The CNPRM is also about trainees, and we work hard every year to ensure that any trainee that is inspired to submit their work to CNPRM is permitted to present in a comfortable and nurturing environment. To honour our emerging scientists, CNPRM 2017 offers at total of 12 trainee awards. Among the many awards given away at the CNPRM, we have four awards of $100 plus registration for CNPRM 2018 kindly sponsored by the CIHR - Institute of Human Development, Child and Youth Health given to the top two oral and top two poster presentations. An additional four oral and four poster presentation awards for our trainees are also to be awarded. Trainee support does not come without cost and this year over $160,000 of sponsorship money was raised to fund the trainees and the meeting logistics. We are grateful to the generosity of so many sponsors from Industry, Research Institutes and University Divisions, Departments and Sections, which enable CNPRM to continue to fully support our young scientists - our perinatal research leaders of tomorrow.

Please take advantage of this meeting to exchange ideas, network and discuss science. We hope you will go home with novel ideas, new research avenues, and breakthrough concepts to explore, as well as new collaborators and friends.

We would like to thank all our guest speakers, delegates, sponsors and attendees, as well as members of our Thematic Committees, workshop organizers, judges and session moderators, who have travelled from far and wide to join us to make this what we are confident will be a memorable meeting. Finally, without the support of the Fairmont Montebello, and our dedicated admin support staff of Karen Burell and Jennifer Cordick, and student (McMaster and Western) volunteers the meeting would be impossible, thank you all!

On behalf of the CNPRM 2017 Organizing Committee, welcome and enjoy!

Dr. Timothy Regnault, PhD

Dr. Deborah Sloboda, PhD

Schulich MEDICINE & DENTISTRY Western

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4th Annual
CANADIAN NATIONAL
PERINATAL RESEARCH MEETING
Montebello, Quebec

McMaster University

BIENVENUE

Bienvenue au 4e Congrès annuel canadien de recherche périnatale! Nous sommes ravis que vous soyez avec nous cette année encore pour écouter et partager les dernières avancées scientifiques dans notre domaine, ici au Fairmont Montebello, Québec.

Comme vous le savez probablement, même si ce congrès canadien n'en est qu'à sa 4e édition nationale, les chercheurs en périnatologie de l'Est et de l'Ouest du pays ont tenu des rencontres scientifiques annuellement depuis près de 40 ans. Le premier congrès national a eu lieu en 2014 à Banff; ce fut un tel succès que tous décidèrent de dorénavant tenir annuellement cette rencontre nationale, alternant l'Ouest (Banff 2014, 2016) et l'Est (Montebello 2015 et cette année, 2017).

Le congrès 2017 semble atteindre un nombre record de participants, tant chercheurs qu'étudiants, soulignant la vitalité et la croissance de la recherche périnatale au Canada, et notre contribution à l'amélioration des soins et politiques de santé des mères et des enfants. Nous accueillons cette année 384 participants. 275 abrégés ont été soumis (65 retenus pour des présentations orales et 210 présentations par affiches – un grand merci aux Comités thématiques pour leur travail de sélection). Durant les sessions plénières, nous entendrons 3 conférenciers renommés invités de l'international. Nous avons ajouté des thèmes d'intérêt au programme, augmentant à 12 sessions thématiques cette année pour répondre aux intérêts du plus grand nombre. Tout comme par les années passées, nous avons en soirée 2 sessions de présentations par affiches. Nouveauté cette année, nous avons aussi 8 ateliers sur des sujets allant de comment obtenir un premier poste de professeur-chercheur à la nutrition néonatale ou comment améliorer les soins en néonatologie en équipe avec des parents-vétérans. Surveillez aussi les rencontres de divers groupes de discussions.

Et surtout, soyez présents au Banquet de jeudi soir!

Le Congrès annuel canadien de recherche périnatale est un congrès qui a la relève scientifique au cœur de ses préoccupations. Chaque année, nous travaillons très fort pour assurer à chaque étudiant qui soumet un abrégé de ses travaux l'occasion de présenter et discuter dans un environnement constructif et chaleureux, et avec un minimum de frais. Pour souligner l'excellence de nos étoiles montantes, le congrès cette année attribuera de nombreux prix : 4 prix de 100$ en plus de l'inscription au congrès 2018 offerts par l'Institut du développement et de la santé des enfants et des adolescents des IRSC aux 2 meilleures présentations par affiche et 2 meilleures présentations orales, en plus de 4 prix pour les présentations par affiche et de 4 prix pour les présentations orales. Ce support des étudiants n'est pas sans coût et cette année encore ce sont plus de $170,000 en sponsorship qui ont été amassés pour couvrir les frais des étudiants et l'organisation du congrès. Nous sommes donc très reconnaissants envers nos partenaires de l'industrie, des instituts et centres de recherche, des services et départements cliniques et universitaires de partout au pays qui, cette année encore, permettent à ce congrès d'exister et aux étudiants d'y être particulièrement bien accueillis.

Nous souhaitons que vous profitiez pleinement de ce congrès pour échanger des idées, « réseauter » et discuter science. Nous espérons qu'après votre séjour vous rentrerez chez vous avec des idées renouvelées, de nouvelles avenues de recherche, des concepts originaux à explorer et surtout des nouveaux collaborateurs et amis.

Nous remercions chaleureusement tous nos conférenciers invités, sponsors et participants, de même que les membres des différents comités thématiques, organisateurs d'ateliers, juges et modérateurs, qui se sont déplacés jusqu'ici pour permettre à ce congrès d'être un événement mémorable! Finalement, il faut souligner le support essentiel et déterminant du Fairmont Montebello, de notre équipe de support administratif Karen Burell et Jennifer Cordick et d'étudiants bénévoles à McMaster et Western U.

Au nom du comité organisateur de l'édition 2017 du Congrès annuel canadien de recherche périnatale, bienvenue, merci d'être là et, surtout, profitez-en bien!

Dr. Timothy Regnault, PhD

Dr. Deborah Sloboda, PhD

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SCIENTIFIC PROGRAM

Tuesday, February 14, 2017	
13:00-17:00	**Registration** [Hotel Lobby]
17:00-19:00	**Poster Session I** [Canada Room] *Author attendance from 17:00 to 19:00*
19:00-21:00	**Dinner: Restaurant aux Chantignoles**

Wednesday, February 15, 2017

07:00-09:00	Breakfast: Restaurant Aux Chantignoles
08:00-08:50	**Parallel Workshops** ***Workshop #1 - Young Investigator Workshop – Getting that 1st faculty position!*** [LE CLUB] ***Workshop #2 - Neonatal feeding in the NICU and beyond*** [MONTEBELLO]
08:45-09:00	**WELCOME AND OPENING REMARKS:** Dr. Timothy Regnault & Dr. Deborah Sloboda

SCIENTIFIC PLENARY SESSION [Room Outaouais]

MODERATORS: Dr. D. SLOBODA & STEPHANIE KERELIUK

09:00-09:45 **PO 1: PLENARY SPEAKER:** Dr. Kent Thornburg – Oregon Health & Science University
What are all of those black holes in the placenta?

Trainee Plenary Presentations

09:45-10:00 **PO 4:** Muhammad Oneeb Rehman Mian
TLR4 antagonism prevents early left ventricular hypertrophy and dysfunction caused by neonatal hyperoxia exposure in rats

10:00-10:15 **PO 5:** Souvik Mitra
Effectiveness of Indomethacin, Ibuprofen and Paracetamol for Patent Ductus Arteriosus (PDA) in preterm infants: A Network Meta-analysis

10:15-10:30 **PO 6:** Usha Rai
Impact of duration of labour on infant gut microbiota

10:30-11:00	Refreshment Break

Trainee Plenary Presentations

11:00-11:15 **PO 7:** Suzanne Demers
Prediction of preeclampsia in nulliparous with uterine artery Doppler

11:15-11:30 **PO 8:** Lisa-Marie Legault
Early embryonic induction of fetal alcohol spectrum disorder leads to DNA methylation perturbations at mid-development in mouse brain and placenta

11:30-11:45 **PO 9:** Jessica Breznik
High fat diet induces premature egress of pro-inflammatory monocytes in reproductively cycling non-pregnant female mice

11:50-13:00	**Parallel Workshops** ***Workshop #3 - RCT: Innovative trials in neonatology: maximize research value, reduce waste*** [QUEBEC ROOM] ***Workshop #4 - Advanced Methods for Perinatal Epidemiology*** [MONTEBELLO] ***Workshop #5 - Improving neonatal care with the help of veteran parents: an overview of current practices*** [LE CLUB]
12:00-13:30	Lunch: Restaurant Aux Chantignoles

CONCURRENT THEMATIC SESSIONS

THEMATIC SESSION 1

Neonatology II - Neurosciences
[LE CLUB]

MODERATOR: Dr. DAN GOLDOWITZ

13:30 **TO 1 - Invited Speaker:** Dr. Jill Zwicker
Prematurity and Developmental Coordination Disorder

14:00 **TO 2 -** Palig Balian
Sildenafil may modulate retinal inflammation following term neonatal hypoxic-ischemic injury

14:15 **TO 3 -** Yang Ding
Measure Blurriness of Neonatal Magnetic Resonance Brain 2D Images: Developing Robust, Simple and Objective Data Quality Control Measures

14:30 **TO 4 -** Manon Ranger
Let's not sugar coat it: Long term adverse effects on the brain of repeated sucrose for pain management in preterm infants using a mouse model

14:45 **TO 5 -** Wyston Pierre
Early non-invasive assessment of neuroprotection in an animal model of neonatal white-matter injury

Perinatal Nutrition & the Gut
[MONTEBELLO]

MODERATORS: Dr. STEPHANIE ATKINSON & CAROLINE MOORE

13:30 **TO 6 - Invited Speaker:** Dr. Megan Azad
Breastfeeding, Gut Microbiota and Child Health

14:00 **TO 7 -** Sangmin (Sarah) Lee
Pregnant Women With Inflammatory Bowel Disease are at Significantly Increased Risk of Vitamin D Insufficiency

14:15 **TO 8 -** Camille Dugas
Impact of Breastfeeding Duration on the Cardiometabolic Risk Profile of Children Born from Mothers with Gestational Diabetes Mellitus

14:30 **TO 9 -** Kate Kennedy
Maternal diet-induced obesity is associated with altered fetal gut development

14:45 **TO 10 -** Jessica Wallace
Diet-induced maternal obesity induces a shift in the maternal intestinal microbiota and is associated with altered maternal intestinal mucus production and M1 macrophage infiltration of the placenta at mid gestation

MFM I - Maternal Medicine
[OUTAOUAIS]

MODERATOR: Dr. EMMANUEL BUJOLD

13:30 **TO 11 - Invited Speaker:** Dr. Stella Daskalopoulou
Arterial stiffness and prediction of pre-eclampsia: can we do better?

14:00 **TO 12 -** Susan O'Rinn
Lacking consensus: results from an international Delphi survey on invasive Placentation

14:15 **TO 13 -** Cedric Gasse
First-trimester mean arterial blood pressure and risk of preeclampsia

14:30 **TO 14 -** Frances Sobierajski
Physical activity patterns and vascular function during pregnancy

14:45 **TO 15 -** Dane DeSilva
MAGnesium sulphate for fetal neuroprotection to prevent Cerebral Palsy (MAG-CP) – a managed knowledge translation project to implement guidelines in Canada

15:00-15:30	Refreshment Break

CONCURRENT THEMATIC SESSIONS

THEMATIC SESSION 2

Reproductive (epi)genetics and Fertility
[LE CLUB]

MODERATORS: Dr. MARC-ANDRE SIRARD & ROSE GHEMRAWI

15:30 **TO 16 - Invited Speaker:** Dr. Jacquetta Trasler
Lifelong consequences of perturbing perinatal epigenetic programs

16:00 **TO 17 -** Patrycja Jazwiec
Characterizing the impact of fetal growth restriction on offspring ovarian follicle growth and development in guinea pigs

16:15 **TO 18 -** Lia Mara Gomes Paim
Binucleation fails to activate a tetraploidy checkpoint and instead causes segregation errors in the preimplantation embryo

16:30 **TO 19 -** Aida Eslami
Parent-of-origin effect in Asthma–GWAS Meta-analysis in three Canadian Cohorts

16:45 **TO 20 -** Cayetana Vázquez-Diez
Spindle assembly checkpoint insufficiency causes chromosome segregation errors in mouse preimplantation embryos

Reproductive Immunology
[MONTEBELLO]

MODERATORS: Dr. ALEXANDER BERISTAIN & BARBARA CASTELLANA

15:30 **TO 21 - Invited Speaker**: Dr. Anne Croy
Is there evidence for lymphocyte-initiated pregnancy failure?

16:00 **TO 22 -** Estefania Sierra
Characterization of the mechanism of action of an anti-IL-6R peptide in an inflammation- and infection-induced preterm birth

16:15 **TO 23 -** Genevieve Genest
IVIg for recurrent pregnancy loss and recurrent implantation failure: experience at the MUHC

16:30 **TO 24 -** Kelly Baines
The Role of Uterine Natural Killer Cells in Immune-Mediated Intrauterine Growth Restriction in Rats

16:45 **TO 25 -** Marie-Eve Brien
Altered maternal immune system profile in PE and postpartum PE: potential contribution to disease progression

Perinatal Epidemiology
[OUTAOUAIS]

MODERATORS: Dr. LINDA DODDS

15:30 **TO 26 - Invited Speaker**: Dr. Sven Cnattingius
Maternal overweight/obesity and offspring risks

16:00 **TO 27 -** Marinela Grabovac
Maternal pre-pregnancy body mass index and gestational weight gain: interprovincial variation and impact on birthweight

16:15 **TO 28 -** Samantha Krueger
Labor outcomes after successful external cephalic version compared to spontaneous cephalic version

16:30 **TO 29 -** Timothy Disher
Neonatal Abstinence Syndrome: A health economic perspective

16:45 **TO 30 -** Alexa Grudzinski
Maternal obesity and health care utilization for mental health conditions in the offspring

17:00–19:00	**Poster Session II – Canada Room** *Author attendance from 17:00 to 19:00*
19:00-21:00	**Dinner: Restaurant Aux Chantignoles**

Thursday, February 16, 2017

07:00-09:00	Breakfast: Restaurant Aux Chantignoles
08:00-08:50	***Workshop #6 - Writing a grant for success and the future!*** [LE CLUB]
08:00-08:50	**Special Group Meeting** - CIHR PTB Network Meeting [QUEBEC ROOM]

SCIENTIFIC PLENARY SESSION [Room Outaouais]

MODERATORS: Dr. GREGORY LODYGENSKY AND CONRAD ROCKEL

09:00-09:45 **PO 2: PLENARY SPEAKER:** Dr. Jeff Neil – Boston Children's Hospital
Diffusion MRI: From Single Cells to Neonates

Trainee Plenary Presentations

09:45-10:00 **PO 10:** Armin Yazdani
Sildenafil Administered After Term Neonatal Hypoxia-Ischemia Increases Mature Oligodendrocytes in the White Matter and Improves Myelination in Rats

10:00-10:15 **PO 11:** Amelie Boutin
Prediction of preeclampsia in nulliparous with baseline maternal risk factors

10:15-10:30 **PO 12:** Giulia Muraca
Perinatal and maternal morbidity and mortality associated with attempted midpelvic operative vaginal delivery and cesarean delivery: a population-based retrospective cohort study

10:30-11:00	Refreshment Break

Trainee Plenary Presentations

11:00-11:15 **PO 13:** Justine Dol
eHealth interventions for parents in neonatal intensive care units: a JBI systematic review

11:15-11:30 **PO 14:** Howard Guo
Therapeutic Potential of Human Umbilical Mesenchymal Stromal Cell-Derived Exosomes in Experimental Bronchopulmonary Dysplasia

11:30-11:45 **PO 15:** Francois Olivier
Efficacy of minimally invasive surfactant therapy in moderate and late preterm infants: A multicenter randomized control trial

11:50-13:00 **Parallel Workshops**
Workshop #7 - A GPS (Guaranteed Pathways to Success) for your career development: What are key drivers? [OUTAOUAIS]
Workshop #8 - Imaging in Perinatal Medicine [MONTEBELLO]

12:00-13:30	Lunch: Restaurant Aux Chantignoles

CONCURRENT THEMATIC SESSIONS

THEMATIC SESSION 3

Paediatric Stem Cells
[LE CLUB]

MODERATORS: Dr. BRIAN COX & Dr. MUHAMMAD ONEEB MIAN

13:30 **TO 31 - Invited Speaker**: Dr. Martin Post
Stem cell-derived alveolar-like macrophages for pulmonary cell therapy

14:00 **TO 32 -** Marissa Lithopoulos
Remote organ injury: neural progenitor cell function is impaired in a neonatal mouse model of chronic lung disease leading to adverse neurodevelopment

14:15 **TO 33 -** Sajit Augustine
Mesenchymal stromal cells in Bronchopulmonary dysplasia: Systematic review and Meta-analysis of preclinical studies

14:30 **TO 34 -** Lannae Strueby
Protective effect of human umbilical cord mesenchymal stromal cell-derived exosomes on multifactorial lung injury in neonatal mice

14:45 **TO 35 -** Joanne Joseph
Endothelial Progenitor Cell-derived Exosomes for Neonatal Pulmonary Hypertension

Nursing and Midwifery
[MONTEBELLO]

MODERATORS: Dr. MARILYN AITA & ANDRÉANE LAVALLÉE

13:30 **TO 36 - Invited Speaker**: Dr. Nancy Feeley
Women at-risk for PTSD symptoms following childbirth: A prospective cohort study

14:00 **TO 37 -** Martin Reichherzer
The Ethics of Family Integrated Care in Neonatology

14:15 **TO 38 -** Erin Hetherington
Vulnerable women report high levels of satisfaction with group prenatal care

14:30 **TO 39 -** Kadeen Briscoe
Parental needs rating by parents and nurses: association with illness severity

14:45 **TO 40 -** Debora Cateni
The effect of method of delivery and psychosocial factors on postpartum sexual satisfaction

DOHaD
[OUTAOUAIS]

MODERATOR: Dr. VERN DOLINSKY

13:30 **TO 41 –Invited Speaker**: Dr. Sarah Kimmins
The Sperm Epigenome Is Implicated In Fertility And Offspring Development

14:00 **TO 42 -** Andrea Constantinof
Predictive Modelling of Behavior through Gene Expression

14:15 **TO 43 -** Andrew Woodman
Prenatal Iron Deficiency Causes Fetal Kidney Hypoxia and Sex-Dependent Upregulation of Cytochrome c Oxidase

14:30 **TO 44 -** Evan Formosa
Maternal Nutrient Restriction (MNR) in Guinea Pigs leads to fetal growth restricted (FGR) offspring with differential rates of organ catch-up growth

14:45 **TO 45 -** Gerald Giesbrecht
Prenatal bisphenol A exposure is associated with sexually dimorphic changes in hypothalamic-pituitary-adrenal axis function in infants

15:00-17:00	**Special Group Meetings** – ReACH Project: Investigators & Collaborators Meeting [QUEBEC ROOM] CIHR - Clinician-Investigator Teams: Performance Measurement Working Group [MONTEBELLO] A Career in Perinatal Epidemiology Research: Advice to Those Beginning Their Journey [OUTAOUAIS]
17:15-18:00	**Business Meeting** [CANADA ROOM]
19:00-21:00	**Gala Dinner** [Outaouais] **"History of Perinatal Research and Meetings in Canada"** David M. Olson, Ph.D., FRCOG Graeme N. Smith MD, PhD, FRCSC

Friday, February 17, 2017

07:00-09:00	Breakfast: Restaurant Aux Chantignoles

SCIENTIFIC PLENARY SESSION [Room Outaouais]

MODERATORS: Dr. DAVID OLSON AND MADISON BEATTY

09:00-09:45 **PO 3: PLENARY SPEAKER:** Dr. Louis Muglia – University of Cincinnati
Human Evolution, Genetics, and Birth Timing

Trainee Plenary Presentations

09:45-10:00 **PO 16:** Julie De Meulemeester
Vascular Function, Structural Changes and Arterial Stiffness Along with High Blood Pressure in Young Adults Born Very Preterm

10:00-10:15 **PO 17:** Gabriel Shapiro
Overall and cause-specific infant mortality among First Nations, Inuit, and Métis populations in Canada

10:15-10:30 **PO 18:** Sophie Tremblay
Microglial depletion prior to a perinatal inflammatory stress aggravates outcomes in mice

10:30-11:00	Refreshment Break

Trainee Plenary Presentations

11:00-11:15 **PO 19:** Marinela Grabovac
What is the safest mode of delivery for extremely preterm breech infants: a systematic review and meta-analyses?

11:15-11:30 **PO 20:** Brittany Moyce
Altered fatty acid and mitochondrial metabolism in the liver of pregnant adiponectin-deficient mice contributes to insulin resistance and gestational diabetes mellitus

11:30-11:45 **PO 21:** Floor Spaans
syncytiotrophoblast extracellular vesicles alter angiotensin II-induced vasoconstriction in mouse uterine arteries

12.30-13:00 **The CNPRM Olson - Smith Punch Out Debate** [Restaurant Aux Chantignoles]
Perinatal Stress and Health 0046etal/Child dEvelopment: The mother is more influencial than the father?

Mother (Western Canada) versus **Father (Eastern Canada)** *moderated by Dr. Deb Sloboda*

Dr. Rhonda Bell, University of Alberta (Lead) — Dr. Janice Bailey, Université Laval (Lead)
Dr. Denise Hemmings, University of Alberta (PI) — Dr. Serge McGraw, Université de Montréal (PI)
Megan Mejer, University of Alberta (Trainee) — Jenna Haverfield, Université de Montréal (Trainee)

12:00-13:30	Lunch: Restaurant Aux Chantignoles

CONCURRENT THEMATIC SESSIONS

THEMATIC SESSION 4

MFM II - Fetal Medicine
[LE CLUB]

MODERATORS: Dr. BARBRA DE VRIJER & Dr. SHERYL CHOO

13:00 **TO 46 - Invited Speaker**: Dr. Mike Seed
Fetal circulatory physiology and brain development in CHD and IUGR

13:30 **TO 47 -** Laurence Soucy-Giguere
Midtrimester intra-amniotic inflammation and development of abnormal gross motor skills in infants

13:45 **TO 48 -** Stephanie Giza
3D Water-Fat MRI of Fetal Fat Development

14:00 **TO 49 -** Stefania Ronzoni
Antenatal management of fetal/neonatal alloimmune thrombocytopenia: should we completely abandon invasive procedures?

14:15 **TO 50 -** Zain Awamleh
Placental microrna expression in pregnancies complicated by intrauterine growth restriction and pre-eclampsia

Neonatology I - Respiration/Ventilation/Cardiology
[MONTEBELLO]

MODERATORS: Dr. ROBERT JANKOV & Dr. LARS MENSE

13:00 **TO 51 - Invited Speaker**: Dr. Grace Parraga
Novel Pulmonary Imaging Biomarkers of Chronic lung disease

13:30 **TO 52 -** Mehdi Shafa
Alveolar Epithelial Cell Therapy Rescues The Lung Phenotype in a Mouse Model of Surfactant protein C Deficiency

13:45 **TO 53 -** Withdrawn

14:00 **TO 54 -** Anastasiya Mankouski
Intermittent hypoxia during recovery from neonatal hyperoxic lung injury causes long-term impairment of alveolar development: a new rat model of bronchopulmonary dysplasia (BPD)

14:15 **TO 55 -** Jean-Claude Lavoie
Impact of parenteral lipid emulsion SMOFLipid and Intralipid on hepatic redox potential of glutathione and DNA methylation in newborn guinea pig

Placental and Fetal Physiology
[OUTAOUAIS]

MODERATOR: Dr. ISABELLA CANIGGIA

13:00 **TO 56 - Invited Speaker**: Dr. John Kingdom
Can Heparin Prevent Severe preeclampsia?

13:30 **TO 57 -** Kathryn Denize
Comparing micorna expression in placentas from active vs. inactive mothers: an exploratory study

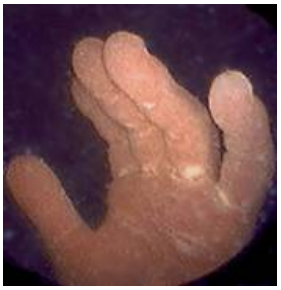
13:45 **TO 58 -** Hua He
Maternal circulating PlGF levels in relation to leptin and adiponectin concentrations in infants born small-for-gestational-age

14:00 **TO 59 -** Kevin Sinclair
Measurement of placental oxygenation in a guinea pig model of intrauterine growth restriction

14:15 **TO 60 -** Withdrawn

14:30-14:45	Refreshment Break

15.00-15:30	**Trainee Awards & Closing Remarks** [OUTAOUAIS]



SEE YOU IN 2018!

Check out our website for update on our 2018 program

www.cnprm.org

ORGANIZING COMMITTEE MEMBERS 2017

The Canadian National Perinatal Research Meeting relies on the excellent guidance and assistance provided by our Organizing Committee. Representing a wide variety of fields within perinatal research, medicine and care, it ensures the conference provides a well-rounded perspective.

MEETING CO-CHAIRS

- **Deborah Sloboda**, Department of Biochemistry and Biomedical Sciences, McMaster University
- **Timothy Regnault**, Department of Obstetrics & Gynaecology, Western University

ORGANIZING COMMITTEE MEMBERS

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- **Shyamala Dakshinamurti**, Children's Hospital Research Institute of Manitoba, University of Manitoba
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- **Jennifer Cordick**, Education Coordinator, Department of Obstetrics & Gynaecology, Western University

PHOTOGRAPHIC CREDITS

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- 3-D photo of fetus from Département de Gynécologie-Obstétrique, CHU Sainte-Justine.

THEMATIC COMMITTEES

DOHaD

- **Convenor: Vernon Dolinsky**, University of Manitoba
- **Shyamala Dakshinamurti**, University of Manitoba
- **Daniel Hardy**, Western University
- **Serge McGraw**, Université de Montréal
- **Anne Monique Nuyt**, Université de Montréal

MFM I - Maternal Medicine

- **Convenor: Emmanuel Bujold**, Université Laval
- **François Audibert**, Université de Montréal
- **Lynne McLeod**, Dalhousie University
- **Jean-Charles Pasquier**, Université de Sherbrooke

MFM II - Fetal Medicine

- **Convenor: Barbra de Vrijer**, Western University
- **Christy-Lynn Cooke**, University of Alberta
- **Genevieve Eastabrook**, Western University

Neonatology I - Respiration/Ventilation/Cardiology

- **Convenor: Robert Jankov**, University of Toronto
- **Anne Monique Nuyt**, Université de Montréal
- **Georg Schmölzer**, University of Alberta
- **Bernard Thébaud**, University of Ottawa

Neonatology II - Neurosciences

- **Convenor: Daniel Goldowitz**, The University of British Columbia
- **Gregory Lodygensky**, Université de Montréal
- **Sylvie Girard**, Université de Montréal
- **Jill Zwicker**, The University of British Columbia

Nursing and Midwifery

- **Convenor: Marilyn Aita**, The University of BC
- **Marjolaine Héon**, Université de Montréal
- **Andréane Lavallée**, Université de Montréal
- **Marie-Josée Martel**, Université du Québec à Trois-Rivières
- **Caroline Paquet**, Université du Québec à Trois-Rivières

Paediatric Stem Cells

- **Convenor: Brian Cox**, University of Toronto
- **Martin Post**, University of Toronto

Perinatal Epidemiology

- **Convenor: Linda Dodds**, Dalhousie University
- **Deshayne Fell**, University of Ottawa
- **Eileen Hutton**, McMaster University
- **K.S. Joseph**, The University of British Columbia
- **Michael Kramer**, McGill University
- **Suzanne Tough**, University of Calgary

Perinatal Nutrition & the Gut

- **Convenor: Stephanie Atkinson**, McMaster University
- **Meghan Azad**, University of Manitoba
- **Sandeep Raha**, McMaster University
- **Wendy Ward**, Brock University

Placental & Fetal Physiology

- **Convenor: Isabella Caniggia**, University of Toronto
- **Paul Delgado Olguin**, University of Toronto
- **David Olson**, University of Alberta
- **Kaiping Yang**, Western University

Reproductive (epi)Genetics and Fertility

- **Convenor: Marc-André Sirard**, Université Laval
- **Jay Baltz**, University of Ottawa
- **Jacquetta Trasler**, McGill University

Reproductive Immunology

- **Convenor: Anne Croy**, Queen's University
- **Alexander Beristain**, The University of British Columbia
- **Caroline Dunk** , University of Toronto
- **Patricia Lima** Queen's University

VENUE

Fairmont Le Château Montebello

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Quebec, Canada
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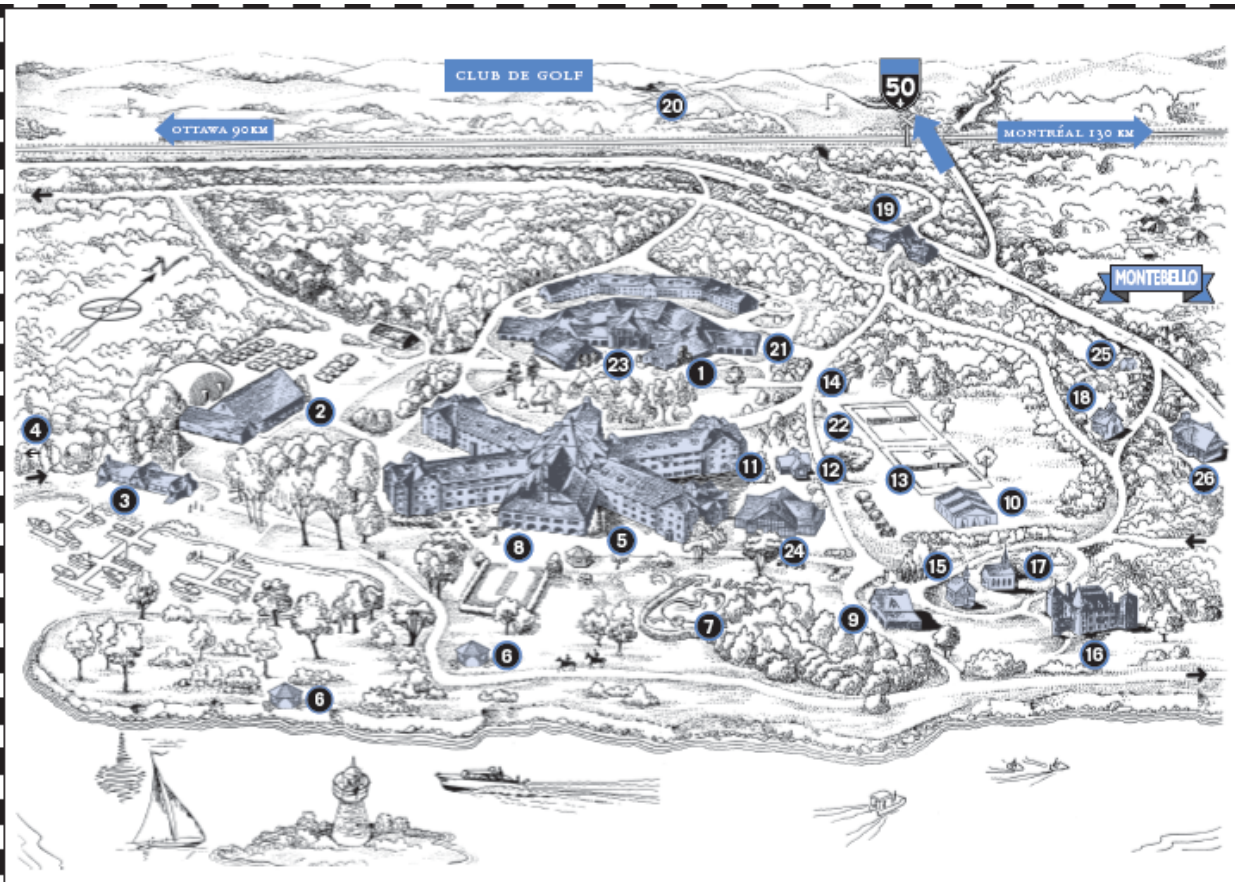
FAX + 1 819 423 1133
chateaumontebello@fairmont.com

www.fairmont.com/montebello



LÉGENDE

1 Motoneige
Ski de fond
Curling
Véhicule tout-terrain
2 Centre sportif
Piscine
Squash • Tennis
Spa
3 Club Nautique
Bateau ponton
Pêche blanche
4 Glissade en pneumatiques
5 Terrasse Le Riverain
6 Gazebos
7 Piscine extérieure
8 BBQ en plein air
9 Écurie • Traîneau à cheval
10 Tente de réception
11 Aire de jeux pour enfants
Golf miniature
12 Chalet des sports
Location d'équipement (été)
13 Courts de tennis extérieurs
14 ÉTÉ : Départ – sentiers de randonnée
HIVER : Départ – pistes de ski de fond • Traîneau à chiens
15 Hangar à grains (Manoir-Papineau)
16 Lieu historique national du Manoir-Papineau
17 Église anglicane
18 Chapelle funéraire Papineau
19 Entrée principale
20 Pavillon du club de golf
21 Salon Héritage
22 Patinoires
23 École de conduite Land Rover Expérience
24 Centre de conférence
25 Maison du Jardinier Camp Explora
26 ChocoMotive : écomusée du chocolat

LEGEND

1 Snowmobiling
Cross-country skiing
All-terrain vehicle
Curling
2 Sports centre
Indoor pool
Squash • Tennis
Spa
3 Yacht Club
Pontoon boat
Ice fishing
4 Tube Sliding
5 Le Riverain Terrace
6 Gazebos
7 Outdoor pool
8 Outdoor BBQ
9 Stables • Sleigh rides
10 SUMMER: Marquee
11 Children's Playground
Mini-golf
12 Sports chalet
Equipment rental (summer)
13 Outdoor tennis courts
14 SUMMER: Start of nature paths
WINTER: Start of cross-country ski trails • Dogsledding
15 Granary of Manoir-Papineau
16 Manoir-Papineau
National Historic Site
17 Anglican Church
18 Papineau Funeral Chapel
19 Main entrance to resort
20 Golf Clubhouse
21 Heritage Room
22 Skating rinks
23 Land Rover Experience
Driving School
24 Conference Centre
25 Gardener's House
Camp Explora
26 ChocoMotive:
Chocolate Economuseum

One of the world's most unique resorts

A BRIEF HISTORY

Fairmont Le Château Montebello is an extraordinary structure with a fascinating history. The resort is located on a site originally known as the *Seigneurie de la Petite-Nation* which belonged to Bishop Montmorency de Laval, a founder of Québec. In the 19th century the property passed into the hands of Joseph Papineau, a member of the Legislative Assembly, and then to his son Louis-Joseph Papineau, who played an important role in the Rebellion of 1837. He constructed Manoir Papineau between 1846 and 1850. His home, on the grounds of the resort, is now the Manoir Papineau National Historic Site, one of the most treasured heritage locations in the area. (The museum and grounds welcome visitors from mid-May through mid-October).

The surrounding picturesque region is known as the Outaouais. The front of the resort overlooks the Outaouais River, one of the waterways used by the first *voyageurs*. And behind, the foothills of the Laurentian mountains rise up to create the rolling landscape.

BUILT IN RECORD TIME

The remarkable log château was built in 1930, at the onset of the Great Depression. The first log was laid on April 7. In June, newspapers across North America told of the completion of the massive log château in only three months.

The unusual structure, in the form of a six-point star, was built of 10,000 hand-cut and set red cedar logs all transported to Montebello directly from the forests of British Columbia by way of the Canadian Pacific Railway.

The project was the dream of Swiss-American H.M. Saddlemire, who was inspired by the châteaux of the Swiss Alps. Finnish master-builder Victor Nymark oversaw the work of as many as 3,500 craftsmen at the peak of construction.

A POPULAR RETREAT

For 40 years, the château was a private retreat – *The Seignory Club* – whose membership included prime ministers, royalty, and Canada's business elite. In 1970, the resort was acquired by Canadian Pacific Hotels Corporation and opened to the public. It quickly became one of the premier resorts in Eastern Canada.

Over the decades, numerous well-known political leaders and celebrities have passed through our doors: former Canadian Prime Ministers Lester B. Pearson and Pierre Elliott Trudeau, President Ronald Reagan, Bette Davis (1939) and Joan Crawford (1940), to name just a few.

HOSTING WORLD LEADERS

In 1981, Fairmont Le Château Montebello played host to the leaders attending the G7 Economic Summit. In 1983, both the Bilderberg congress and the NATO conference were held here. In 1989, the 17th Annual Conference of New England Governors and Eastern Canada Premiers was convened at the "log castle." And in 2007 the resort hosted the North American Leaders Summit attended by President Bush, President Calderon and Prime Minister Stephen Harper.

Un endroit unique au monde

NOTRE HISTOIRE

Le site du Fairmont Le Château Montebello est riche en histoire. La Seigneurie de la Petite-Nation, comme connue auparavant, avait appartenu tout d'abord au premier évêque de la Nouvelle-France, Monseigneur de Laval, un fondateur de Québec. Au 19e siècle, la propriété devint le domicile de Joseph Papineau, un membre de l'Assemblée législative ainsi que de son fils Louis-Joseph Papineau, personnage important au moment de la Rébellion en 1837. La maison Papineau bâtie par Louis-Joseph entre 1846 et 1850 demeure aujourd'hui un témoignage de cette phase historique. D'ailleurs elle est maintenant musée, le Lieu historique national du Manoir-Papineau, et accueille des visiteurs du monde entier (de la mi-mai jusqu'à la mi-octobre).

Cette région est tout aussi scénique qu'historique. La rivière des Outaouais, la route des premiers voyageurs, jalonne l'hôtel. Les montagnes des Laurentides s'élèvent à l'arrière de celui-ci.

CONSTRUIT EN UN TEMPS RECORD

Les trois bâtiments de ce chef d'oeuvre architectural furent construits en 1930, au début de la Grande Dépression. L'installation de la première poutre se fit le 7 avril 1930. En juin, les journaux signalaient la fin de la construction d'un monumental château de bois rond en trois mois seulement.

Cet hôtel de dimensions uniques au monde, ayant la forme d'une étoile à six pointes, est composé de 10 000 poutres de cèdre rouge de la Colombie-Britannique qui furent transportées par les chemins de fer du Canadien Pacifique.

Le projet était l'œuvre d'un américain d'origine suisse, H.M. Saddlemire, qui s'était inspiré des grands hôtels des Alpes suisses. Un contremaître

finlandais, Victor Nymark, dirigea le chantier qui, au plus fort de la construction, regroupait 3 500 ouvriers.

ÉTABLISSEMENT PRISÉ

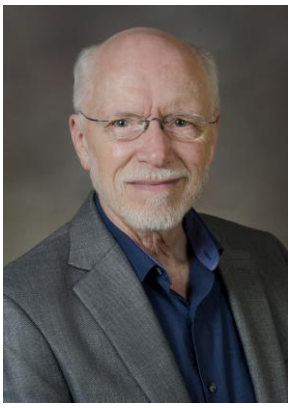
Connu initialement comme le Club Seigniory, Le Château Montebello est opéré depuis 1970 par la Corporation Hôtelière Canadien Pacifique. Maintenant connu sous le nom de Fairmont Le Château Montebello, l'endroit a accueilli d'innombrables célébrités qui ont fait de cet endroit leur halte favorite. Ce sont des personnalités de la scène politique telles que Lester B. Pearson, Pierre Elliott Trudeau, Ronald Reagan et plusieurs autres, des vedettes du cinéma telles que Bette Davis (1939) et Joan Crawford (1940) qui ont passé les portes du Club Seigniory.

HÔTE DE PERSONNALITÉS POLITIQUES

En 1981, Fairmont Le Château Montebello faisait les manchettes internationales, lorsque les Chefs d'État des pays les plus industrialisés du monde s'y rencontraient lors du Sommet Économique. Il en a été de même au moment de la tenue des Réunions de Bilderberg et de l'OTAN en 1983, et de la 17e Conférence annuelle des Gouverneurs de la Nouvelle Angleterre et des Premiers Ministres de l'est du Canada en 1989. En 2007, Fairmont Le Château Montebello a reçu le président américain Bush, le président mexicain Calderon et le premier ministre Stephen Harper lors du sommet annuel des chefs de gouvernement nord-américain.

GUEST SPEAKER BIOPROFILES

PLENARY SESSION SPEAKERS



Kent Thornburg, Ph.D.
Oregon Health and Science University

What are all of those black holes in the placenta?
[Wednesday, February 15]

Kent L. Thornburg, PhD, is the M. Lowell Edwards Endowed Chair and Professor of Medicine in the Knight Cardiovascular Institute at the Oregon Health & Science University. He holds joint professorships in the Departments of Physiology & Pharmacology, Obstetrics & Gynecology and Biomedical Engineering. He directs the Center for Developmental Health in the Knight Cardiovascular Institute and the OHSU Bob and Charlee Moore Institute for Nutrition & Wellness. He studies how women adapt to pregnancy and the roles of maternal diet and body composition in regulating fetal growth and lifelong health. He collaborates with scientists in England, New Zealand, Switzerland, Finland, Australia and India. He oversees clinical studies in rural Oregon and Alaska. Kent Thornburg serves regularly on advisory panels at the National Institutes of Health, the American Heart Association and the Children's Heart Foundation and serves on the medical advisory board of the Preeclampsia Foundation. He is director of translational research training for the Knight Cardiovascular Institute and holds multiple grants from the NIH. He recently co-chaired the task force to determine the 10 year vision of the developmental origins of health and disease for the National Institute of Child Health and Human Development.

Jeff Neil, MD, PhD
Boston Children's Hospital

Diffusion MRI: From Single Cells to Neonates
[Wednesday, February 15]

Workshop #7 - A GPS (Guaranteed Pathways to Success) for your career development: What are key drivers?
[Thursday, February 16]

Jeff Neil is a Pediatric Neurologist with a PhD in Neuroscience. He is past president of the International Society for Magnetic Resonance in Medicine. His clinical specialty is Neonatal Neurology, and much of his clinical practice consists of serving as a consultant in the neonatal intensive care units at Boston Children's, Brigham and Woman's, and Beth Israel Hospitals in Boston. His research is focused on understanding brain development and injury in infants. He has spent two decades researching diffusion magnetic resonance imaging from both technical and clinical viewpoints.

Louis J. Muglia, MD PhD
University of Cincinnati College of Medicine

Human Evolution, Genetics and Birth Timing
[Thursday, February 16]

Dr. Muglia is Co-Director of the Perinatal Institute, Director of the Center for Prevention of Preterm Birth and Vice Chair for Research at Cincinnati Children's Hospital Medical Center, and Professor of Pediatrics at University of Cincinnati College of Medicine. In addition, he serves as Principal Coordinating Investigator of the March of Dimes Prematurity Research Center Ohio Collaborative. Dr. Muglia has been a leader in the analyses of the molecular pathways leading to birth. These studies have evolved to specifically focus on the mechanisms controlling the timing for birth in humans using genetics and comparative genomics. The goal of the Muglia laboratory is to understand the molecular machinery comprising this biological clock to prevent human preterm birth.
Among Dr. Muglia's achievements are more than 200 publications and many awards, including the Society of Pediatric Research Young Investigator Award, and election to the American Society for Clinical Investigation and Association of American Physicians. In 2013, Dr. Muglia was elected to membership in the National Academy of Medicine. Dr. Muglia earned his Doctor of Medicine (1988) and Doctor of Philosophy (1986) degrees from the University of Chicago. He received a Bachelor of Science degree in biophysics from the University of Michigan in 1981.

THEMATIC SESSION SPEAKERS

Meghan Azad
University of Manitoba

Breastfeeding, Gut Microbiota and Child Health
[Wednesday, February 15]

Dr. Meghan Azad draws on dual expertise in basic science (biochemistry and genetics) and clinical research (epidemiology and pediatrics) to conduct translational research on the developmental origins of chronic disease. Her postdoctoral research on the infant gut microbiome was awarded the Canadian Medical Association Journal Bruce Squires Award for research "most likely to impact clinical practice". Her current research program is focused on maternal nutrition, breastfeeding, and breast milk composition in the development and prevention of childhood obesity and allergic disease. Recent findings from the Azad lab show that breastfeeding may prevent wheezing during infancy, and that consuming artificial sweeteners during pregnancy may predispose offspring to obesity.

Dr. Azad co-leads the Manitoba site of the Canadian Healthy Infant Longitudinal Development (CHILD) Study, a national pregnancy cohort following 3500 children to understand how early life experiences shape lifelong health (www.canadianchildstudy.ca). She also co-leads the Population Health Pillar for the Manitoba Developmental Origins of Chronic Disease Network (DEVOTION, www.devotionnetwork.com), and the Maternal, Fetal and Child Health Working Group for the new Canadian Urban Environmental Health Research Consortium (CANUE). Dr. Azad also serves on the Executive Council for the International Society for Research in Human Milk and Lactation, and the Breastfeeding Committee of Canada.

Sven Cnattingius
Karolinska Institutet

Maternal overweight/obesity and offspring risks
[Wednesday, February 15]

Sven Cnattingius studied medicine at Uppsala University and graduated in 1975. He became Board Certificate in Obstetrics and Gynecology in 1982 and defended his thesis in 1984. He is working at Karolinska Institutet since 1997 and became professor in reproductive epidemiology in 1997.

Sven Cnattingius research includes environmental risk factors for pregnancy complications and adverse health effects on the fetus/infant. Such risk factors include maternal smoking and snuff use and maternal overweight/obesity. He has also studied familial factors related to pregnancy complications and offspring health, and the long-term effects of pregnancy on offspring and maternal health (predominantly focused on cardiovascular and cancer morbidity).

Sven Cnattingius present research is predominantly focused on: Maternal overweight, obesity and weight gain during pregnancy with respect to infant and childhood risks; Loss of a close relative during pregnancy (as a measure of stress) and risks of pregnancy complications and complications in the newborn; Long-term effects of pregnancy for the mother; The tendency to repeat pregnancy and newborn complications across generations; Asphyxia during delivery.

Anne Croy
Queen's University

Is There Evidence for Lymphocyte-Initiated Pregnancy Failure?
[Wednesday, February 15]

Anne Croy received her DVM from University of Guelph and PhD in Immunology from University of Toronto. She developed her interests in reproductive biology and uterine Natural Killer (uNK) cells as a PDF at Brock University. From 2004-2016, Dr. Croy held the Tier 1 Canada Research Chair in Reproduction, Development and Sexual Function at Queen's University, Kingston where she recently became an adjunct and emeritus professor in the Department of Biomedical and Molecular Sciences. Dr. Croy is widely recognized for her findings on the essential role of interferon gamma production in pregnancy-associated uterine spiral arterial remodeling and for the roles of uNK cells in promotion of early post implantation decidual angiogenesis. Her central research interest are in preeclampsia, including its impacts of the vascular and neurological development of children whose gestations were complicated by this maternal syndrome. Her recent collaborative studies address the decidual immune system in late pregnancy failures linked with food-borne pathogens or autoimmune disease.

Stella Daskalopoulou
McGill University

Arterial stiffness and prediction of pre-eclampsia: can we do better?
[Wednesday, February 15]

Dr. Stella S. Daskalopoulou is an Internist with special interest in Vascular Medicine. She is a tenured Associate Professor of Medicine, Department of Medicine (Divisions of Internal Medicine and Experimental Medicine), Faculty of Medicine, McGill University.
Dr. Daskalopoulou's research program centers around the identification of early markers of vascular impairment and maintenance of vascular health, with a focus on cardio-metabolic diseases, women's health, and vascular disease prevention.
She performs research in hypertension, arterial stiffness in subjects with different cardiovascular risk factors, including pre-eclampsia, hypertension, diabetes, and smoking, as well as in atherosclerotic disease where she is working towards the identification of novel pathways of atherosclerotic plaque instability.
Dr. Daskalopoulou has established and directs the Vascular Health Unit at the McGill University Health Centre (MUHC), which includes a clinical and a wet-bench lab, and where she is conducting her vascular research projects. She is the co-Leader of the Cardiovascular Health Across the Lifespan (CHAL) Program of the Research Institute of the MUHC, and the Director of the Scholarly Activity Rotation for McGill Internal Medicine Residents at the Montreal General Hospital.
She has over 135 high-quality peer-reviewed journal publications, and over 3000 citations of her work, with an h-index of 31. She has received research funding from several agencies, including Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, and Fonds de recherche du Québec - Santé (> $3.5 million as a Principal/co-Principal Investigator).
She is the Chair of the Central Review Committee of the Hypertension Canada Guidelines. She is the treasurer of the North American Artery Society.
She holds several personal awards, including, among others: the Department of Medicine Early Career Staff Research Award; the Hypertension Canada Jacques-de-Champlain New Investigator Award for significant dedication and contributions to research and health services in Canada; the Young Researcher Award of Excellence from the HSFQ; the Canadian Foundation for Women's Health Research Award; the Bourse FRSQ - La Société Québécoise d'Hypertension Artérielle Jacques-de-Champlain; and the Canadian Society of Internal Medicine New Investigator Award.

Nancy Feeley
McGill University

Women at-risk for PTSD symptoms following childbirth: A prospective cohort study
[Thursday, February 16]

Nancy Feeley RN PhD is Associate Professor, Ingram School of Nursing, McGill University, and Senior Researcher at the Centre for Nursing Research and Lady Davis Research Institute of the Jewish General Hospital in Montreal. She holds a Senior Research Scholar Award from the Fonds de la recherche du Québec Sante (FRQS). She is also Co-Director of the provincially funded Quebec Network on Nursing Intervention Research (RRISIQ). Her program of research focuses on parents' psychological adjustment and parenting in the perinatal period with a particular focus on parents of NICU infants.

Sarah Kimmins
McGill Centre for the Study of Reproduction

The Sperm Epigenome Is Implicated In Fertility And Offspring Development
[Thursday, February 16]

Dr. Sarah Kimmins received her Ph.D. from Dalhousie University in 2003 and completed her post-doctoral training at the Institut de Génétique et de Biologie Moleculaire et Cellulaire in Strasbourg, France. She was appointed to the Department of Animal Science in the Faculty of Agricultural and Environmental Sciences in September of 2005 and is a tenured Associate Professor. She is an associate member of the Department of Pharmacology and Therapeutics, Faculty of Medicine at McGill. She holds a Tier II Canada Research Chair in Epigenetics, Reproduction and Development and is the Associate Director for the McGill Center for the Study of Reproduction (2014-2017).

John Kingdom
University of Toronto

Can Heparin Prevent Severe preeclampsia?
[Friday, February 17]

John Kingdom graduated from Trinity College Dublin Medical School in 1984 and undertook Residency Training Programs in Paediatrics and Obstetrics-Gynaecology in Glasgow. He developed his research interests in the placenta during a Medical Research Council (UK) Research Fellowship. He did his Maternal-Fetal Medicine Fellowship at University College Hospital, London, followed by three years as Assistant Professor. In 1998 he was recruited to his current position as a Clinician-Scientist in Maternal-Fetal Medicine at Mount Sinai Hospital in Toronto. He established the Placenta Clinic with his colleague Dr. Rory Windrim in the Maternal-Fetal Medicine Division in 1999. His basic and clinical research interests in Placental Development and Pathology are currently funded by the Canadian Institutes of Health Research and a variety of donors; he has previously been funded also by the Ontario Physicians' Services Incorporated Foundation and the Alternate Funding Plan Innovation Fund of Mount Sinai Hospital-University Health Network. He has held the Rose Torno Chair at Mount Sinai Hospital since 2005. He directed the University of Toronto Maternal-Fetal Medicine Fellowship Program for ten years until 2009. In 2011 he was President of the US-based Perinatal Research Society. In 2012 he was appointed Head of the Division of Maternal-Fetal Medicine at the University of Toronto and more recently was elected to the Chair of Obstetrics & Gynaecology at the University of Toronto, effective July 2013. John has published over 240 original peer review publications and supervises a wide range of Clinical and Basic Science Trainees. His current research focuses on improving clinical outcomes in women at risk of “placental insufficiency”, advanced imaging methods in IUGR pregnancies and the non-anticoagulant actions of heparin in-vitro and in-vivo.

Grace Parraga
Western University

Novel Pulmonary Imaging Biomarkers of Chronic Lung Disease
[Friday, February 17]

Dr. Parraga’s laboratory is focused on understanding the underlying mechanisms of disease using novel imaging technologies as tools in patient-based research. An important goal of the lab is to validate imaging intermediate endpoints of respiratory disease as potential therapeutic targets. Dr. Parraga completed her PhD in Biochemistry at the University of Washington in Seattle Washington and after completing post-doctoral studies at the Biozentrum, University of Basel, (Basel, Switzerland), she joined F. Hoffman La Roche AG as a Scientist in Pharmaceutical Research and Development. In 2004, she returned to academic research at Robarts Research Institute, Western University. Dr. Parraga’s work has been published in Science, PNAS, Circulation, Radiology, Thorax, ERJ and AJRCCM with over 80 peer-reviewed publications in the last 3 years. She currently serves as a member of the Canadian Respiratory Research Network (CRRN) Steering committee and leads the CRRN imaging platform. She also co-Chairs with Dr Teresa To, the Mentoring and Training committee of the Canadian Lung Association RENASCENT program. Her pulmonary research is currently funded by CIHR Operating grants, Network grant, and the National Science and Engineering Research Council Discovery and Accelerator grants.

Martin Post
University of Toronto

Stem Cell-derived Alveolar Macrophages for Cell Therapy
[Thursday, February 16]

Dr. Martin Post received his PhD from the University of Utrecht, The Netherlands, in 1982. Following postdoctoral research training at Harvard Medical School, he was appointed as an Assistant Professor at Harvard in 1985. This was followed by a move to The Hospital for Sick Children, Toronto in 1986. Here he is the Head and Senior Scientist of the Physiology and Experimental Medicine Program at the Hospital for Sick Children and Professor of Physiology, Pediatrics and Laboratory Medicine & Pathology and at the University of Toronto. His discovery research is focused on pulmonary development, injury and repair. He has authored more than 300 scientific papers, reviews and book chapters and holds a Canada Research Chair in Fetal, Neonatal and Maternal Health. He directs the Centre for Study of Complex Childhood Diseases, a Canadian-Foundation of Innovation-funded translational research initiative, supporting interventional studies in preclinical models and in patients. He is also the Scientific Director of the Analytical Facility for Bioactive Molecules enabling Metabolomic research in Toronto and beyond. He has received numerous awards, including the distinguished Canadian Institutes of Health Research Lectureship in Respiratory Sciences for life-time achievement in respiratory sciences in 2013.

Mike Seed
University of Toronto

Fetal circulatory physiology and brain development – insights from performing MRI in the setting of CHD and IUGR
[Friday, February 17]

Mike Seed was appointed as a pediatric cardiologist and radiologist at SickKids in Toronto in 2011. He is an assistant professor of Pediatrics, Medical Imaging and Obstetrics and Gynecology at the University of Toronto. He is an Associate Scientist at the SickKids Research Institute and an Associate Member of the Institute of Medical Science. Mike is from England and went to medical school at the University of Newcastle-upon-Tyne in the United Kingdom, where he also undertook his basic specialist training in pediatrics. He moved to Leeds for his residency in Radiology and then completed fellowships in cardiac MRI and pediatric cardiology in Toronto. Mike's clinical role at SickKids involves a combination of general inpatient and outpatient cardiology and cardiac imaging. In partnership with his colleagues in Neurology and Neonatology, he co-founded the Cardiac Neurodevelopment Program in 2015. His research has focused on the relationship between fetal and neonatal cardiovascular physiology and brain development. Mike lives in Mississauga with his wife Nina, who is a pediatric radiologist at Macmaster, and their two boys, Sam (4) and Nick (2).

Jacquetta Trasler
McGill University

Lifelong consequences of perturbing perinatal epigenetic programs
[Wednesday, February 15]

Dr. Jacquetta Trasler is a James McGill Professor in the Departments of Pediatrics, Human Genetics and Pharmacology & Therapeutics at McGill University. She is a Senior Scientist and directs the Developmental Genetics Laboratory at the Montreal Children's Hospital and Research Institute of the McGill University Health Centre (RI-MUHC). She has held a number of leadership roles including as Director of Pediatric Research and Deputy Director/CSO of the RI-MUHC, Director of the McGill MD-PhD Program and President of the Canadian Fertility and Andrology Society. Dr. Trasler's research focuses on understanding the molecular and developmental regulation of gene expression in the male and female germlines with implications for the resulting embryos, including specific interests in DNA methylation and genomic imprinting and the molecular and cellular targets for drug effects on germ cells. In clinical studies she is examining the potential of assisted reproductive technologies, infertility, drug treatment and folate deficiency and supplementation to alter the human epigenome.

Jill Zwicker
The University of British Columbia

Prematurity and Developmental Coordination Disorder
[Wednesday, February 15]

Dr. Jill Zwicker is an Assistant Professor in the Department of Occupational Science and Occupational Therapy at the University of British Columbia. She completed her undergraduate training in psychology and clinical training in occupational therapy at Queen's University, a Master of Arts in Educational Psychology (Learning & Development) at the University of Victoria, a PhD in Rehabilitation Sciences from the University of British Columbia, and Post-Doctoral training in Pediatrics (Developmental Neuroscience) at the University of British Columbia. Jill uses advanced neuroimaging techniques to better understand how the brain differs in children with and without developmental coordination disorder (DCD) and whether brain structure and function can change with rehabilitation intervention. She is also interested in the relationship of prematurity and DCD and is examining early brain development and motor outcomes of premature newborns.

WORKSHOPS AND WORKSHOP SPEAKERS

WEDNESDAY, FEBRUARY 15

08:00-08:50

WORKSHOP #1 - YOUNG INVESTIGATOR WORKSHOP – GETTING THAT 1ST FACULTY POSITION! [LE CLUB]

CONVENORS/SPEAKERS: Drs. GRAEME SMITH (QUEEN'S) AND TIMOTHY REGNAULT (WESTERN)

Outline: *Provide trainees with insight and ideas for how to get the first faculty position in north american institutes (MD and PHD).*

WORKSHOP #2 - NEONATAL FEEDING IN THE NICU AND BEYOND [MONTEBELLO]

CONVENORS/SPEAKERS: Drs. ORLANDO DA SILVA (WESTERN) AND CATHERINE POUND (OTTAWA)

Outline: *To develop an educational and practical program to increase breastfeeding in the Neonatal Intensive Care Unit and for the term infant post-discharge from hospital. The workshop aims to describe the problems that mothers face with breastfeeding, determine when to step in and manage breastfeeding problems, discuss the evaluation and management of low milk supply, recognize and manage slow weight gain, understand the role of the pediatrician it terms of supporting breastfeeding, review the current state of breastfeeding knowledge of Canadian physicians and to discuss educational initiatives that have been piloted.*

11:50-13:00

WORKSHOP #3 - RCT: INNOVATIVE TRIALS IN NEONATOLOGY: MAXIMIZE RESEARCH VALUE, REDUCE WASTE [QUEBEC ROOM]

CONVENOR: Dr. THIERRY LACAZE (CALGARY)

Outline: *Health care research is being criticized for a lack of validity and practical impact and for unacceptable research waste. While critics state that "most published research findings are false", neonatal clinical research should make a difference for child health outcomes. The extent to which this goal is attained can be appraised by the research questions addressed, information gain, relevance and patient centeredness, feasibility, transparency, and value for money of the research effort. Recent evidence suggests that most clinical research fails to be useful because of its design and conduct. While much of this is controversial, the child health research community has developed and is implementing strategies that reduce avoidable research waste and enhance impact. The objectives of the workshop are to 1) review the main reasons for the existence of non-useful clinical trials and research waste, 2) examine the current reform in neonatal drug research that sets new trial standards, 3) review a suite of modern tools for interoperable neonatal health research that help produce clinical research that is useful at a reduced cost.*

SPEAKER: Dr. MARTIN OFFRINGA

WORKSHOP #4 - ADVANCED METHODS FOR PERINATAL EPIDEMIOLOGY [OUTAOUAIS]

CONVENORS: Dr. LINDA DODDS (DALHOUSIE) AND ERIN HETHERINGTON (CALGARY)

Outline: *Propensity score methods are a set of tools for control of confounding in observational data. Propensity score-adjusted estimates can be easier to interpret than regression-adjusted estimates. This workshop will provide a review of the foundations of propensity score methods, demonstrate their use through examples, and discuss some extensions of propensity score methods.*

SPEAKER: Dr. ROBERT PLATT

11:50-13:00 CONTINUED

WORKSHOP #5 - IMPROVING NEONATAL CARE WITH THE HELP OF VETERAN PARENTS: AN OVERVIEW OF CURRENT PRACTICES [MONTEBELLO]

CONVENOR: Dr. ANNE MONIQUE NUYT (MONTREAL)

Outline: *Recently, veteran NICU (Neonatal Intensive Care Unit) parents have become increasingly involved to provide peer-to-peer support to parents of sick neonates. This unique form of support optimizes the integration of families in neonatal care. Veteran NICU parents also assume other roles in clinical care, research, administration and/or teaching, but those roles are rarely described in the literature. We have also identified gaps in knowledge relative to recruitment and training, development and evaluation of programs, primary responsibility and remuneration. This workshop will provide an overview of the activities performed by veteran NICU parents and how to practically integrate parents in different settings/situations.*

SPEAKERS:

Dr. CLAUDE JULIE BOURQUE
Dr. ANNIE JANVIER
GINETTE MANTHA
Dr. AHMED MOUSSA
KATE ROBSON

THURSDAY, FEBRUARY 16

08:00-08:50

WORKSHOP #6 - WRITING A GRANT FOR SUCCESS AND THE FUTURE! [LE CLUB]

CONVENORS/SPEAKERS: Drs. WILLIAM FRAZER (SHERBROOKE), SANDRA DAVIDGE (ALBERTA) AND STEPHEN LYE (TORONTO)

Outline: *Get the latest up to date changes on Perinatal grant opportunities in North America.*

11:50-13:00

WORKSHOP #7 - A GPS (GUARANTEED PATHWAYS TO SUCCESS) FOR YOUR CAREER DEVELOPMENT: WHAT ARE KEY DRIVERS? [LE CLUB]

CONVENORS: Drs. DOUGLAS SWANSON (UBC) AND GREGORY LODYGENSKY (MONTRÉAL)

Outline: *Our two experts will share insights into developing clinical research programs and where they see career opportunities for clinical rehabilitation, clinical trials, and family/community engagement. They are also prepared to discuss how to create a research program and build collaborations, the importance of mentorship, challenges/strategies in funding this type of work, and key Knowledge Translation strategies to bring impact to the clinical and patient communities.*

SPEAKERS:

Dr. ANNETTE MAJNEMER
Dr. JEFF NEIL

WORKSHOP #8 - IMAGING IN PERINATAL MEDICINE [MONTEBELLO]

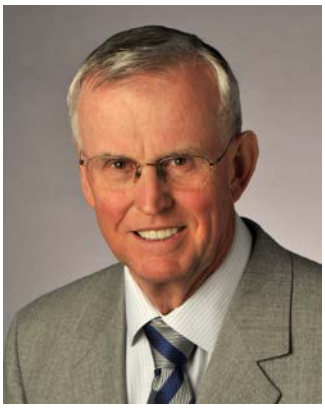
CONVENOR: Dr. CHARLIE MCKENZIE (WESTERN)

Outline: *Attendees will learn about the latest challenges and opportunities in using medical imaging techniques in perinatal medicine.*

SPEAKERS:

Dr. JOHN SLED
Dr. PIA WINTERMARK

BANQUET SPEAKERS



David M. Olson, Ph.D., FRCOG is Professor of Obstetrics and Gynecology, Pediatrics and Physiology at the University of Alberta in Edmonton, Canada. Educated at Augustana University (Sioux Falls, SD), the University of Minnesota, St. Louis University, and the University of Western Ontario (London, Ont), he served as the founding director or co-director of the University of Alberta Perinatal Research Centre, the CIHR Group in Perinatal Health and Disease, the CIHR Strategic Training Initiative in Maternal-Fetal-Newborn Health Research, the AIHS Interdisciplinary Preterm Birth and Healthy Outcomes Team, the GAPPS Inflammatory Pathways to Preterm Birth Team, and the WUN/MOD-sponsored OPERA (Optimal Pregnancy Environment Risk Assessment) program. He is a founding board member of the Child Health Research Institute (London, Ontario), The Mogenson Trust in Physiology (Western University), The Alberta Centre for Child, Family and Community Research (now PolicyWise), the International Pregnancy Research Alliance, and has served several national and international societies in elected office. He organized the annual Western Perinatal Research Meeting for twenty-one years in Banff and was the first organizer of the Canadian National Perinatal Research Meeting in 2014. His laboratory has published >170 papers primarily on the interactions of inflammatory mediators, prostaglandins and cytokines, that transform the uterus from the state of pregnancy to that of delivery at term and preterm, and he and his collaborators are studying the effects of chronic stress and abuse on pregnancy outcomes. He has raised >$40 M for research. He and his collaborators are developing new diagnostics and risk prediction models for adverse pregnancy and newborn outcomes, and they are developing efficacious new therapeutics to delay preterm delivery and protect the fetus from inflammatory harm. He has received a US PCT patent for a new diagnostic. He has received national and international recognition for his achievements. He collaborates with scientists and programs around the world and is a dedicated supporter of the Canadian National Perinatal Research Meeting.

Graeme N. Smith MD, PhD, FRCSC (Professor and Head, Obstetrics & Gynaecology, Anatomy & Cell Biology and Imaging Services, Kingston General Hospital Queen's University).

Dr. Smith completed a combined MD/PhD at the University of Western ON in 1992 under the supervision of Dr. John Patrick. He obtained his FRCSC in Obstetrics & Gynaecology at Queen's University and completed subspecialty training in Maternal-Fetal Medicine at the University of Toronto. Dr. Smith joined the Division of MFM, Obstetrics & Gynaecology at Queen's University in 1999. In July 2013, Dr. Smith was appointed Department Head, Obstetrics and Gynaecology. Dr. Smith divides his time between High Risk Obstetrics and Clinical/Basic science research.

Dr. Smith is a Maternal-Fetal Medicine (MFM) clinician scientist at Kingston General Hospital/Queens University who established the Queen's Perinatal Research Unit (Basic Science and Clinical research laboratories). Dr. Smith is a recipient of a Canadian Institutes of Health Research (CIHR) New Investigators award and a Premier's Research Excellence Award. He has received the highest research recognition at Queen's University in receiving the Basmajian Research Award and the Chancellor's Research Award. He was the Principal Investigator for the CIHR funded Canadian Preterm Labour Nitroglycerin Trial and the CIHR/HSF funded Pre-eclampsia (PE) New Emerging Team (PE-NET) project which helped to establish that the developments of complications in pregnancy, specifically PE, are novel pregnancy-related CVR indicators. He has over 200 peer-reviewed publications and has been/is involved with over 80 peer-reviewed grant funded studies; from basic science to multi-centre randomized placebo controlled trails. He has supervised over fifteen graduate students (MSc and PhD) and dozens of clinical research trainees (medical students and residents).

Dr. Smith's research focuses on PE as a marker of cardiovascular disease and potential therapeutics for the treatment of PE. His primary research interests pertain to adverse pregnancy outcomes as a marker of future maternal health. He developed The MotHERS Program (Mothers Health Education, Research and Screening) (www.themothersprogram.ca) to improve maternal health and outcomes.

Dr. Smith is married to Dr. Susan Chamberlain, also an obstetrician/gynaecologist, and has a 15 year old son and a 13 year old daughter. He has many interests outside of Academic Obstetrics and has previously completed the Ironman Triathlon.

2016 AWARDS OF EXCELLENCE RECIPIENTS

Congratulations to last year's Award of Excellence recipients, whose CNPRM 2017 registration has been generously sponsored by CIHR-IHDCYD:

PARENTAL STRESS IN LATE PRE-TERM INFANTS AND ITS ASSOCIATION WITH CHILD DEVELOPMENT

Muhammad Kashif Mughal, University of Calgary

Introduction: There is a relationship between parenting stress with preterm birth (PTB); mothers and fathers experiences are different. Late preterm infants (LPI; 340-366) account for approximately 75% of all preterm births. Recent studies have depicted increased risk for short-term and long-term morbidities in lpi that may be related to rapid brain growth during the last 6 to 8 weeks of gestation. Under the age of 6 years, LPI are at increased of developmental delays, behavioral and emotional problems compared to term infants. However, limited research has focused association of child development and parenting stress in LPI under 6 months of age. **Objective:** The aim of the study is to examine parenting stress in mothers and fathers of LPI and its association with child development in infants at 4 months corrected age. **Methods:** A total of 111 first-time biological parents of LPI were recruited from two Canadian cities between December 2008 and June 2011. The parenting stress index (PSI) is a self-reported scale with two domains: parent domain reflecting stress as parents, and child domain reflecting perceptions of child temperament and behavior. The ages and stages questionnaires 3rd edition (ASQ-3) measures child development on five domains: communication, gross motor, fine motor, problem-solving, and personal-social. A pearson correlation was carried out to examine the relationship between the PSI parent and child domain scores, and ASQ-3 domain scores. T-tests were used to compare mothers and fathers on PSI parent and child domains. **Results:** Mean ages of fathers and mothers were 34.12 and 31.93 years, respectively. The mean gestational age of infants was 356 (range 34- 36 weeks) and 57% were male. 79% of fathers and 81% of mothers had college education or higher; 80% of families had a household income of $80,000 or above. A statistically significant negative correlation was found between mothers' PSI parent domain stress and ASQ-3 communication score. A significant negative correlation was found between fathers' psi parent domain stress and asq-3 gross motor score. A significant negative correlation was found between PSI parent domain stress (both parents) and ASQ-3 personal-social scores. Compared to fathers, mothers reported significantly greater stress in the psi parent domain. **Conclusion:** Fathers and mothers report different types of stress associated with being the parent of LPI. High levels of fathers' stress negatively impacted child gross motor development and high stress in mothers' negatively impacted child's communication. Fathers and mothers may need different types of support and intervention to manage their stress associated with parenting LPI.

ARRAY ANALYSIS OF G-PROTEIN COUPLED RECEPTORS IN HUMAN MYOMETRIUM: EXPLORING NOVEL TARGETS FOR CLINICAL MANAGEMENT OF LABOUR

Daniela Urrego, University of Calgary

Introduction: Clinical management of labour is currently limited to a small number of targets used to modulate myometrial activation and contraction. Many of are G-protein coupled receptors (GPCRs), including those for prostaglandin (PG)F2a, PGE2 and oxytocin. The GPCR receptor family can elicit both pro-contractile and pro-relaxatory effects in myometrial smooth muscle by signalling via Gq (contractile) and Gi (pro-contractile) or Gs proteins (pro-relaxatory). There is a distinct spatial distribution of many receptor types in the upper and lower myometrium at term that is related to the ability of each tissue segment to respond differently to stimuli for example PGE2 and oxytocin. Spatiotemporal changes in receptor expression, mediating myometrial contractility, may complicate clinical interventions that target these receptors. To improve therapeutic approaches for labour management it is necessary to understand when and where clinically targeted receptors are expressed in the myometrium, and also to identify other regulated receptors as candidate therapeutic targets. **Objective:** To identify the diversity of GPCRs expressed in the term uterus, and compare upper versus lower segment and labour versus non-labour. We hypothesise that additional pro-contractile and pro-relaxatory GPCRs are spatiotemporally regulated in the myometrium. **Methods:** Paired upper and lower segment myometrial biopsies were obtained, with patient consent, following caesarean section deliveries at term (37-40 weeks gestation) with labour (TL) or not in labour (TNL). Total RNA was isolated and reverse transcribed into cDNA for real-time PCR-based array detection of transcripts encoding 370 different GPCRs. Expression data was analyzed using theRT2 Profiler PCR Array Data Analysis Software (v3.5) t-test. **Results:** Out of 370 GPCRs screened 98 were identified to be expressed in the myometrial samples analyzed. Several Gs, Gi and Gq coupled GPCRs were differentially -expressed in a temporally- (TNL versus TL) and spatially- (upper versus lower) dependent manner (Figure 1). As expected our array identified expression patterns for genes well studied in parturition including oxytocin, relaxin/insulin-like family, and β-adrenergic receptors. We also found expression patterns for other genes for which roles in labour have not been studied including numerous orphan receptors, tachykinin, vasoactive intestinal peptide, and α-adrenergic receptors. **Conclusion:** A distinct GPCR expression profile is observed in a spatial- (lower and upper segment) and temporal- (labour-status) dependent manner. It is unlikely that a single GPCR/ target will signal the start of labour; rather more complex and subtle changes of multiple GPCRs are involved. Determining the subtle changes in GPCR expression may lead to the identification of new targets for the manipulation of labour, either the induction of labour at term, or indeed the inhibition of preterm labour.

CIHR IRSC | Institute of Human Development, Child and Youth Health
Institut du développement et de la santé des enfants et des adolescents

PLENARY SESSION

ABSTRACTS

Invited Plenary Speaker

PO 1

WHAT ARE ALL OF THOSE BLACK HOLES IN THE PLACENTA?

Kent Thornburg, Ph.D.
M. Lowell Edwards Chair
Professor of Cardiovascular Medicine
Director, Center for Developmental Health, Knight Cardiovascular Institute
Director, Bob and Charlee Moore Institute for Nutrition & Wellness

In the early years of fetal programming research both animal and human data showed associations between adult onset chronic disease and birthweight. Fetal biologists immediately recognized that differences in fetal growth throughout the whole of gestation implied differences in placental function. However, little additional insight existed into the role of the placenta in determining adult disease risk. That is until it was discovered that Finnish midwives/nurses in Helsinki had measured not only birthweight but also placental weight, length and width and cord length at birth in over 20,000 cases. From these data it was possible to determine that gross placental shape and size predicts hypertension, heart failure, sudden cardiac death, coronary artery disease, diabetes mellitus, asthma, lung cancer, Hodgkin's Lymphoma and reduced lifespan. However, the placenta is not an isolated organ - -placental size and shape interact with maternal body phenotype. Thus, for example, short mothers with small placentas in combination impart disease risk beyond either alone. Small babies with large placentas are also at risk for cardiovascular disease. All of these associations are observational and do not prove cause and effect. Thus, we are left with enormous gaps between descriptive relationships and biological explanations. The scientific community is now saddled with a number of large questions, black holes as I call them, which underlie a significant portion of modern chronic disease prevalence without explanation. The most important of these include:
1) What is the role of pre-pregnancy maternal body composition in determining adult onset disease in offspring?
2) How is placental shape and thickness determined?
3) Why is placental lipid transport closely tied to fetal growth?
4) To what degree does placental size, shape and function drive epigenetic modifications in fetal organs?
5) Does placental function directly affect aging of offspring cardiovascular system?
6) What is the link between placental inflammation and enduring smoldering inflammation in offspring?
Understanding these "black holes" in our knowledge is required before rational therapies to improve fetal growth can be proposed.

Trainee Plenary Presentations

PO 4

TLR4 ANTAGONISM PREVENTS EARLY LEFT VENTRICULAR HYPERTROPHY AND DYSFUNCTION CAUSED BY NEONATAL HYPEROXIA EXPOSURE IN RATS.

Muhammad Oneeb Rehman Mian[1], Ying He[1], Anik Cloutier[1], Thuy Mai Luu[2], Anne Monique Nuyt[2]
[1]Fetomaternal and Neonatal Pathologies Axis, Research Center, and [2]Department of Pediatrics, Sainte-Justine University Hospital, University of Montreal, Canada

Introduction: Preterm birth is associated with altered pro-oxidant and proinflammatory status early in life (1). This disequilibrium can be carried into adulthood and contribute to increased risk of cardiovascular diseases (CVD). Our lab has shown in rats that transient neonatal exposure to high O2, a well-established model of prematurity-related prooxidative conditions, leads to early CV inflammation and remodeling (2). TLR4 signaling is a critical link between inflammation and the pathogenesis of CVD (3). Whether programmed innate activation, via TLR4 signaling, impacts long term CVD is unknown. **Objective:** In an established rat model of preterm birth related-conditions (neonatal high O2 exposure) we intend to investigate whether neonatal TLR4 antagonist treatment versus saline will prevent the development of early CV dysfunction. **Methods:** Male Sprague-Dawley pups were kept with their mother in 80% O2 or

room air from day (P) 3 to 10 of life. Pups were treated with intraperitoneal injections of TLR4 antagonist LPSRS (100 µg/kg) or vehicle (0.9% NaCl) at P3, P6 and P9 (concomitant to O2 exposure; n=8-9 per group, max 3 animals/group/liter). At 4 weeks, body weights were measured and left ventricular (LV) echocardiography was performed under isoflurane anesthesia (2%) using VEVO 3100 system (VisualSonics). Comparisons across groups were made using one-way ANOVA with Tukey HSD post-hoc test. **Results:** Body weight of pups exposed to hyperoxia and treated with vehicle or LPS-RS (101 ± 2 g and 106 ± 2 g) was lower compared to room air controls (117 ± 2 g, P<0.01). Compared to room air vehicles, vehicle-treated hyperoxia animals exhibited increased LV mass index (3.8 ± 0.1 vs 3.3 ± 0.1 mg/g, P<0.05), reduced ejection fraction (74 ± 2 vs 82 ± 1 %, P<0.05) and fractional shortening (43 ± 2 vs 52 ± 2 %, P<0.01), reduced cardiac output index (0.43 ± 0.02 vs 0.56 ± 0.03 ml/min/g, P<0.01), and decreased mitral E-to-A wave ratio (1.3 ± 0.1 vs 1.7 ± 0.1, P<0.01). In LPSRS-treated hyperoxia animals, the LV mass index (3.4 ± 0.1 mg/g), ejection fraction (79 ± 2 %), fractional shortening (48 ± 2 %), cardiac output (0.48 ± 0.02 ml/min/g), and mitral E-to-A wave ratio (1.7 ± 0.1) was not changed compared to room air vehicles. **Conclusion:** TLR4 antagonism prevents early LV hypertrophy and mild systolic and diastolic dysfunction caused by neonatal exposure to hyperoxia.
REFERENCES: 1. Burton GJ et al. Best Pract Res Clin Obstet Gynaecol 2011;25:287–299. 2. Bertagnolli M et al. Hypertension 2014;63:143-150. 3. Bomfim et al. Endocrinol Metabol Syndrome S8:002.

PO 5

EFFECTIVENESS OF INDOMETHACIN, IBUPROFEN AND PARACETAMOL FOR PATENT DUCTUS ARTERIOSUS (PDA) IN PRETERM INFANTS: A NETWORK META-ANALYSIS

Souvik Mitra[1,2], Ivan D Florez[1,3], Maria E. Tamayo[3], Yuang Zhang[1], Behnam Sadeguirad[1], Adriana M. Zea[1,3], Lawrence Mbuagbaw[1], Thuva Vanniyasingam[1], Lehana Thabane[1]
[1]Dept of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada, [2]Division of Neonatal-Perinatal Medicine, Dalhousie University, Halifax, Canada, [3]Dept of Pediatrics, University of Antioquia, Medellin, Colombia

Introduction: Different pharmacotherapeutic interventions have shown effectiveness in the management of patent ductus arteriosus (PDA) in preterm infants. However, it is unclear which ones confer advantage over the rest. **Objective:** To determine the relative effectiveness of all the available interventions for closure of a hemodynamically significant (hs) PDA using Bayesian network meta-analysis. **Methods:** We conducted a systematic review of all randomized controlled trials (RCTs) evaluating intravenous (IV) or oral (PO): indomethacin, ibuprofen and paracetamol compared among them or to placebo for hs-PDA in preterm infants. Studies evaluating prophylactic pharmacotherapy were excluded. The primary outcome was primary closure of an hs-PDA. Secondary outcomes were need for a second course or surgical closure. We searched Medline, Embase, CENTRAL and grey literature upto June 2016. Two reviewers independently screened studies, extracted information, and assessed the risk of bias. A Bayesian network meta-analysis was performed to combine the pooled direct and indirect estimates for each outcome. The Surface under the Cumulative Ranking (SUCRA) probabilities of being the best to worst interventions was computed. The analysis was performed using the OpenBUGs software (v 3.2.3).The review was registered on PROSPERO international registry of systematic reviews (CRD4201501579! 7). **Results:** In total 421 studies were retrieved, and 65 studies (4,397 infants) with 16 different comparisons were included (Figure 1). Indomethacin, ibuprofen and paracetamol were better than placebo to achieve PDA closure. In the ranking the best 3 interventions for achieving closure were PO-high-dose ibuprofen(Prob=0.93), PO-paracetamol(Prob=0.76), and IV-high-dose ibuprofen (Prob=0.75) (Table 1). Placebo(Prob=0.008) and IV-regular dose ibuprofen(Prob=0.29) were ranked the worst interventions for PDA closure compared with the rest. PO-high-dose ibuprofen was also the best intervention for reducing the requirement of second course (Prob=0.85) or surgical closure (Prob=0.99). **Conclusion:** Among preterm infants with hs-PDA, PO high dose ibuprofen seems to be the best intervention for achieving PDA closure followed by PO paracetamol and IV high-dose Ibuprofen. The first of its kind Bayesian network meta-analysis may help guide neonatologists and practice guideline developers choose the best pharmacotherapeutic option based on available evidence.

PO 6

IMPACT OF DURATION OF LABOUR ON INFANT GUT MICROBIOTA

Usha Rai[1], Theodore Konya[2], David S. Guttman[3], Allan B Becker[4], Piushkumar J Mandhane[1], Stuart E Turvey[5], Padmaja

Subbarao[6], Malcolm R Sears[7], James A Scott[2], Andrea M. Haqq[1], Radha Chari[8], Anita L Kozyrskyj[1] and the CHILD study investigators
[1]Pediatrics, University of Alberta, [2]Dalla Lana School of Public Health, University of Toronto, [3]Cell and Systems Biology, University of Toronto, [4]Pediatrics & Child Health, University of Manitoba, [5]Pediatrics, UBC, [6]Pediatrics, University of Toronto, [7]Firestone Institute for Respiratory Health, McMaster University, [8]Obstetrics and Gynecology, University of Alberta

Introduction: Labour dystocia is the leading cause of primary C-section (CS) (Barber et al 2011). CS is associated with divergent gut microbial colonization in infants (Azad et al 2015). Since the pioneer gut colonizers play a pivotal role in immune-programming and regulation of host energy harvest and adiposity, infant gut microbiota have profound implications for long-term health consequences. Protracted labour is often intertwined with prolonged rupture of membranes, risk of chorioamnionitis, accumulation of lactate, maternal overweight and greater CS-risk. Thus, duration of labour may impact the infant gut microbiota by influencing the opportunity of microbial seeding of newborn gut. **Objective:** To explore the association between duration of labour and infant gut microbiota. **Methods:** The study involved a subset of 1028 infants from the Canadian Healthy Infant Longitudinal Development (CHILD) national birth cohort. Data on labour and birth characteristics were obtained from hospital birth charts. Infant fecal samples were collected 3 to 4 months after delivery, and fecal microbiota characterized by Illumina high-throughput gene sequencing of the hyper-variable V4 region of 16S rRNA. Microbiota taxon abundance and diversity were compared between infants based on duration of labour using Mann-Whitney U-test. **Results:** Approximately 1 in 5 infants were born after total active labour longer than 12 hours (n=922, 21.1%) and 2nd stage longer than 2 hours (n=871, 19.3%). Preliminary analysis, pending adjustments for mode of delivery and other co-variates, showed that total labour duration longer than 12 hours was associated with increased abundance of family Clostridiaceae (p=0.001) (of phylum Firmicutes). With 2nd stage longer than 2 hours, genus Clostridium (p =0.001) of the family Clostridiaceae and genus Citrobacter of the family Enterobacteriaceae (and phylum Proteobacteria) (p=0.045) showed greater abundance, while genus Bifidobacterium (of phylum Actinobacteria) was depleted (p=0.001). **Conclusion:** Our findings provide evidence of association between duration of labour and changes to infant gut microbial composition at 3 to 4 months of age. Prolonged labour duration may contribute to infant gut dysbiosis, and may herald long-term health risks.

PO 7

PREDICTION OF PREECLAMPSIA IN NULLIPAROUS WITH UTERINE ARTERY DOPPLER

Suzanne Demers, Amélie Boutin, Cédric Gasse, Olivier Drouin, Mario Girard, Emmanuel Bujold

Introduction: Uterine artery (UtA) Doppler has been used to identify women at high-risk of preeclampsia (PE) for the last two decades. Recent evidences showed that such women could benefit from low-dose aspirin initiated in early pregnancy. However, there is a current controversy about the predictive value of UtA Doppler in the first-trimester of pregnancy. **Objective:** To evaluate the performance of UtA Doppler in the first-trimester for the prediction of preeclampsia. **Methods:** We conducted a prospective cohort study of pregnant nulliparous women with a singleton and live fetus at their 11-13 weeks visit. Participants with fetuses with morphological or chromosomic anomaly leading to medical abortion were subsequently excluded. UtA Doppler was performed on both uterine sides using the Fetal-Medicine Foundation (FMF) guidelines by certified technicians. The mean UtA pulsatility index (PI) were calculated and reported in multiple of median (MoM) adjusted for gestational age was used to as independent variable. Using ROC curves analyses, we calculated the screening performance [area under the curve (AUC)] of mean UtA PI MoM for the prediction of PE, preterm PE and early-onset (<34 weeks) PE, as well as detection rates (DR) at specific false-positive rates (FPR) of 5%, 10% and 25%. **Results:** Out of 4804 nulliparous women recruited at a mean gestational age of 13.0±0.6 weeks, we observed 246 (5.1%) cases of PE, 34 (0.7%) of preterm PE, and 10 (0.2%) cases of early-onset PE. We observed that the mean UtA PI was not associated with the risk of PE [AUC= 0.51 (95%CI: 0.47 – 0.55, p=0.700)] However, first-trimester mean UtA PI was significantly associated with the risk of preterm PE [AUC= 0.65 (95%CI: 0.54 – 0.77, p=0.008)] and particularly early-onset PE [AUC= 0.80 (95%CI: 0.64 – 0.97, p=0.001)]. At false-positive cut-off rates of 5%, 10% and 25%, we could have predicted 21%, 35% and 56% of preterm PE and 30%, 50% and 70% of early-onset PE, respectively. **Conclusion:** First-trimester UtA Doppler is associated with the risk of preterm and early-onset PE but

not with term PE. Its predictive values preclude its use as single first-trimester marker for the prediction of PE in low-risk population but could be beneficial in combination with other markers

PO 8

EARLY EMBRYONIC INDUCTION OF FETAL ALCOHOL SPECTRUM DISORDER LEADS TO DNA METHYLATION PERTURBATIONS AT MID-DEVELOPMENT IN MOUSE BRAIN AND PLACENTA

Lisa-Marie Legault[1,2], Virginie Bertrand-Lehouillier[1,2], Roxane Landry[1], Maxime Caron[1], Daniel Sinnett[1,2], Serge McGraw[1,2]
[1]Centre de Recherche du CHU Sainte-Justine, Montréal, Canada, [2]Département de Biochimie, Faculté de Médecine, Université de Montréal, Canada

Introduction: Prenatal alcohol exposure (PAE) is known to altered epigenetic profiles in cells during brain development and be part of the molecular basis underpinning Fetal Alcohol Spectrum Disorders (FASD) etiology. However, the consequences of a PAE during early embryonic life on the future epigenetic landscape of the brain remain unknown. **Objective:** Our research hypothesis is that a PAE during pre-implantation will initiate DNA methylation dysregulation. Consequently, we believe that these original epigenetic alterations will be perpetuated and amplified in the developing brain, leading to abnormal brain functions associated to FASD. **Methods:** To test this, we instigated FASD in mouse 8-cell embryos by injecting ethanol at 2.5 days of pregnancy (E2.5). We collected FASD (ethanol) and control (saline) E10.5 embryos/placentas. Genome-wide quantitative DNA methylation profiles of forebrains and placentas were established by Reduced Representation Bisulfite Sequencing. **Results:** Results : A comparison of all our FASD samples (n=12) vs all controls samples (n=8) showed 686 differentially methylated tiles (DMTs) in the forebrain and 2942 DMTs in the placenta. Further analysis also brought to us that males and females embryos seem to response differently to ethanol exposure. Interestingly, we exposed 21 specific regions abnormally methylated in both FASD forebrain and placenta samples. **Conclusion:** Our study establishes that early embryonic PAE can cause epigenetic dysregulations that leads to permanent alteration in the future epigenetic program of brain cells. The epigenetic dysregulations also observed in FASD placental tissues allow us to believe that the placenta could be use for epigenetic FASD screening at birth. Altogether, our results allow us to have a better understanding of how epigenetic perturbations can alter the normal function of the brain and lead to neurodevelopmental disorders present in children with FASD.

PO 9

HIGH FAT DIET INDUCES PREMATURE EGRESS OF PRO-INFLAMMATORY MONOCYTES IN REPRODUCTIVELY CYCLING NON-PREGNANT FEMALE MICE

Jessica A. Breznik, Christian Schulz, Kevin P. Foley, Jonathan D. Schertzer, Deborah M. Sloboda, Dawn M. E. Bowdish

Introduction: Few laboratory studies on obesity have focussed on females due to the inherent challenges in controlling for interactions between reproductive metabolic responses that occur over the estrous cycle. Therefore we set out to characterize and compare female metabolic adaptation and immune function in the context of obesity whilst controlling for reproductive stage. In obesity, changes in microbial metabolism are thought to result in decreased intestinal barrier function and translocation of bacterial products into circulation, which stimulate a low-grade chronic inflammatory response. Maturation of monocytes (macrophage precursors) to a pro-inflammatory phenotype is characteristic of this inflammation, with their subsequent infiltration into adipose tissue. It is unknown whether reproductive hormones affect monocyte maturation. These data will inform a female baseline response to a high fat diet which can then be used to investigate obesity during pregnancy. **Objective:** To characterize high fat-induced changes in female intestinal permeability and soluble and cellular inflammation while controlling for reproductive stage. **Methods:** Female C57BL/6 wildtype mice were fed either standard chow (3% kcal fat n=5) or high fat diet (60% kcal fat n=9) from 4 weeks of age for 6 weeks. Weight gain and kcal consumption were monitored weekly. Fasting blood glucose, gonadal and mesenteric fat weight, and transcellular intestinal permeability were measured at endpoint, serum and tissues were collected for future analyses. Blood and bone marrow immune cell populations were analyzed by flow cytometry. At each outcome measure, vaginal smears were analyzed for reproductive stage. **Results:** Females fed high fat diet had significantly more gonadal and mesenteric fat and higher overall body weight. High fat diet led to an increase in pro-inflammatory monocytes in circulation and elevated fasting glucose levels. Intestinal permeability was not different with dietary treatment. In these preliminary data changes in monocyte populations, fasting glucose, and intestinal permeability do

not appear to correlate with reproductive stage. **Conclusion:** High fat diet feeding for 6 weeks in young female mice caused increased adiposity that was associated with an egress of immature pro-inflammatory monocytes from bone marrow and metabolic changes characteristic of obesity. Initial analyses suggest that this change is not further influenced by female reproductive cycle stage.

Invited Plenary Speaker

PO 2

Diffusion MRI: From Single Cells to Neonates

Jeff Neil, MD, PhD
Boston Children's Hospital

Diffusion magnetic resonance imaging (MRI) is widely used in the clinical setting because of its capacity to show brain injury within minutes of its occurrence. The contrast between normal and injured tissue is a result of a rapid reduction in water displacements (also known as water apparent diffusion) in injured brain. Remarkably, the biophysical principles underlying this change in apparent diffusion are not yet understood. We will review studies of water apparent diffusion aimed at elucidating these mechanisms in three systems: 1) single frog oocytes, 2) HeLa tumor cells, and 3) cultured rodent glia and neurons. Diffusion MRI is also useful for evaluating tissue microstructure. In this application, information is obtained relating to differences in water apparent diffusion along different axes of tissue. For example, water apparent diffusion in white matter is greater parallel to axons than perpendicular to them, a phenomenon known as diffusion anisotropy. We will review the application of tissue anisotropy measures to assessment of cortical and white matter development in human preterm infants

Trainee Plenary Presentations

PO 10

SILDENAFIL ADMINISTERED AFTER TERM NEONATAL HYPOXIA-ISCHEMIA INCREASES MATURE OLIGODENDROCYTES IN THE WHITE MATTER AND IMPROVES MYELINATION IN RATS

Armin Yazdani[1], Virginie Bleau[1], Zehra Khoja[1], Pia Wintermark[1]
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Introduction: Neonatal encephalopathy remains a leading cause of mortality and morbidity worldwide. Neonatal encephalopathy often leads to severe white matter injury that hinders repair of the developing brain and leads to long-term neurological impairments. We have shown that sildenafil decreased brain injury following term neonatal hypoxia-ischemia; however, the mechanism remains unknown for now. Sildenafil has been shown to increase oligodendrocyte progeny in the ischemic brain of the middle-aged mouse. Sildenafil may thus also be useful in newborns to improve the myelination capability by increasing oligodendrogenesis following hypoxia-ischemia. **Objective**: To determine how myelination and oligodendrogenesis are impaired in the central nervous system after neonatal hypoxia-ischemia (HI) at term-equivalent age and whether sildenafil may modulate this activation. **Methods:** Neonatal HI was induced in male Long-Evans rat pups at postnatal day 10 (P10) by left common carotid ligation followed by 2-hour exposure to 8% oxygen. Sham operated rat pups served as control. Both groups were administered 0 (vehicle), 2, 10 or 50 mg/kg of sildenafil twice daily by oral gavage, starting from 12 hours post-HI for 7 consecutive days. At P30, rats were sacrificed and their brains extracted. Hematoxylin and eosin staining was performed to analyze the structure of the myelin sheath. Olig2 and CC-1 immunostaining were performed to assess the proportion of mature oligodendrocyte to total oligodendrocytes. **Results**: HI caused a significant decrease in myelin sheath thickness in the corpus callosum and left external capsule compared to sham vehicle rats. Sildenafil (all dosage) reverted the myelin sheath thickness back to levels comparable to sham vehicle rat animals. There were no significant differences in the number of total oligodendrocytes or mature oligodendrocytes between HI vehicle and sham vehicle rat in the corpus callosum or left external capsule. High doses of sildenafil (50mg/kg) significantly increased the number of total oligodendrocytes as well as mature oligodendrocytes in the corpus callosum. There were no changes in number of total and mature oligodendrocytes in the left external capsule after sildenafil. **Conclusion**: Oral sildenafil, especially at higher dosage, may increase oligodendrogenesis following neonatal hypoxic-ischemia. This is probably one of the involved mechanisms through which sildenafil administrated following term neonatal hypoxia-ischemia decreases brain injury by improving myelination and the structural integrity of white matter.

PO 11

PREDICTION OF PREECLAMPSIA IN NULLIPAROUS WITH BASELINE MATERNAL RISK FACTORS

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Introduction: Low-dose aspirin initiated in early pregnancy reduces the risk of preterm and early-onset preeclampsia (PE) in high-risk women. Therefore, there is growing interest for the early prediction of PE and its preterm form in order to target women that could benefit from prophylactic interventions. Several risk factors (including chronic diseases, obesity, advanced maternal age) have been associated with the risk to develop preeclampsia and could potentially be used to identify high-risk women. **Objective:** To evaluate the performance of baseline maternal risk factors in the prediction of preeclampsia. **Methods:** We conducted a prospective cohort study of pregnant nulliparous women with a singleton and living fetus at their 11-13 weeks visit. Participants with fetuses with morphological or chromosomic anomaly leading to medical abortion were excluded. Maternal age, body mass index (BMI), history of chronic hypertension, diabetes mellitus, chronic renal disease, rheumatoid arthritis, and antiphospholipid syndrome were used to develop multivariate logistic regression models of prediction of PE, preterm PE and early-onset (<34 weeks) PE. Using ROC curves analyses, we calculated the screening performance [area under the curve (AUC)], as well as detection rates (DR) at specific false-positive rates (FPR) of 5%, 10% and 25%. **Results:** Out of 4804 nulliparous women recruited at a mean maternal age of 28.9±4.1 years old with a BMI of 25.0±5.0 kg/m2, complete observations were obtained in 4713 participants (98%). We observed 246 (5.1%) cases of PE, 34 (0.7%) of preterm PE, and 10 (0.2%) cases of early-onset PE. Combining all maternal risk factors in predictive models, we obtained an AUC= 0.64 (95%CI: 0.55 to 0.72, p=0.006) for PE; an AUC= 0.69 (95%CI: 0.61 to 0.78, p<0.001) for preterm PE, and an AUC= 0.72 (95%CI: 0.60 to 0.85, p=0.02) for early-onset PE. At false-positive cut-off rates of 5%, 10% and 25%, we could have predicted 15%, 21% and 44% of PE, 12%, 27% and 56% of preterm PE and 10%, 20% and 70% of early-onset PE, respectively. **Conclusions:** The performance of the optimal prediction models using maternal risk factors only for the identification of pregnancies at high-risk of PE, preterm PE and early-onset PE is moderate and should not be use alone in clinical practice. National guidelines should be changed to consider other markers for optimal identification of high-risk women and optimal use of aspirin during pregnancy.

PO 12

PERINATAL AND MATERNAL MORBIDITY AND MORTALITY ASSOCIATED WITH ATTEMPTED MIDPELVIC OPERATIVE VAGINAL DELIVERY AND CESAREAN DELIVERY: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

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Introduction: Increased use of operative vaginal delivery has been advocated as a strategy to curb the rising rate of cesarean delivery, however, there is limited comparative information regarding perinatal and maternal outcomes between operative vaginal and cesarean delivery. The decision between these delivery options is most uncertain at midpelvic station. **Objective:**To quantify severe perinatal and maternal morbidity/mortality associated with attempted midpelvic operative vaginal delivery compared with cesarean delivery. **Methods:** We conducted a retrospective cohort study of all term singleton operative vaginal and cesarean deliveries carried out in the second stage of labour in British Columbia from 2004 to 2014. The primary outcomes were severe perinatal morbidity/mortality (including neonatal convulsions, assisted ventilation, severe birth trauma, 5–minute Apgar <4, and perinatal death) and severe maternal morbidity (including severe postpartum haemorrhage, shock, sepsis, cardiac complications, obstetric embolism and acute renal failure). Logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals (CI) after stratifying by indication (dystocia or fetal distress). Absolute effects were quantified by calculating adjusted rate differences and the adjusted number needed to treat (NNT). **Results:** The study included 10,901 deliveries; 5,057 with dystocia and 5,844 with fetal distress. Among deliveries with dystocia, attempted midpelvic operative vaginal delivery was associated with higher rates of severe perinatal morbidity/mortality compared with cesarean delivery (forceps AOR 2.29, 95% CI 1.28–4.11, NNT 93; vacuum AOR 2.92, 95% CI 1.46–5.83, NNT 63; Table 1). Rates of severe maternal morbidity/mortality were similar following midpelvic operative vaginal delivery and cesarean delivery. Among deliveries with fetal distress, there was a marginally significant increase in severe perinatal morbidity/mortality (AOR

1.51, 95% CI 1.00–2.29, NNT 104) and a significant increase in severe maternal morbidity (AOR 2.32, 95% CI 1.23–4.37, NNT 115) in the attempted midpelvic forceps group (Table 1). Severe perineal lacerations rates were high among all midpelvic operative vaginal deliveries, ranging from 8.5% to 23.0%. **Conclusions:** Attempted midpelvic operative vaginal delivery is associated with higher rates of severe perinatal morbidity/mortality, though these associations vary by indication and instrument. Birth and obstetric trauma rates are substantially increased following attempted midpelvic operative vaginal delivery.

PO 13

EHEALTH INTERVENTIONS FOR PARENTS IN NEONATAL INTENSIVE CARE UNITS: A JBI SYSTEMATIC REVIEW

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INTRODUCTION: There is an emerging trend to increase the use of eHealth interventions in neonatal intensive care units (NICUs). Technology related to web cameras and interactive learning platforms is becoming more advanced, with many hospitals and NICUs interested in implementing technology to enhance and expand their family-centered care environments. Although there is substantial literature regarding paternal and maternal experiences in the NICU environment, little is known about the "virtual" experience of parents and the role these advanced eHealth interventions have on parent-related and infant outcomes. **OBJECTIVES:** To examine the effect of eHealth interventions used in the NICU on parent-related and infant outcomes. **METHODS:** We systematically searched PubMed, CINAHL, PsycINFO and EMBASE from inception to August 2016 using key terms for neonatal, parents, eHealth, education, and communication. Inclusion criteria were peer-reviewed empirical studies published in English related to eHealth interventions in the NICU focused on parents or primary care providers of infants. Exclusion criteria were interventions not associated with, or initiated outside of, the NICU and eHealth interventions not targeted at parents. **RESULTS:** Based on the primary search strategy, 2,617 articles were identified. After the removal of duplicates (n=77) and those meeting the exclusion criteria (n=2,542), 25 full-text articles were retrieved and screened. Using the Joanna Briggs Institute (JBI) methodology for the conduct of systematic reviews, n=10 articles were critically appraised and n=8 met acceptable inclusion. eHealth interventions varied considerably in design. The examination of effect was limited due to variability in study methodology and measurement instruments used. Most consistently reported parent-related outcomes were on the use of eHealth interventions (n=4) or on the acceptance and satisfaction by parents (n=4). On neonatal-related outcomes, most studies reported either on length of stay (n=5) or parental presence or interaction (n=3). However, outcomes were not always significant and due to difference in reporting on all outcomes, no quantitative synthesis of data was possible. **CONCLUSION:** Despite the push for the use of eHealth interventions in the NICU, there remains a paucity of significant data to evaluate the effectiveness of existing neonatal eHealth interventions on the impact on parent-reported and infant outcomes. Future studies need to focus on evaluating the impact of eHealth interventions on broader outcomes including length of stay, parental presence, parental knowledge, and confidence.

PO 14

THERAPEUTIC POTENTIAL OF HUMAN UMBILICAL MESENCHYMAL STROMAL CELL-DERIVED EXOSOMES IN EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA

Howard Guo, BSc; Chanèle Cyr-Depauw, MSc; Arul Vadivel, PhD; Shumei Zhong, MSc; Bernard Thébaud, MD, PhD.

Introduction: Bronchopulmonary dysplasia (BPD) is the most common complication of extreme prematurity. This chronic lung disease develops as a consequence of oxygen and positive-pressure ventilation. Infants who suffer from BPD exhibit arrest in alveolar and lung vascular growth, and are also predisposed to long-term consequences including pulmonary hypertension, emphysema, and asthma. Currently, there is no treatment for BPD. MSCs are multipotent stem cells which have attracted attention due to their multi-lineage potential and immunomodulatory properties. Human umbilical cord MSCs can repair the lungs in rat models of BPD. The therapeutic effects of MSCs were enacted in a paracrine manner, rather than by lung engraftment. Recent findings have shown MSCs to secrete exosomes, which are nano-size cell vesicles crucial for cell-cell interactions. **Objective:** To demonstrate that exosomes mediate the therapeutic benefit of MSCs in a rat model of BPD. **Methods:** Newborn rat pups were exposed to 95% oxygen in a

Plexiglas chamber from postnatal (P) day 4 to P14 to produce a rat model of BPD. Human umbilical-cord MSCs (100,000 cells) or MSC-derived exosomes (produced from 100,000 cells) were administered intra-tracheally at P4. Lung function tests were performed on anesthetised animals using Flexivent on P21. Lungs were harvested at P22 for lung morphology, which was quantified on formaldehyde-fixed lung sections using the mean linear intercept (MLI). **Results:** Hyperoxia significantly reduced survival at P21 compared to control, room air housed animals. MSC-derived Exos significantly improved survival, whereas MSC had no effect on survival. MSC and MSC-derived Exos had no adverse effect on survival in control animals. Hyperoxia reduced lung compliance significantly compared to controls. MSC-derived Exos significantly improved lung compliance, whereas MSCs had no effect on lung compliance. MSC and MSC-derived Exos had no adverse effect on lung compliance in control animals. Hyperoxia led to fewer and larger alveoli reminiscent of histological features seen in human BPD. MSCs and MSC-derived Exos improved lung histology. This was confirmed statistically by using the MLI: the MLI was significantly worse (increased) in hyperoxia compared to control RA animals. MSCs and MSC-derived Exos significantly improved the MLI. MSC and MSC-derived Exos had no adverse effect on lung architecture in control animals. **Conclusions:** MSCs exert their therapeutic benefit through excretion of exosomes in a rat model of BPD. Exosomes may thus represent an avenue towards generating a cell-free treatment for BPD in the future.

PO 15

EFFICACY OF MINIMALLY INVASIVE SURFACTANT THERAPY IN MODERATE AND LATE PRETERM INFANTS: A MULTICENTER RANDOMIZED CONTROL TRIAL

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Introduction: Minimally invasive surfactant therapy (MIST) is a new strategy to avoid invasive mechanical ventilation (IMV) in respiratory distress syndrome (RDS).
Objective: The primary aim of this study was to test MIST as means of avoiding IMV exposure and pneumothorax occurrence in moderate and late preterm infants (32 – 36 weeks' gestational age (GA)) affected by RDS. **Methods**: This is a parallel-group randomized controlled trial including 3 Canadian neonatal intensive care units. Moderate and late preterm infants presenting with RDS were eligible in their first 24 hours of life. They were all stabilized on nasal continuous positive airway pressure (NCPAP). Participants were randomized by blocks stratified for GA, to standard management or to the intervention (MIST) immediately after inclusion. Inclusion criteria were: a requirement of a fraction of inspired oxygen (fiO2) of 35% and NCPAP support of 6 cm of water (H2O) to maintain a minimal saturation of 90%. The adverse combined primary outcome included either exposure to IMV or presenting a pneumothorax requiring a chest tube insertion in the first 3 days of life. Clinical failure criteria were used to prevent bias on intubation decision. The primary outcome was analyzed using bivariate and multivariate logistic regressions. The analysis was made by intention to treat approach. **Results:** Among 45 randomized patients, 24 were assigned to MIST and 21 to standard management. All patients were included in the analysis. Height infants (33%) in the intervention group presented with the adverse primary outcome versus 19 (90%) in the standard management group (absolute risk reduction 0,57, 95% confidence interval: 0,54-0,60, number needed to treat 1,75). Seven out of height patients from the intervention group reached the primary outcome for being exposed to IMV and one for presenting a pneumothorax. None of the patients have reached the clinical failure criteria. In the control group, 18 out of 19 patients reached the primary outcome for being exposed to IMV and one for presenting a pneumothorax. **Conclusion:** Minimally invasive surfactant therapy for RDS management in moderate and late preterm infants was associated with a significant reduction of IMV exposure and pneumothorax occurrence.

Invited Plenary Speaker

PO 3

HUMAN EVOLUTION, GENETICS, AND BIRTH TIMING

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Despite the large public health burden ensuing from preterm birth, relatively little progress has been made to date in reducing its incidence. In part, this shortcoming emerges from the incomplete understanding of the control of the normal timing for parturition in women and how these mechanisms become disrupted to result in delivery of a premature infant. Extrapolation of findings in animal models to human pregnancy to reveal mechanisms has resulted in only limited insights. Over the last decade, the ability to use human cohorts as sources of information to lead to new mechanistic insights into disorders such as prematurity have increased enormously. Linkage of large-scale epidemiological and electronic medical record information, with biological specimens and pregnancy outcomes, provides important substrates for new, high dimensional, cross-platform analytic approaches. Genome-wide association, genome sequencing, proteomics, metabolics and microbiome characterization studies have recently begun to come to fruition, with encouraging new findings. In this presentation, genes identified in genome-wide and comparative genomic studies of the maternal and fetal genome for association with birth timing will be described. Many of these genes exhibit unique patterns of evolutionary emergence across species reinforcing the physiological differences they exhibit. To explore the mechanisms by which these genes exert their effects, gene knockout, knockin, and humanized mouse models have been developed and recent findings will be presented.

Trainee Plenary Presentations

PO 16

VASCULAR FUNCTION, STRUCTURAL CHANGES AND ARTERIAL STIFFNESS ALONG WITH HIGH BLOOD PRESSURE IN YOUNG ADULTS BORN VERY PRETERM.

Julie De Meulemeester*, Rafael Oliveira Fernandes*, Muhammad Oneeb Rehman Mian,Jean-Luc Bigras, Rong Wu, Thuy Mai Luu, Anne Monique Nuyt.*co-first
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Introduction: Preterm birth is associated with increased blood pressure(BP) in adulthood. Experimental data indicate that deleterious perinatal conditions can impact vascular structure and function. Measures of vascular function are established markers of cardiovascular(CV) outcome **Objective:** Determine whether young adults born very preterm(PT) versus term(T) present vascular structural differences and dysfunction along with increased BP. **Methods:** 87 pairs of young adults born PT (gestational age <29 weeks) and T, matched for age(T:23±2;PT:23±2yrs), sex(55% female), and socio-economic status were studied. Measurements: Blood pressure(24-hour ABPM and office BP); US measures of brachial flow-mediated dilatation(FMD) and hyperaemic velocity, carotid intima-media thickness(cIMT), aorta-, brachial- and carotid diameters, and arterial stiffness indices (Pulse Wave Velocity(PWV)), arterial distension(Syst-Dias diameters), beta-stiffness and Petersen Indices). The cIMT to lumen ratio was calculated. Hyperaemic velocity was defined as the velocity-time integral at 15 seconds(VTI15sec) after cuff release. T-tests were performed. **Results:** Mean height(T:170±8;PT:165±9cm), weight(T:69±15;PT:61±12kg), BMI(T:24±4;PT:22±4kg/m2)and BSA(T:1.8±0.2;PT:1.7±0.19m2) were significantly lower in PT. ABPM systolic(T:116±8;PT:119±9mmHg) and diastolic(T:66±5;PT:68±5mmHg) BP were significantly higher in PT whereas office BP values were not statistically different. FMD was not different but VTI15sec(T:33±1;PT:28±9cm,P<0.01) was significantly reduced in PT. Aortic diameter, both systolic(T:2.68±0.30;PT:2.49±0.20 cm,P<0.01) and diastolic(T:2.36±0.28;PT:2.20±0.19cm,P<0.00), were smaller in PT, but were similar when corrected for BSA. Carotid diameter was lower in PT during systole(T:0.65±0.04;PT:0.62±0.05 cm,P<0.01) but not diastole. Brachial diameter was similar between T and PT. cIMT did not differ between groups, but cIMT to lumen ratio (T:7.8±1.0; PT:8.2±1.0%,P<0.05) was significantly increased in PT.

PWV was not different whereas arterial distension of the aorta(T:0.31±0.06;PT:0.29±0.05cm,P<0.01) and carotid(T:0.09±0.01,PT:0.07±0.01cm,P<0.01) were reduced in PT. Moreover, in the carotid, beta stiffness(T:3.7±0.5;PT:4.5±0.8,P<0.00) and Petersen Index(T:303±58;PT:379±75,P<0.01) were increased in PT. **Conclusion:** Young adults born extremely PT exhibit some degree vascular dysfunction, changes in the arterial structure and stiffness which, along with increased blood pressures, may predispose them to early-onset CV disease. Considering the accumulating evidence,extreme PT birth should be considered as screening factor for CV risk assessment

PO 17

OVERALL AND CAUSE-SPECIFIC INFANT MORTALITY AMONG FIRST NATIONS, INUIT, AND MÉTIS POPULATIONS IN CANADA

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Introduction: Infant mortality is a strong indicator of perinatal health, reflecting pre-pregnancy health status and access to and effectiveness of prenatal and delivery care. However, no comparisons of overall and cause-specific infant mortality have previously been reported from a nationally representative sample of First Nations, Inuit and Métis (FNIM) compared with non-Indigenous populations **Objective:** To compare infant mortality rates, including neonatal and postneonatal mortality and cause-specific mortality rates, for FNIM and the non-Indigenous populations in Canada. **Methods:** Data were from the 2006 Canadian Birth-Census Cohort, a study of births between May 2004 and May 2006 created by linking Canadian birth registration data with the 2006 long-form Canadian census. The long-form census was distributed to 100% of enumerated households on First Nations reserves and remote Inuit communities, and to a 20% sample of enumerated Canadian households in other areas. FNIM identity was ascertained using the census questionnaire item: “Is this person an Aboriginal person, that is, North America Indian, Métis or Inuit (Eskimo)?” Infant mortality rates were calculated using birth and death registration data for all singleton pregnancies. Cause of death was determined from ICD-10 codes on infant death registrations. **Results:** The cohort included 13,506 births to First Nations, 1,730 Inuit, 2,267 Métis and 112,112 non-Indigenous mothers. Overall infant mortality rates were 9.2 (95% CI 7.5, 11.3) per 1,000 among First Nations, 12.3 (9.9, 15.2) among Inuit and 10.5 (7.1, 15.5) among Métis, compared to 4.4 (4.2, 4.7) for the non-Indigenous population. Neonatal deaths made up approximately three-fourths of all infant deaths in the non-Indigenous population (neonatal death rate = 3.4 (3.1, 3.6) per 1,000 live births, postneonatal death rate = 1.1 (0.9, 1.3) per 1,000 neonatal survivors). Postneonatal deaths accounted for a larger proportion of infant deaths in the FNIM populations and ranged from 3.1 to 5.1 per 1,000, compared to neonatal death rates ranging from 4.4 to 7.5 per 1,000. Major causes of infant death differed between the combined FNIM populations and the non-Indigenous population and varied somewhat between the different FNIM groups. The most striking difference was due to sudden infant death syndrome (SIDS), which contributed 46% of postneonatal deaths in the combined FNIM population, compared to 23% of postneonatal deaths in the non-Indigenous population. **Conclusion:** These data present the first cause-specific infant mortality rates on a national sample of FNIM Canadians and highlight the need to reduce rates of SIDS in Indigenous populations.

PO 18

MICROGLIAL DEPLETION PRIOR TO A PERINATAL INFLAMMATORY STRESS AGGRAVATES OUTCOMES IN MICE

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Introduction: Extreme preterm infants are exposed to multiple stressors including perinatal cerebellar haemorrhage (CBH) and postnatal infection, two major risk factors for neurodevelopmental impairments. Microglia are a key player in inflammatory responses after injury. Given the duality of microglial involvement in inflammatory as well as in noninflammatory functions across the central nervous system, they may play a central role in the pathogenesis of cerebellar injury in developing brains. **Objective:** By using a transgenic mouse model allowing microglia depletion, the role of microglial cells on short- and long-term outcomes in perinatal cerebellar haemorrhage and early inflammation

will be studied. **Methods:** Conditional transgenic model dependent on diphtheria toxin (DT) intracerebellar injection to deplete CX3CR1-positive cells expressing an inducible diphtheria toxin receptor, unilateral intraparenchymal CBH was induced in transgenic mouse pups (CX3CR1CreER-EYFP/WT:R26iDTR/WT or WT/WT) by a local injection of bacterial collagenase (0.15U/g) at postnatal day 2 (P2) combined with an intraperitoneal lipopolysaccharide (LPS) injection (300µg/kg) to mimic an early inflammatory state (EIS) (total of 8 groups, n=256). Survival, weight gain and sensorimotor reflexes were measured during the neonatal period followed by behavioral testing at P45-P65 to assess locomotor activity, motor coordination, anxiety and memory. Cerebellar tissues were collected at P2, P15 and P65-85 for neurohistological studies. **Results:** Significant microglia depletion was reached 24 hours after tamoxifen and DT treatment. A residual level of microglial cells in treated mice (26.6±6.9%) compared to control mice (100.0±11.1%) (****P=0.0001) is found at P2 prior to insult exposure. Survival is mainly affected by being exposed to DT (50%) or to CBH (48,6% to 54,6%) compared to control (71,4%) or vehicle-exposed mice (62,6%). Amongst survivors, LPS exposure favors survival of CX3CR1CreER-EYFP/WT:R26WT/WT mice (78.3%) compared to CX3CR1CreER-EYFP/WT:R26iDTR/WT mice (21.7%) (**P=0.0067). During the neonatal period, CX3CR1-depleted mouse pups exposed to EIS have smaller brains compared to non-depleted mice (**P=0.0095) or CX3CR1-depleted mouse pups exposed to vehicle (**P=0.0056) without significant changes in body weight compared to all groups. Functional assessment reveals a significant delay of grasping acquisition in CX3CR1-depleted pups exposed to EIS compared to non-depleted mice (**P=0.0045) or CX3CR1-depleted pups exposed vehicle (****P<0.0001). **Conclusion:** Microglia-depleted mice exposed to early inflammation have worse neonatal outcomes including smaller brains and delay in grasping acquisition compared to non-depleted mice, suggesting a potential neuroprotective role of microglial cells after EIS insult.

PO 19

WHAT IS THE SAFEST MODE OF DELIVERY FOR EXTREMELY PRETERM BREECH INFANTS: A SYSTEMATIC REVIEW AND META-ANALYSES?

Grabovac M, Karim JN, Isayama T, Korale Liyanage S, Beyene J, McDonald SD

Introduction: The safest mode of delivery for extremely preterm (<28 weeks) breech infants is unknown. At term, major obstetric practice guidelines (SOGC, ACOG, RCOG) state Caesarean delivery decreases mortality and morbidity for breech babies, but no comment is made for extremely premature infants, 30-35% of whom are breech. **Objective:** The objective of this systematic review was to determine the safest mode of delivery for actively resuscitated extremely preterm breech infants between 22+0 to 27+6 weeks' gestation in high-income countries. **Methods:** Cochrane Central, MEDLINE, EMBASE, CINAHL and clinicaltrials.gov were searched from Jan 1, 1994–Aug 18, 2016. Randomized controlled trials (RCT) and observational studies were included. Outcomes after Caesarean section (CS) and vaginal delivery (VD) were compared. Our primary outcomes were death before discharge and severe intraventricular hemorrhage (IVH; grade III/IV) stratified by gestational age (22+0–24+6; 25+0–26+6; 27+0–27+6). Two reviewers independently screened full texts. Authors were contacted for information on active resuscitation, data by gestational week, and use of antenatal corticosteroids. Risk of bias was assessed using the Cochrane Risk of Bias tool for RCTs and the modified Newcastle Ottawa Scale in observational studies. Random-effects (inverse variance) models were used for meta-analysis to calculate unadjusted odds ratios and 95% confidence intervals. **Results:** Eleven observational studies and one RCT were included, as they reported on our primary outcomes of death before discharge and severe IVH by gestational age with a total of 2593 and 569 infants, respectively (Table1). In actively resuscitated infants at 22+0–27+6, 31.8% delivered by Caesarean section and 60.8% of delivered vaginally died before discharge. Caesarean was associated with a 51% reduction in death before discharge (OR 0.49, 95% CI 0.29-0.82). Furthermore, 7.8% and 16.7% of infants suffered severe IVH in the Caesarean and vaginal birth groups, respectively. The odds of severe IVH in infants delivered by Caesarean section were reduced by 50% (OR 0.50, 95% CI 0.27-0.92) at 22+0–27+6. **Conclusion:** Caesarean section was associated with a halving of the odds of either death before discharge or severe intraventricular hemorrhage in actively resuscitated breech infants <28 weeks compared in those delivered vaginally.

PO 20

ALTERED FATTY ACID AND MITOCHONDRIAL METABOLISM IN THE LIVER OF PREGNANT ADIPONECTIN-DEFICIENT MICE CONTRIBUTES TO INSULIN RESISTANCE AND GESTATIONAL DIABETES MELLITUS

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Dolinsky

Introduction: Gestational diabetes mellitus (GDM) is a common pregnancy-related health condition. While genetics, lifestyle and diet contribute to development of GDM, evidence suggests that low levels of adiponectin increases the risk for GDM. Adiponectin is a fat derived hormone that improves the sensitivity of tissues to insulin. **Objective:** To confirm whether adiponectin deficiency causes fatty liver during pregnancy, ultimately contributing to the development of GDM. **Methods:** We compared the glucose and insulin tolerance of pregnant (3rd trimester) adiponectin-/- (strain B6;129-Adipoqtm1Chan/J) and wild-type mice, and assessed parameters of hepatic metabolism, including mitochondrial function and fatty acid metabolism. We assessed the impact of adiponectin supplementation by administering adenovirus mediated full length adiponectin at the end of the second trimester of pregnancy, and comparing to control containing GFP. **Results:** In the third trimester, pregnant adiponectin-/- mice exhibited fasting hyperglycemia regardless of diet (9.2mmol/L vs. 7.7mmol/L in controls, $p<0.05$). These mice display impaired glucose and insulin tolerancerelative to wild-type controls. Pregnant adiponectin-/- mice develop hepatic steatosis, including a 3-fold elevation in hepatic triglycerides ($p<0.05$). This was associated with altered hepatic lipid metabolism, including a 2.5 fold increase in fatty acid synthase expression ($p<0.05$), elevated circulating free fatty acids, triglycerides and cholesterol. Nearly 2-fold reduction ($p<0.05$) in maximal mitochondrial respiration was observed via oxidative flux analyzer in hepatocytes of adiponectin -/- mice. Hepatocytes from pregnant adiponectin-/- mice dramatically reduced respiratory capacity when using fatty acids alone, and display elevated synthesis and secretion of triglycerides and cholesterol. Gestational weight gain and food consumption were similar in knockout and wild-type mice. Adiponectin supplementation to pregnant adiponectin-/- mice significantly improved glucose tolerance, prevented fasting hyperglycemia, and attenuated fatty liver development. **Conclusion:** Results show that adiponectin deficiency is associated with altered hepatic lipid metabolism and hepatic steatosis during pregnancy. Consequently, adiponectin deficiency contributes to med-gestation insulin resistance and hyperglycemia characteristic of GDM. Moreover, adiponectin supplementation rescues the effects of adiponectin deficiency on insulin sensitivity and hepatic lipid metabolism.

PO 21

SYNCYTIOTROPHOBLAST EXTRACELLULAR VESICLES ALTER ANGIOTENSIN II-INDUCED VASOCONSTRICTION IN MOUSE UTERINE ARTERIES

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Introduction: The development of hypertension and proteinuria in preeclampsia (PE) is thought to be due to the release of placental factors, including syncytiotrophoblast extracellular vesicles (STBEVs), leading to maternal endothelial dysfunction. Plasma levels of STBEVs are higher in women with preeclampsia. The lectin-like oxidized LDL receptor-1 (LOX-1) is a multi-ligand scavenger receptor and LOX-1 expression is increased in vessels from women with PE. To further investigate a role for LOX-1 in pathological pregnancies, we propose to use genetically modified mice. **Objective:** We hypothesized that STBEVs activate LOX-1 and contribute to vascular dysfunction in mouse uterine arteries, and that this effect will not be evident in LOX-1 KO mice. Our aim was to investigate the role of STBEVs and the LOX-1 receptor in vascular dysfunction using LOX-1 deficient (knock-out; KO) mice. **Methods:** Uterine arteries were obtained from late pregnant (gestational day 18; term = day 19) C57BL/6 (WT) and LOX-1-KO mice. Isolated vessels were incubated for 24hrs in the absence (n=4) or presence of STBEVs (200 µg/ml, n=4). A recent report showed that LOX-1 activation is associated with AT-1 receptor activation, and vice versa. We therefore used angiotensin II (Ang II) mediated vasoconstriction using wire myography to assess vascular (dys)function. **Results:** Our results showed that responsiveness to Ang II was increased after incubation with STBEVs as compared with controls, i.e. a prolonged response to Ang II was observed (AUC: 3.3±0.9 controls vs. 4.9±0.9 STBEVs; $p<0.03$) in uterine arteries from WT mice. In uterine arteries from LOX-1 KO mice this response to STBEV-incubation was not observed (AUC: 4.1±2.3 controls vs. 3.5±2.0 STBEVs). **Conclusion:** STBEVs induced hyper-responsiveness to Ang II which was LOX-1 dependent. Further studies are required to determine the mechanisms: i.e. whether this effect is AT-1 receptor mediated and whether AT-1 receptor expression is altered by STBEV activation of LOX-1. In addition, the possible activation of LOX-1 by STBEVs in

the WT mice will be further investigated using LOX-1 blocking antibodies. These data indicate that elevated levels of circulating STBEVs in pregnancy could contribute to the development of vascular dysfunction via the LOX-1 receptor.

THEMATIC SESSION

ABSTRACTS

NEONATALOGY II: NEONATAL NEUROSCIENCES

TO 1 Invited Speaker

PREMATURITY AND DEVELOPMENTAL COORDINATION DISORDER

Dr. Jill Zwicker

While the incidence of cerebral palsy is declining, infants born preterm remain at high risk for poor motor outcomes. Up to 50% of very preterm infants may have a condition called developmental coordination disorder (DCD), an under-recognized motor disorder of unknown etiology. DCD affects the child's ability to perform and learn motor skills, such as using a knife and fork, tying shoelaces, printing, or riding a bicycle. This presentation will highlight clinical risk factors and brain imaging studies that suggest possible predictors of DCD and potential avenues for prevention and improved motor outcomes. A pilot study of rehabilitation intervention for very preterm preschool-age children with DCD will also be presented.

Trainee Thematic Presentations

TO 2

SILDENAFIL MAY MODULATE RETINAL INFLAMMATION FOLLOWING TERM NEONATAL HYPOXIC-ISCHEMIC INJURY

Palig Balian, Armin Yazdani [1], Annie Wing Hoi Poon [1], Zehra Khoja [1], Pia Wintermark [1]
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Introduction: Birth asphyxia constitutes one of the main causes of newborn death around the world. Surviving newborns often develop long-term neurological complications (including visual impairments) due to injuries to their brain and retina. Treatment with sildenafil has been shown to improve retinal injuries following term neonatal asphyxia; however, the mechanism explaining this improvement remains yet to be elucidated. **Objective:** To determine how sildenafil improves retinal injuries following term neonatal asphyxia. **Methods:** Neonatal hypoxia-ischemia (HI) was induced in male Long-Evans rat pups at postnatal day 10 (P10) by left common carotid ligation followed by 2-hour exposure to 8% oxygen. 12 hours following HI, animals were randomly administered 0 (vehicle), 2, 10 or 50 mg/kg of sildenafil for 7 consecutive days. At P30, rats were sacrificed and their eyes were extracted. Immunohistochemistry was performed to examine retinal ganglion cells (Brn3a), bipolar cells (Chx10), astrocytes (GFAP) and microglia (Iba1) in order to assess the neuronal count and the inflammatory response in the retina following HI and the impact of the sildenafil treatment. **Results:** In the retina, HI caused a decrease in the number of retinal ganglion cells and bipolar cells, as well as an increase in inflammation marked by an increase in the number of astrocytes. Sildenafil treatment restored the number of retinal ganglion cells and bipolar cells. Furthermore, the treatment reduced neuroinflammation by decreasing the number of astrocytes. **Conclusion:** Sildenafil seems to prevent neuronal death and modulate inflammation. Further research is needed to better understand the link between these findings and how they improve retinal injuries.

TO 3

MEASURE BLURRINESS OF NEONATAL MAGNETIC RESONANCE BRAIN 2D IMAGES: DEVELOPING ROBUST, SIMPLE AND OBJECTIVE DATA QUALITY CONTROL MEASURES

Yang Ding, Sabrina Suffren, Genevieve Blain, Canadian Neonatal Brain Platform, Gregory A. Lodygensky
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Introduction: Large-scale magnetic resonance imaging (MRI) studies in newborns is difficult since the data is often hard to collect and aggregate. The Canadian Neonatal Brain Platform is a new initiative supported by Brain Canada to facilitate multi-center neonatal brain imaging studies and collect clinical neonatal brain MRI with shared common protocols across the country to build a powerful large scale neonatal brain registry. This requires the platform to enforce imaging data quality control to help researchers identify and isolate problematic scans easily with objective metrics to ensure scanner temporal stability and consistency. Over the past two decades, there have been numerous advancement in 2D image processing algorithm for image quality metrics. **Objective:** Here we tested the most commonly used image

blurriness measuring algorithms on neonatal brain data acquired through typical T2-weighted clinical MRI protocol to evaluate the feasibility of utilizing these metrics as measures of clinical image quality **Methods:** Twenty-eight algorithms were identified from the recent image processing literature. We validate the algorithms against 51 preterm newborns scanned at term who has been undergoing the identical clinical Turbo Spin Echo T2 brain acquisition sequence on a Siemens 1.5T Avanto clinical scanner (TR = 6480ms, TE = 106ms, 20 Transverse Slices). For each slice of the acquisition from the patients, it is rated independently and blindly into four tiers: “very bad”, “bad”, “good”, “very good”. We then tested all the algorithms against the performance of human rater to check correspondence. **Results:** Of the 28 algorithms tested, three algorithms were excluded from analyses due to processing time. All remaining 25 algorithms identified significant differences among the four categories of clinical brain images: for each algorithm ANOVA test of the quality metric derived from each category ($p < 0.001$, DoF(3, 1016)). In the follow up pairwise comparisons, 21 algorithms showed that worst images tend to have lowest metrics and were most statistically distinct from all other categories of the images ($p < 0.001$). Although statistically distinguishable, metric derived from any single algorithm is not yet sufficient to clearly classify the the images individually into the four human defined categories. Further refinement with additional weighting of different algorithms in machine learning context is underway to improve the classification accuracy. **Conclusion:** Our ongoing work demonstrate the feasibility of using blurring metrics to indirectly gauge the quality of the T2-weighted brain MRI images and majority of the blurring metric algorithms tested statistically distinguished poor images from higher quality images. Future works need to focus on establishing a reliable and applicable cutoffs while incorporating other medical imaging metrics to increase the robustness of these metrics to screen out poor images among T1 T2, fcMRI and DTI data.

TO 4

LET'S NOT SUGAR COAT IT: LONG TERM ADVERSE EFFECTS ON THE BRAIN OF REPEATED SUCROSE FOR PAIN MANAGEMENT IN PRETERM INFANTS USING A MOUSE MODEL

Sophie Tremblay*, Manon Ranger*, Cecil MY Chau, Jacob Ellegood, Jason P. Lerch, Liisa Holsti, Daniel Goldowitz§, Ruth E. Grunau§

*These authors contributed equally to this work; §These authors share senior authorship equally.

Introduction: Currently, oral sucrose is administered routinely to reduce pain of minor procedures in premature infants and is recommended as standard care in international guidelines. Thus, clinical equipoise no longer exists for randomized controlled trials of sucrose use for pain. No human or animal studies on effects of early repeated sucrose exposure on long-term brain development have been done in the context of pain. **Objective:** To examine the effects of repeated neonatal sucrose treatment before an intervention on long-term brain structure in mice. **Methods:** Neonatal C57Bl/6J mice (n = 109, 46% male) were randomly assigned to one of two treatments (vehicle vs sucrose) and one of three interventions (handling, touch or needle-prick). Mice received 10 interventions over a 12h period (daytime) daily from postnatal day 1 to 6 (P1-P6). A single dose of 24% sucrose (0.1-0.2mg of sucrose/g weight) or vehicle was given orally 2 min before each intervention. At P85-95, mice were anesthetized and intracardially perfused with 4% paraformaldehyde (PFA) containing 2mM ProHance. The brains were scanned using a multi-channel 7.0 Tesla MRI. Volumes of 159 independent brain regions were obtained using advanced registration with a pre-existing classified atlas. **Results:** Early repetitive sucrose exposure in mice resulted in widespread smaller volumes in multiple brain regions including cortical, subcortical grey and white matter structures. Precisely, after correcting for whole brain volume and multiple comparisons, mice that received sucrose compared to vehicle had smaller white matter volumes in the corpus callosum, stria terminalis, and fimbria ($P < 0.0001$). Cortical and subcortical grey matter was also affected by sucrose with smaller volumes of hippocampus and cerebellum ($P < 0.0001$). These significant changes in adult brain were found irrespective of the type of intervention (i.e. received painful procedure or not) in the neonatal period. **Conclusion:** This study provides the first evidence of long-term adverse effects of repetitive sucrose exposure in neonatal mice and raises concerns for the use of this standard pain management practice during a period of rapid brain development in the very preterm population.

TO 5

EARLY NON-INVASIVE ASSESSMENT OF NEUROPROTECTION IN AN ANIMAL MODEL OF NEONATAL WHITE-MATTER

INJURY

Wyston C. Pierre[1,2], Luis Akakpo[3], Irène Londono[1], Frédéric Lesage[3], Philippe Pouliot[3], and Gregory A Lodygensky[1,2].
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Introduction: Inflammation-induced white matter injury (WMI) in preterm babies is associated with well-known neurocognitive impairments. Early monitoring of neuroprotection with a non-invasive tool such as magnetic resonance imaging (MRI) could greatly improve the development of therapeutic approaches. Among neuroprotective agents, Anakinra, an antagonist of interleukin-1 receptor (IL-1Ra), has previously showed beneficial effects in animal models of WMI. **Objective:** Using diffusion tensor imaging (DTI), a non-invasive monitoring tool, we evaluated the early neuroprotective effect of IL-1Ra in neonatal rats subjected to WMI. **Methods:** P3 Sprague-Dawley rats received LPS (1mg/kg) or sterile saline injections in the left corpus callosum. A subset of rats receiving LPS was treated with three i.p. injections of IL-1Ra (2 mg/kg). 24h post-injection, 13 animals (7 sham, 3 LPS, 3 LPS+IL-1Ra) were imaged on a 7 tesla scanner. DTI was acquired using spin echo standard sequence with dual scheme with b-values of 0 and 700 s/mm2 with a voxel resolution of 230 x 120 x 600 µm. ROIs were placed on the ipsilateral cingulum. Kruskal¬-Wallis test was used for statistical comparisons. Results are normalized with the sham group. Apoptosis and inflammatory status were assessed in the three groups. **Results:** Similar to previous results (Lodygensky et al. Pediatric Res 2014), LPS injection caused a decrease in diffusivity in the acute phase. This decrease is significantly limited for animals treated with IL-1Ra. Fractional anisotropy did not come out as a reliable biomarker for assessing acute WMI. Primary blind qualitative evaluation of apoptosis revealed a sharp decrease in fractin expression in treated animals. Furthermore, IL-1Ra treatment decreased RNA expression of pro-inflammatory genes iNOS, IL-1β, TNF-α and IL-6. **Conclusion:** DTI allowed early detection (in the 24h post-injury) of neuroprotective effect of IL-1Ra which correlated with a reduction of pro-inflammatory gene expression. More animals are currently being scanned with thorough quantitative immunohistochemistry analysis and evaluation of pro- and anti-inflammatory gene expression. Our results suggest DTI is a non-invasive tool allowing early monitoring of therapeutic response in neonates.

PERINATAL NUTRITION AND THE GUT

TO 6 Invited Speaker

BREASTFEEDING, GUT MICROBIOTA AND CHILD HEALTH

Dr. Meghan Azad

Breast milk provides optimal nutrition to support infant growth and development. Breastfeeding is associated with reduced risks of infection, allergic disease and obesity later in childhood. These beneficial effects appear to be mediated, in part, by the gut microbiome – a complex microbial community that is established at birth and develops rapidly during infancy, influencing host metabolism and immunity throughout the lifespan. Breast milk drives gut microbiome development by providing a source of probiotic microbes and prebiotic oligosaccharides. These associations and mechanisms are being studied in The Canadian Healthy Infant Longitudinal Development (CHILD) pregnancy cohort of 3500 infants followed through early childhood. Ongoing research in the CHILD cohort and recent evidence from other studies will be discussed.

Trainee Thematic Presentations

TO 7

PREGNANT WOMEN WITH INFLAMMATORY BOWEL DISEASE ARE AT SIGNIFICANTLY INCREASED RISK OF VITAMIN D INSUFFICIENCY

Sangmin (Sarah) Lee[1], Amy Metcalfe[1,3], Yvette Leung[2], Maitreyi Raman[2], Catherine J Field[7], Nicole Letourneau[4,6], Elnaz Ehteshami Afshar[2], Nastaran Sharifi [2,6], Henry Ntanda [5], Remo Panaccione[2], Gilaad G. Kaplan[1,2], Cynthia H. Seow[1,2] on behalf of the University of Calgary IBD Centre and the APrON team.

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Introduction: Inflammatory bowel disease (IBD) consists of Crohn's Disease (CD) and Ulcerative Colitis (UC). Previous studies have suggested that up to 80% of patients with CD and up to 45% of patients with UC are vitamin D insufficient. This may be a result of gastrointestinal inflammation, malabsorption or decreased intake. Vitamin D insufficiency increases the risk of adverse pregnancy outcomes including preterm birth and small for gestational age infants. However, the prevalence of vitamin D insufficiency in pregnant women with IBD is currently unknown. **Objective:** To assess the prevalence of vitamin D insufficiency in pregnant women with and without IBD. **Methods:** An observational study was conducted on 2 cohorts of pregnant women between 2009-2016. The Alberta Maternal-fetal Outcomes in IBD cohort provided 122 pregnant women (CD, n=73; UC, n=49; mean age(SD):31.83.64 years) while there were 638 pregnant women without IBD from the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort (mean age(SD):32.44.36 years). 25(OH)D levels from both cohorts were reported in nmol/L. Vitamin D insufficiency was defined as <75 nmol/L. Chi-square test was used to compare the proportion of women with vitamin D insufficiency with and without IBD. Subgroup analysis was conducted for pregnant women with vitamin D deficiency (25(OH)D <50 nmol/L). Logistic regression was used to examine the prevalence of vitamin D insufficiency in women with and without IBD after adjusting for the potential confounders of season and ethnicity. **Results:** Amongst pregnant women without IBD, 154 (24.1%; 95%CI=21.0-27.6%) were vitamin D insufficient compared to the 47.9% (95%CI=36.7-59.4%) pregnant women with CD (p<0.01) and 59.2% (95%CI=44.8-72.0%) with UC (p<0.01). Only 3.44% (95%CI=2.28-5.19%) pregnant women without IBD, 6.85% (95%CI=2.86-15.5%) with CD (p=0.15), and 12.2% (95% CI=5.55-24.9%) with UC (p<0.01) were vitamin D deficient. Pregnant women with IBD, whether diagnosed with CD (crude OR=2.89, 95%CI=1.77-4.74) or UC (crude OR=4.56, 95%CI=2.41-8.29), were more likely to be vitamin D insufficient than pregnant women without IBD. Women with IBD were at increased risk of vitamin D insufficiency during pregnancy even after adjusting for season and ethnicity [CD (adjusted OR=3.83, 95%CI=2.22-6.61); UC (adjusted OR=6.64 95%CI=3.37-13.1)]. **Conclusion:** Pregnant

women with IBD were more likely to be vitamin D insufficient than women without IBD. Further, the rate of vitamin D insufficiency was higher amongst pregnant women with UC than pregnant women with CD, contrary to what is reported in the non-pregnant IBD population. As vitamin D status is easily monitored and corrected with supplementation, health professionals should focus on vitamin D status of pregnant women with IBD as this may improve materno-fetal outcomes.

TO 8

IMPACT OF BREASTFEEDING DURATION ON THE CARDIOMETABOLIC RISK PROFILE OF CHILDREN BORN FROM MOTHERS WITH GESTATIONAL DIABETES MELLITUS.

Camille Dugas[a,b], Michèle Kearney[a,b], Roxanne Mercier[a,b], Julie Perron[b], André Tchernof[a,b,c], Isabelle Marc[c], S. John Weisnagel [c,d], Julie Robitaille[a,b,c]
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Introduction: Children born from mothers with gestational diabetes mellitus (GDM) are at high risk of developing cardiometabolic alterations later in life. Maternal breastfeeding has been demonstrated to improve health of children born from an uncomplicated pregnancy, but this relation is unclear among children exposed to GDM in utero. **Objective:** The aim of this study was to evaluate the impact of breastfeeding duration on the cardiometabolic risk profile of children born from mothers with GDM. **Methods:** To date, 104 children exposed to GDM participated in this ongoing project. Fasting lipid and glycemic profiles, weight, height, waist circumference, body composition and blood pressure were measured. Pearson correlations were performed to assess the association between total breastfeeding duration (including exclusive and non-exclusive breastfeeding) or exclusive breastfeeding duration and the cardiometabolic risk profile of children. Children were also divided into groups according to the median duration of total or exclusive breastfeeding and cardiometabolic profiles were compared between groups using ANOVA. Adjustments for children's age, sex and BMI were performed. **Results:** Mean age was 6.1±2.5 years. Mean duration of total and exclusive breastfeeding were respectively 8.7±7.4 and 4.0±2.0 months. Total breastfeeding duration was associated with a significant decrease in fat mass percentage ($r=-0.34$, $p=0.047$) and in glycated hemoglobin (A1C) levels ($r=-0.29$, $p= 0.01$). Children breastfed >8 months had lower levels of A1C than those breastfed ≤8 months (5.18±0.25% and 5.34±0.27%, respectively, $p=0.01$). Exclusive breastfeeding duration was not significantly associated with the cardiometabolic risk profile of children. **Conclusion:** Our results suggest that prolonged exposure to breast milk is associated with a better cardiometabolic health profile among children exposed to GDM in utero. Promoting breastfeeding among women with GDM could be a good strategy to prevent cardiometabolic alterations among this population of high-risk children.

TO 9

MATERNAL DIET-INDUCED OBESITY IS ASSOCIATED WITH ALTERED FETAL GUT DEVELOPMENT.

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Introduction: Studies have shown that maternal diet-induced obesity (DIO) is associated with offspring obesity, reduced gut barrier function and shifts in the gut microbiota. While maternal gut microbes are likely the initial colonizers of the offspring intestines, altered fetal gut development may change gut barrier function, thus influencing the ecological niches available to colonizing microbes, shaping postnatal gut microbial communities. The gut barrier is known to be influenced by inflammation, mucin proteins and by bacterial metabolites including short-chain fatty acids (SCFAs). **Objective:** To examine the impact of maternal DIO on fetal gut barrier development and whether this is associated with increased inflammation. **Methods:** Female C57BL/6 wildtype (Wt) mice were fed either a control (chow; n=7) or a high fat (HF; 60% kcal from fat; n=8) diet for 8 weeks prior to mating. After confirmation of pregnancy, maternal weight gain and food intake were recorded. Fetal small and large intestines were collected at term, from which mRNA was extracted and analyzed by quantitative PCR. **Results:** In both male and female fetuses, maternal DIO increased mRNA levels of

fetal gut Muc2, the principal secreted mucin, ($p<0.001$) as well as mRNA levels of the tight-junction protein occludin ($p<0.001$), and increased the expression of the SCFA receptor GPR43 ($p<0.001$) and LPS receptor TLR-4 ($p=0.0316$). Female gut IL-10 mRNA levels were modestly increased ($p=0.0525$), while IL-6 mRNA levels were modestly increased in males ($p=0.0690$). **Conclusion:** We show that key factors associated with fetal gut barrier function and inflammatory signalling are altered by maternal DIO. Whether the increased GPR43 levels are associated with shifts in SCFAs is unknown, but appears to be associated with changes in fetal mucin levels and heightened inflammatory signalling. These signalling pathways appear to be sex specific. The impact of maternal DIO on fetal gut development at term gestation has implications for the offspring microbiota, as both the maternal microbial inoculation and fetal intestinal environment contribute to its composition. Given the established impact of the gut microbiota on host health, this may represent a pathway by which maternal DIO programs offspring health throughout life.

TO 10

DIET-INDUCED MATERNAL OBESITY INDUCES A SHIFT IN THE MATERNAL INTESTINAL MICROBIOTA AND IS ASSOCIATED WITH ALTERED MATERNAL INTESTINAL MUCUS PRODUCTION AND M1 MACROPHAGE INFILTRATION OF THE PLACENTA AT MID GESTATION.

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Introduction: We have previously shown that maternal obesity results in shifts in maternal intestinal microbiota throughout gestation. **Objective:** We investigated whether these intestinal microbial shifts were correlated with maternal metabolic indices and associated with maternal intestinal and placental inflammation at mid gestation. **Methods:** C57BL/6 female mice were fed a high-fat (HF; 60% kcal fat) or control (CON) diet 6 weeks prior to mating and throughout gestation (n=10). Maternal weight, food intake and fecal samples were collected at gestational day (GD) 0.5, 6.5, 10.5 and 14.5. At GD 14.5, dams underwent an intestinal permeability assay and maternal intestinal and placental tissues were collected. The maternal intestinal microbiota was investigated via sequencing of the 16S rRNA gene variable 3 (V3) region. Target genes associated with maternal intestinal and placental inflammation were assessed by qPCR. **Results:** HF females weighed more than CON at mating and throughout gestation. At GD 14.5, maternal blood glucose, serum insulin and leptin levels were higher in HF dams. Pregnancy induced a maternal intestinal microbial shift that was further modulated by obesity. The relative abundance of maternal intestinal Ruminococcaceae and Lachnospiraceae correlated with maternal glucose, insulin and leptin levels. Maternal intestinal permeability was unchanged by pregnancy or obesity. Maternal intestinal mRNA levels of intestinal mucin protein, Muc5ac, were elevated in HF dams. Although fetal and placental weights were similar between groups, HF placentae displayed elevated mRNA levels of TLR-4, TRAF6 and NFκB and MCP1, F4/80 and TNF-α compared to CON. These inflammatory findings were associated with increased mRNA levels of nutrient transporters GLUT1, 3 and SNAT2 in HF placentae. **Conclusion:** Both obesity and pregnancy shifted the maternal intestinal microbiota and shifts were characterized by changes in the relative abundance of taxa involved in intestinal mucus and short-chain fatty acid production. Maternal obesity was associated with altered intestinal mucus production, elevated M1 macrophage infiltration and altered placental nutrient transport. These data suggest a microbial-immune interaction in mediating the impacts of obesity on maternal adaptation to pregnancy.

MATERNAL FETAL MEDICINE I: MATERNAL MEDICINE

TO 11 Invited Speaker

ARTERIAL STIFFNESS AND PREDICTION OF PRE-ECLAMPSIA: CAN WE DO BETTER?

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There is currently lack of accurate clinical tools to predict pre-eclampsia. Specifically, previously proposed predictive tools, including angiogenic factors and uterine artery Doppler, have low or inconsistent predictive abilities, and thus they are not reliable for population screening. Although placental pathogenic processes associated with pre-eclampsia initiate in the first trimester, the clinical manifestations of pre-eclampsia develop in the second half of pregnancy, i.e., weeks to months later.

Arterial stiffness, a composite indicator of arterial health, has recently been identified as a potential tool to assess risk of pre-eclampsia and other hypertensive disorders in pregnancy. We performed a longitudinal cohort study of consecutive pregnant women at high risk for pre-eclampsia with a singleton pregnancy, the REVEAL (pRedictivE Value of artEriAl stiffness in the development of pre-ecLampsia) study. Participants were recruited within their first trimester and arterial stiffness measurements were performed every four weeks from recruitment to delivery, once within 24 h after delivery at bedside, and at 6-12 weeks post-partum. Blood was drawn at the end of each trimester and post-partum to measure angiogenic/antiangiogenic factors associated with pre-eclampsia, of which the soluble fms-like tyrosine kinase 1 to placental growth factor (sFlt-1/PlGF) ratio is known to have the best predictive properties, while a uterine artery Doppler was performed at weeks 22-24. REVEAL's overarching objective was to fill important knowledge gaps with respect to the ability of arterial stiffness to predict the development of pre-eclampsia and recovery post-partum in high-risk pregnant women with a singleton pregnancy. We assessed 1) temporal changes in arterial stiffness during pregnancy and up to 6-12 weeks post-partum of those women who develop vs those who do not develop pre-eclampsia, and 2) a) the predictive value for pre-eclampsia of arterial stiffness (according to level and timing) as compared with the predictive value of specific angiogenic factors or/and uterine artery Doppler. In addition to pre-eclampsia, we assessed the composite outcome of pre-eclampsia, gestational hypertension and gestational diabetes. Results of the REVEAL study will be presented, as well as other related evidence during pregnancy and post-partum.

Trainee Thematic Presentations

TO 12

LACKING CONSENSUS: RESULTS FROM AN INTERNATIONAL DELPHI SURVEY ON INVASIVE PLACENTATION

Susan O'Rinn[1,2] , Cheyanne Reed [1], Leedan Cohen[1,2], Alex Kiss[1,2], Nir Melamed[1,2], John Kingdom[2,3], Jon Barrett[1,2], On behalf of the International IP Consensus Steering Committee
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Objective: The objective of this study was to determine best practices for screening, diagnosing, and managing placenta accreta, increta, and percreta – invasive placentation (IP) - by surveying experts worldwide. **Methods:** A modified Delphi survey was used to assess current expert opinion and practice regarding IP. 56 potential experts were identified for participation using the following inclusion criteria: expertise in maternal fetal medicine (MFM), obstetrics, gynecology, anesthesiology, interventional radiology, hematology or transfusion medicine; geographic diversity; and previous clinical guideline development or recommendation from the steering committee. 41 (68%) agreed to participate with >83% of respondents completing each survey round. The survey was administered via SurveyMonkey Inc. and consisted of three rounds, each with three sections: screening; diagnosis; and management (ante-natal, pre-operative, operative and post-operative subsections). Survey development was guided by a 15 person steering committee with a total of 210 survey items generated from existing guidelines and scientific literature. Each item was

rated on a 5-point Likert scale and consensus was defined as greater than 70% agreement across two rounds. **Results:** Consensus was achieved for 63 (30%) items while 147 (70%) items did not achieve consensus. Non-consensus items included: termination of pregnancy; timing of Caesarean delivery; management of bleeding and blood product requirements; balloon use and placement; incision type; conservative approach vs. hysterectomy; and treatment of adherent placenta. Significant differences in responses were only found for 13 (6%) items between MFMs and all other specialties and for 21 (10%) items between North American and European experts. Rater consistency across rounds was 81%. **Conclusion:** We conclude that despite the increasing prevalence of IP worldwide, it is clear there is a lack of consensus amongst experts on how best to screen, diagnose and manage this potentially serious obstetrical complication. The majority of survey items were culled from existing guidelines but the results suggest that experts do not necessarily endorse these practice recommendations. This research highlights the divergence between existing clinical guidelines and expert opinion and suggests the need for future research to better address IP.

TO 13

FIRST-TRIMESTER MEAN ARTERIAL BLOOD PRESSURE AND RISK OF PREECLAMPSIA

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Introduction: There is growing interest for the early prediction of preeclampsia (PE) using a combination of markers including maternal blood pressure. In a case-cohort study, we previously observed that mean arterial blood pressure using an automated device was superior to manual measurement for the prediction of PE. **Objective:** We aimed to evaluate the predictive value of mean arterial pressure (MAP) using blood pressure taken by an automated device during the first trimester of pregnancy to predict preeclampsia. **Methods:** We performed a prospective observational cohort study of nulliparous pregnant women recruited over the first trimester of pregnancy in two academic centers. MAP was calculated from blood pressure measured using an automated device validated for pregnant women, on both arms simultaneously and taking a series of recordings (minimum of 2) until stability was reached. All participants were followed until delivery and each pregnancy complications were noted. We computed the multiples of the median (MoM) of the log10MAP while adjusting for gestational age at measurement. ROC curves analyses were performed and the screening performance [area under the curve (AUC)] of MAP was calculated. Optimal cut-off values of MAP to predict PE were identified along with their sensitivities and specificities. P-value <0,05 were used to describe a significant association. The results were stratified for early onset (EO), preterm and term preeclampsia and multi linear regression was used to develop a predictive model. **Results:** We included 4733 adult nulliparous women, with a mean maternal age of 28.9 years old (STD=4.1), and BMI of 25 (STD=5). Fourty-nine (1%) participants were lost to follow-up. The current study included 292 cases of PE (10 early onset PE, 33 preterm PE and 241 term PE). We observed that MAP was significantly associated with the risk of PE (AUC: 0.742; 95%CI: 0.711 - 0.773). The first-trimester MAP could predict 58% of term PE, 70% of preterm PE (p<0.001) and 70% of EO-PE (p=0.002), with a 25% false- positive rate. Moreover, MAP could predict 36% of term PE, 49% of preterm PE (p<0.001) and 60% of EO-PE (p=0.002), with a 10% false-positive rate. **Conclusion:** Mean arterial blood pressure measured during the first trimester of pregnancy is useful to identify women at high-risk of preeclampsia, mostly in its preterm forms. However, the detection rate of PE by MAP should be combined with other markers to attain higher discriminative level and be integrated into clinical practice.

TO 14

PHYSICAL ACTIVITY PATTERNS AND VASCULAR FUNCTION DURING PREGNANCY.

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Introduction: Prenatal exercise is established to improve maternal health outcomes, yet 85% of pregnant women in North America fail to meet the current physical activity guidelines. Concurrent with low levels of moderate to vigorous physical activity (MVPA), pregnant women engage in high levels of sedentary (sitting) time. In non-pregnant populations, MVPA and sedentary behaviour are independent risk factors for cardiovascular disease including high blood pressure. Although blood pressure is controlled by many factors it is intimately related to baroreflex gain (BRG) and arterial

stiffness. The impact of pregnancy, MVPA and sedentary behaviour on BRG and arterial stiffness is not well understood. **Objective:** The purpose of this study was to determine the influence of MVPA and sedentary behaviour during pregnancy on maternal arterial stiffness and baroreflex gain. We hypothesized that increased MVPA and decreased sedentary behaviour would be independently correlated with increased BRG and decreased arterial stiffness. **Methods:** Data from 49 third trimester (31.6 ± 3.4 weeks) normotensive pregnant women (30.9 ±3.2 years) were included in the present study. Peripheral (carotid-finger) arterial stiffness was assessed using pulse-wave velocity (PWV) analysis (tonometer to finger photoplethysmography). Spontaneous BRG was calculated as the slope of the relationship between fluctuations in systolic blood pressure (SBP) and heart rate (HR). Objective measures of MVPA and sedentary behaviour were collected over a 7-day period using accelerometry. **Results:** Sixteen women were classified as active (ACT; >150 minutes of MVPA per week) while the rest were inactive (INACT; <150 minutes of MVPA). ACT engaged in less sedentary behaviour (ACT: 65.6 ± 6.9% vs. INACT: 72.0 ± 7.9%) and more MVPA (ACT: 287 ± 109 min/week vs. INACT: 77 ± 41 min/week) than INACT. After controlling for age, weeks gestation, pre-pregnancy body mass index, sedentary behaviour and light physical activity, women who engaged in more MVPA had increased BRG (r=-0.327, p=0.018) and decreased PWV (r=-0.471, p=0.003). However, after controlling for age, weeks gestation, pre-pregnancy body mass index, MVPA and light physical activity we found no correlation between percent of the day spent sedentary and BRG (r=-0.019, p>0.05) or PWV (n=43,r=0.187, p>0.05). **Conclusion:** The results of the current study found moderate correlations between MVPA (but not sedentary behaviour) and both BRG and PWV during pregnancy. These data suggest that engaging in greater amounts of MVPA during pregnancy is beneficial for vascular function.

TO 15

MAGNESIUM SULPHATE FOR FETAL NEUROPROTECTION TO PREVENT CEREBRAL PALSY (MAG-CP) – A MANAGED KNOWLEDGE TRANSLATION PROJECT TO IMPLEMENT GUIDELINES IN CANADA

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Introduction: Canadian guidelines (2011) recommend magnesium sulphate (MgSO4) for women at risk of imminent birth at <32-34 weeks to reduce the likelihood of cerebral palsy in the child. MAG-CP was a managed knowledge

translation (KT) intervention for this guidance. **Objective:** Using managed KT, we aimed to increase the 'optimal' use of MgSO4 (i.e., MgSO4 use when and only when indicated) to 80% of eligible women over four years (2011-15). **Methods:** KT activities included a national interactive online e-learning module and at MAG-CP tertiary perinatal sites, educational rounds, focus group discussions, and surveys of practice change barriers and facilitators. Participating sites contributed data on pregnancies with threatened very preterm birth using the Canadian Perinatal Network (CPN) database. MgSO4 use for fetal neuroprotection (NP) was tracked prior to (Jan 2009-May 2011) and during (Jun 2011-Sept 2015) implementation of managed KT. The primary outcome was 'optimal' MgSO4 use (i.e., administration when and only when indicated) over time, evaluated by generalized estimating equation logistic regression ($p<0{\cdot}05$ significant). Also analyzed were national trends in MgSO4 use for fetal NP and associated neonatal resuscitation, using the Canadian Neonatal Network (CNN) database. **Results:** There were 5800 women with imminent preterm birth who were eligible for MgSO4 for fetal NP: 2657 pre-KT (17 centres) and 3143 during KT (11 centres). For MgSO4 use for fetal NP, KT was associated with: an increase in optimal use (35.8% to 71.7%, $p<0.001$), a decrease in underuse (64.2% to 17.9%, $p=0.005$), and a small increase in suboptimal use (too early or at ≥32 weeks) (0.6% to 10.4%, $p=0.010$). There was substantial between-center variability in use of MgSO4. Maternal hypotension was uncommon during MAG-CP (7/1512, 0.5%). Nationally, intensive neonatal resuscitation decreased ($p=0.024$) despite rising MgSO4 for fetal NP use ($p< 0.001$). **Conclusion:** Multifaceted KT was associated with significant increases in appropriate use of MgSO4 for fetal NP to over 70%, and associated with neither important maternal nor neonatal risks. Further investigation is warranted to understand the remaining challenges and explain between-centre differences in practice. Future directions include analyses of the association of MgSO4 use and cerebral palsy incidence using data from the Canadian Neonatal Follow-Up Network (CNFUN).

REPRODUCTIVE (EPI)GENETICS AND FERTILITY

TO 16 Invited Speaker

LIFELONG CONSEQUENCES OF PERTURBING PERINATAL EPIGENETIC PROGRAMS

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DNA methylation is the best characterized epigenetic modulator and has been shown to have essential functions in the germline and embryo as well as in genomic imprinting. Genomic imprinting involves the formation of an epigenetic 'mark' at specific loci in a parent-of-origin-specific manner leading to monoallelic expression of a subset of genes in the offspring. Abnormalities in DNA methylation are associated with perturbations in growth, placental function, neurobehavioral processes, and carcinogenesis. A number of studies have linked an increased incidence of rare genomic imprinting disorders, associated with alterations in the methylation of imprinted genes, as well as birth and growth defects in children, to assisted reproductive technologies and/or infertility. Such findings are biologically plausible since spermatogenesis, oogenesis and early embryo development are key times when genomic methylation patterns are erased, acquired and maintained. We will present examples of mouse and human studies showing that compromised oocyte quality, manipulation of gametes and culture conditions and paternal factors can affect the acquisition and/or maintenance of DNA methylation and result in adverse outcomes in the offspring.

Trainee Thematic Presentations

TO 17

CHARACTERIZING THE IMPACT OF FETAL GROWTH RESTRICTION ON OFFSPRING OVARIAN FOLLICLE GROWTH AND DEVELOPMENT IN GUINEA PIGS

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Introduction: Intrauterine growth restriction (IUGR) results in metabolic and reproductive dysfunction in offspring. Previous experimental and clinical studies have demonstrated that low birth weight (LBW) females enter puberty early, have reproductive cycle irregularity, and a loss of ovarian follicles early in life. **Objective:** To determine the impact of offspring age and maternal nutrient restriction (MNR)-induced fetal growth restriction (FGR) on factors mediating follicle growth and development in prepubertal and young adult guinea pig offspring. **Methods:** Dunkin-Hartley guinea pig sows were randomized to either control (CON; 26.4% kcal protein, 13.3% kcal fat, 60.3% kcal carbohydrates) or nutrient-restricted (MNR) diets prior to mating. Nutrient-restricted sows were fed 70% of the average food intake per kilogram of body weight of the control group until day 34 of pregnancy after which food intake increased to 90% of the CON group. At birth, offspring were classified as appropriate-for-gestational age (AGA) if > 95 g or FGR if < 85 g. Offspring ovaries were collected at postnatal day 26 (P26, prepubertal) and P111 (young adult). Ovarian mRNA levels of key follicular regulatory genes were measured using RT-qPCR. The effect of offspring age and maternal diet on gene expression levels mediating folliculogenesis was evaluated. **Results:** With age, both AGA and FGR offspring exhibited increased ovarian expression of mediators of ovarian steroidogenesis and steroid action, LHR (pAge<0.0001) and AR (pAge<0.0001), and decreased ovarian expression of key follicle promoting factor, BMP7 (pAge<0.0001), compared to prepubertal offspring. Ovarian expression of gonadotropin receptor, FSHR (pAge=0.0153) was decreased in FGR offspring compared to prepubertal offspring. Offspring that were growth restricted in utero demonstrated significant reductions in key ovarian follicle growth factors including; anti-mullerian hormone (AMH; pDiet=0.0004), insulin-like growth factor receptor (IGFR; pDiet=0.0038), growth differentiation factor 9 (GDF9; pDiet=0.0452), and androgen receptor (AR; pDiet=0.0023). We observe these effects primarily in young adult offspring, suggesting that the impacts of IUGR appear early in the post-pubertal period. **Conclusion:** Fetal growth restriction was associated with significant changes in key regulators of ovarian follicle growth and steroid regulation. Collectively, these data support the concept that the prenatal intrauterine environment is a key mediator of postnatal ovarian development.

TO 18

BINUCLEATION FAILS TO ACTIVATE A TETRAPLOIDY CHECKPOINT AND INSTEAD CAUSES SEGREGATION ERRORS IN THE PREIMPLANTATION EMBRYO.

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Introduction: Embryo binucleation is commonly observed in human embryos. In somatic cells, binucleation leads to tetraploidy, which in turn causes a G1 arrest. However the consequences of binucleation and tetraploidy in the preimplantation embryo are poorly understood. **Objective:** To understand the impact of binucleation and tetraploidy in the mammalian preimplantation embryo. **Methods:** To induce binucleation, mouse embryos were treated with Cytochalasin B or Latrunculin at the 4-cell stage. Fixed and live cell imaging was performed to evaluate embryo development, cell cycle progression and chromosome segregation errors. Embryos were stained with Alexa-Phalloidin (plasma membrane) and Hoechst (DNA). Embryo ploidy was analyzed after binucleation using CREST (kinetochores) or CENP(A) (centromeres), along with Hoechst and Alexa-Phalloidin. For detailed analysis of S-phase dynamics, we performed live cell imaging using H2B:RFP (chromosomes) and the S-phase marker PCNA:EGFP. Finally, we performed live embryo imaging using H2B:RFP-expressing and Tubulin:GFP-expressing embryos during the first and second divisions after binucleation to observe chromosome segregation dynamics. Live and fixed images were acquired using either confocal or structured illumination microscopy. **Results:** The number of cells within binucleated embryos increased similarly to diploid cells, indicating that binucleation does not prevent embryonic cell divisions. Cells within binucleated embryos possessed approximately double the amount of kinetochores and centromeres as the control diploid group, confirming that binucleation leads to tetraploidy. Using live imaging of PCNA:GFP we observed that S-phase occurred in binucleated embryos with normal temporal dynamics. Regarding chromosome segregation errors, we observed that embryos that had been binucleated possessed substantially greater numbers of micronuclei than the control diploid group ($P<0.05$). Consistent with this, with live cell imaging, we observed higher rates of abnormal divisions as compared to the control group ($P<0.05$), including lagging chromosomes, chromosome misalignment, and chromosome bridges. Live imaging of Tubulin:GFP reveals that chromosome missegregation may be a result of altered microtubule dynami! cs. **Conclusion:** We conclude that embryos lack a tetraploidy checkpoint, and we propose that tetraploidy may be a previously unappreciated stepping stone to the generation of aneuploid cells in embryos.

TO 19

PARENT-OF-ORIGIN EFFECT IN ASTHMA–GWAS META-ANALYSIS IN THREE CANADIAN COHORTS

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Introduction: Asthma is a complex disease caused by a combination of genetic and environmental factors. Heritability is estimated to range between 0.48- 0.79. To date, 44 significantly associated SNPs have been identified by 23 asthma genome-wide association studies (GWAS) ($p<10-6$). The consensus is that the main genetic effects of these common SNPs (with modest effects) do not fully explain the heritability of asthma. Genomic imprinting is a potential mechanism which may explain some of the 'missing heritability'. Imprinting is an epigenetic phenomenon where the expression of genes depends on their parental origin (parent-of-origin effect). Imprinting effects have been reported in the development of many complex diseases. **Objective:** Identify candidate genomic regions for imprinting in asthma. **Methods:** To identify candidate genomic regions for imprinting we used GWAS data from three family-based studies (two parents and one offspring). These studies are: 1) the Canadian Asthma Primary Prevention Study (CAPPS), a high-risk asthma birth cohort and, 2) the Study of Asthma Genes and Environment (SAGE), a population-based asthma

birth cohort 3) the Saguenay-Lac-Saint-Jean Québec Familial Collection (SLSJ), a founder population of French-Canadians. We used a likelihood-based variant of the Transmission Disequilibrium Test. Parent-of-origin effects in SLSJ as well as the combined CAPPS and SAGE were performed by including parental sex as a modifier in the analysis. Meta-analysis was conducted using the results of SLSJ and the joint analysis of CAPPS and SAGE weighted by the number of informative transmissions for each study. **Results:** In SLSJ, 7 SNPs showed significant parent-of-origin effects with p<10-5 (252 trios with asthmatic children). In the joint analysis of CAPPS and SAGE, 13 SNPs showed significant parent-of-origin effects with p<10-5 (148 trios with asthmatic children). Notably, in the joint analysis of CAPPS and SAGE, we identified a parent-of-origin effect at a known imprinted gene, CTNNA3. This gene was previously identified in a GWAS study of occupational asthma. Of all significant results in those two analyses (p<10-5), 12 out of 20 of the SNPs were in or near Long non-coding (lnc)RNA genes. LncRNAs are known to be involved in genomic imprinting and gene regulation. Meta-analysis resulted in two SNPs with significant parent-of-origin effects with p<10-5 in the genes SLC39A10 and LNX2/POLR1D. **Conclusion:** We identified several SNPs showing parent-of-origin effects in asthma.

TO 20

SPINDLE ASSEMBLY CHECKPOINT INSUFFICIENCY CAUSES CHROMOSOME SEGREGATION ERRORS IN MOUSE PREIMPLANTATION EMBRYOS

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Introduction: Chromosome segregation errors during early embryonic divisions result in embryos comprising a mixture of euploid and aneuploid cells. While mosaic aneuploidy is observed commonly in human embryos, how and why it arises remains elusive. In somatic cells, the spindle assembly checkpoint (SAC) is the major cellular safeguard against aneuploidy, delaying the onset of anaphase until all chromosomes have been correctly attached to spindle microtubules. **Objective:** To examine the presence, strength and sensitivity of the SAC in preimplantation embryos. **Methods:** Female CD1 mice were super-ovulated and mated with male mice. Two-cell embryos were harvested from oviducts 48hrs after and cultured in vitro. Microinjection of H2B:RFP mRNA was performed to fluorescently label chromosomes allow visualization of chromosome segregation dynamics by confocal live cell imaging. **Results:** We performed fast-acquisition live imaging of H2B:RFP-expressing embryos under standard conditions and found uncorrected, pre-anaphase misaligned chromosomes in ~5% of divisions, suggesting that SAC function is weak in early mouse embryos. To ascertain whether a SAC operates in preimplantation development, embryos were treated from the two-cell to blastocyst stage with the specific SAC inhibitor AZ3146. Immunofluorescence analysis revealed a higher incidence of micronuclei after SAC inhibition (p=0.038). Consistent with this, live imaging experiments show that SAC inhibition results in premature anaphase with increased chromosome misalignment and chromosome segregation errors such as lagging chromosomes (p=0.002). In addition SAC inhibition was capable of overcoming mitotic arrest induced by high concentrations of the spindle poison Nocodazole. Thus, a SAC operates in embryos. We next probed SAC strength by exposing embryos for 16h to different Nocodazole concentrations. Embryos only arrested in mitosis at the highest concentrations tested, despite significant spindle damage and increased segregation errors at lower concentrations (range: 1nM-1µM, with 100nM and 1µM causing ~45% and 99% mitotic arrest, respectively). Furthermore, we performed live imaging of embryos in low doses of Nocodazole (10nM), we observe no anaphase delay despite and increased rate of chromosome mis-segregation, suggesting that a failure to activate SAC signaling in response to spindle damage results in chromosome segregation errors. **Conclusion:** Taken together, our results demonstrate that embryos possess a SAC that does limit chromosome mis-segregation, but it is not sufficiently sensitive or robust to prevent all errors. SAC insufficiency provides a potential mechanistic explanation for mosaicism.

REPRODUCTIVE IMMUNOLOGY

TO 21 Invited Speaker

IS THERE EVIDENCE FOR LYMPHOCYTE-INITIATED PREGNANCY FAILURE?

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Introduction: The capacity of the immune system and of uterine lymphocytes to initiate pregnancy failure is not sufficiently defined. Particularly unclear is whether immune involvement is a primary or secondary event. In the absence of pregnancy, endometrial decidualization recruits lymphocytes, suggesting their physiological roles are conceptus-independent. Between implantation and midgestation, uterine Natural Killer (uNK) cells are the dominant decidual immune cells. Physiological roles of murine and human uNK cells are promotion of decidual cell maturation and decidual angiogenesis and vascular remodeling. This includes initiation of spiral arterial remodeling prior to their interval of trophoblast-associated remodeling. **Objective:** To characterize decidual lymphocyte interactions during pre-placental stages of mouse pregnancy and to address decidual immune system alterations in experimental pregnancy failures due to maternal bacterial infection or autoimmune disease. **Methods:** Whole mount immunohistochemistry was applied to live, hemisected implantation sites from C57BL/6 (B6) mice to define interacting lymphocyte lineages under physiological conditions. The intracellular bacterium Salmonella enterica serovar Typhimurium (S.Tm) was given intravenously to gd12.5 susceptible and congenic, resistant B6 mice whose implant sites were examined by histopathology 48-72h later. The mouse model of fetal/neonatal autoimmune thrombocytopenia (NFAIT) was studied at gd14.5 when >50% of conceptuses show hemorrhagic failure due to fetal platelet deficits induced by maternal antibodies to beta 3 integrin. **Results:** Dynamic changes in immune cell subsets occur in early decidua with synapse formation between immune cell subtypes. UNK cells initially conjugate with antigen presenting cells and then with CD8+ T cells. Conjugations with trophoblast first occurred at gd9.5 but were rare. In bacterial infection, immune cell responses were absent or limited. Fetal losses were attributed to S.Tm colonization of yolk sac. In NFAIT, a pathological uNK cell was defined that unexpectedly expanded in number during late pregnancy. These cells killed extravillous but not placental trophoblasts via antibody-dependent cell-mediated cytotoxicity (ADCC). Fetal hemorrhages, growth retardation and deaths were reduced/eliminated by maternal NK cell reduction or inactivation. **Conclusion:** Time course studies that include rigorous histopathology and immunohistology are essential in reaching appropriate, unbiased on the importance of the immune system for initiation of pregnancy loss.

Trainee Thematic Presentations

TO 22

CHARACTERIZATION OF THE MECHANISM OF ACTION OF AN ANTI-IL-6R PEPTIDE IN AN INFLAMMATION- AND INFECTION-INDUCED PRETERM BIRTH

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Introduction: Preterm birth (PTB) is defined as delivery before 37 weeks of gestation and it is a health concern, ranked as the leading cause of mortality under 5 years old. PTB is difficult to address because of its multifactorial aetiology where just infection has been determined as a causal link. Current studies have shown that one common process in PTB is the presence of an inflammatory process. Some studies have shown a significant increase of IL-6 levels before the onset of PTB and there have been some efforts to use this cytokine as a potential biomarker of PTB. Some of the detrimental effects on the neonate have been shown to be related to the increasing levels of IL-6 in amniotic fluid, fetal blood and gestational tissues. **Objective:** Here we present the characterization of an IL-6R antagonist small peptide designed by our group and named 633, in a mouse LPS-and or IL-6-induced PTB model. **Methods:** We analyze the efficacy of 633 to reduce IL-6-induced proinflammatory genes ex vivo in gestational tissues (placenta, uterus and fetal

membranes). **Results:** During this work, we showed that 633 can modulate IL-6 signalling by blocking the STAT3 pathway without affecting the Akt and Erk1/2 pathway. Peptide 633 showed a dose response inhibitory effect of IL-6-induced IL-1β, IL-6 and TNFα gene expression in HEK-IL-6R cells and of TNFα gene expression in mice uterus (IC50 0.76, 2.07, 0.26 and 1.05nM, respectively). **Conclusion:** We have shown the efficacy of 633 in preventing IL-6- and LPS-induced PTB in mice, by selectively blocking the gene expression of some PTB inducing proteins in leukocytes, uterus and fetal membranes; and downregulating the levels of CRP in maternal blood and IL-1β in amniotic fluid. 633 is also able to increase neonatal survival and rescue neonatal weight. All this results set up the capacity of 633 to be a potential prophylactic treatment for PTB by reducing the inflammation outcome and will also encourage research the potential of 633 to reduce neonatal morbidity.

TO 23

IVIG FOR RECURRENT PREGNANCY LOSS AND RECURRENT IMPLANTATION FAILURE: EXPERIENCE AT THE MUHC

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Introduction: IVIg has emerged as a potential therapy for idiopathic immune-mediated RPL and RIF. However, due to study heterogeneity and lack of biomarkers to diagnose immune mediated reproductive failure (IMRF), there is controversy surrounding its use for this indication. To fully take advantage of IVIg's immunomodulatory potential, we believe that it must be given at sufficient doses (400-800 mg/kg) before implantation. We have developed a standardized protocol for patients suspected IMRF. **Objective:** To evaluate whether our IVIg protocol is safe and effective as a last resort therapy in a non-selected population of women with RPL and RIF. **Methods:** This was a single center, non-randomized pilot study conducted at the Allergy-Immunology Clinic of the Montreal General Hospital (MUHC). We included patients 18-42 years old with > 4 miscarriages, or > 3 good quality embryo transfer (ET) failures who did not have any contraindications to IVIg therapy. IVIg (or equivalent doses of subcutaneous immunoglobulin (scIg)) 40g (<65kg) or 50g (≥65 kg) was administered 5-10 days before embryo transfer. If successful pregnancy ensued, IVIg was given monthly until 32-34 weeks. The addition of low dose Aspirin or LMWH was left to the discretion of the treating obstetrician and we excluded patients receiving other immunomodulators. We then prospectively followed these patients every 3 months during pregnancy and 1 month after delivery to determine the efficacy and safety of IVIg. **Results:** 15 patients undergoing IVF were included from 08/2014-01/2016. 13/15 (86%) have either delivered healthy neonates (9/15) or are doing well with intact pregnancies >12 weeks of GA (4/15); 2/15 (13%) patients failed their ET and there were no miscarriages or stillbirths reported. In the subgroup analysis, successful outcomes were seen in 7/9 (77%) patients with primary RIF, 2/2 (100%) with secondary RIF, 3/3 (100%) with primary PRL and 1/1 (100%) with secondary RPL. There were 7 cases of IVIg related side effects: 6/15 (40%) patients reported transient mild post-infusion headaches; one patient developed hypotension and chills during her first IVIg infusion but tolerated subsequent scIg. IVIg was discontinued prematurely (both at 24 weeks) in 2 patients, one was hospitalized for renal colic at 26 weeks and another developed prolonged hypotension at needle insertion. Obstetrical complications were reported in 2 patients, one developed gestational diabetes and delivered prematurely at 34 6/7 weeks because of HELLP syndrome, another was put on bed rest at 27 weeks because of PTL and delivered a healthy child at term. There was one fetal abnormality reported; one child was born with mild hydrocephalus. **Conclusion:** Our IVIg protocol appears to be safe and may be effective for patients with suspected IMRF undergoing IVF and our results justify the need for a properly designed RCT.

TO 24

THE ROLE OF UTERINE NATURAL KILLER CELLS IN IMMUNE-MEDIATED INTRAUTERINE GROWTH RESTRICTION IN RATS

Kelly Baines and Stephen Renaud

Introduction: Pregnancy is an immunological paradox, where two genetically foreign individuals – mother and fetus – coexist in harmony. The mechanisms facilitating this immunological tolerance are not well understood; however, the uterus contains a unique population of immune cells belonging to the natural killer (NK) lineage that likely have a key

role in promoting fetal tolerance. Uterine NK cells are purported to promote uterine vascular remodeling as well as facilitate placental and fetal development during pregnancy. We hypothesize that exposure to an immune stimulus early in pregnancy disrupts normal functioning of uterine NK cells, thereby impacting uterine vascular remodeling and fetal growth. **Objective:** To determine the effect of polyinosinic-polycytidylic acid (polyI:C), an immune stimulant and potent activator of NK cells, on fetal and placental growth and development. **Methods:** 1, 5, or 10mg/kg polyI:C, or saline as a control, was injected into gestational day (GD) 8.5 pregnant rats under control conditions or following NK cell depletion using anti-asialo GM1 antibodies. Changes in uterine cytokine production were assessed by qRT-PCR two and six hours following injection of saline or polyI:C. Fetal growth was assessed five and ten days following polyI:C or saline injection by measurement of fetal weight and crown-rump length. **Results:** Dams injected with 10 mg/kg polyI:C exhibited a 15% decrease in fetal weight and a 4% decrease in fetal crown-rump length, without affecting fetal viability. Decreased fetal weight correlated with increased production of inflammatory cytokines (interferon-gamma, tumour necrosis factor-alpha, and interleukin-6) in both spleen and implantation sites, and increased perforin expression within implantation sites. Interestingly, immunodepletion of NK cells prior to injection of 10 mg/kg polyI:C resulted in a 38% decrease in fetal weight compared to control animals, indicating that uterine NK cells have a role in preventing fetal growth restriction caused by polyI:C exposure. **Conclusion:** Administration of polyI:C to pregnant rats resulted in elevated cytokine production and fetal growth restriction that was exacerbated by a lack of uterine NK cells.

TO 25

ALTERED MATERNAL IMMUNE SYSTEM PROFILE IN PE AND POSTPARTUM PE: POTENTIAL CONTRIBUTION TO DISEASE PROGRESSION

Marie-Ève Brien[1,2,3], Cyntia Duval[1,2,4], Ines Boufaied[1,2], Sylvie Girard[1,2,3,4]
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Introduction: Preeclampsia (PE) is a leading cause of mortality and morbidity which affects 5-8% of pregnancies worldwide. PE is characterized by hypertension after 20 weeks of gestation and proteinuria. The placenta plays a central role in PE and its removal remains the only cure, however, it cannot explain PE occurring in the postpartum period (PPPE). Systemic maternal inflammation is known to be associated with PE and could be key to the understanding of PPPE. **Objective:** Our aim was to determine the circulating inflammatory profiles in women with pregnancies complicated with PE or PPPE as compared to term uncomplicated pregnancies in relation with inflammation at the maternal-fetal interface. **Methods:** We recruited women with uncomplicated term pregnancies (Ctrl, N=20), pregnancies complicated with PE (PE, N=20) or normal term pregnancies with postpartum occurrence of PE (PPPE, N=20). Blood samples were collected to determine the circulating immune profile by flow cytometry and placental biopsies obtained for histological and inflammatory mediators analysis. **Results:** Analysis of the maternal circulating immune cells revealed that PE and PPPE had distinct profiles characterized by increased percentage of CD8+ cytotoxic and Th1 T cells as well as NKT cells in PE. On the other hand, in PPPE, we detected increased in NK cells, monocytes and CD4+ T cells. These distinct profiles were also seen in the levels of circulating levels of endogenous mediators of inflammation (damaged-associated molecular pattern, DAMPs), such as elevated uric acid in both PE and PPPE but with HMGB1 being increased in the maternal circulation only in PPPE. At the maternal-fetal interface increased syncytial knots were seen in PE placentas but no morphological changes were observed in PPPE. Interestingly, high levels of immune cell infiltration were detected in placentas from women that later developed PPPE only, suggesting a prenatal initiation of the pathology. **Conclusion:** Our work showed unique maternal immune profiles in PE vs PPPE with a primarily involvement of the adaptive immune system (T lymphocytes) in PE and of the innate immune system (monocytes) in PPPE. This highlight the involvement of the maternal immune system in both pathologies. Furthermore, we saw immune cells infiltration in the placenta of women that will later develop PPPE suggesting a prenatal initiation of the pathology. In-depth understanding of these changes will allow better understanding of the mechanisms linking the immune system to PE and PPPE.

PERINATAL EPIDEMIOLOGY

TO 26 Invited Speaker

MATERNAL OVERWEIGHT/OBESITY AND OFFSPRING RISKS

Sven Cnattingius[1], Stefan Johansson[1], Martina Persson[1], and Eduardo Villamor[1,2]
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Introduction: Overweight and obesity is increasing in prevalence worldwide, and the presently reported increase in the severe forms of obesity is a growing concern. **Objective:** Using population-based nation-wide Swedish registries, we have studied associations between maternal body-mass index (BMI) in early pregnancy and risks of preterm birth, infant mortality, and asphyxia-related neonatal complications. We have also studied if weight gain or weight loss between successive pregnancies influences risks. **Methods:** We conducted several nation-wide cohort studies including all live singleton births at ≥22 completed gestational weeks in Sweden. Using the person-unique national registration number, individual record-linkages were performed between between the Swedish Medical Birth Register, the National Patient Register, and the Cause of Death Register. Odds Ratios or Hazard Ratios (HR) and 95% confidence intervals were calculated, and generally also adjusted for maternal age, country of origin, education level, cohabitation with partner, height, smoking, maternal epilepsy, and year of delivery. **Results:** Compared with normal weight women (BMI 18.5 to <25) risks of preterm delivery increased with overweight (BMI 25 to <30) and increasing obesity (BMI >30). Risk of spontaneous preterm delivery increased with BMI among obese women. Risk of medically indicated preterm delivery increased with BMI among overweight and obese women regardless of gestational age.1 Risk of infant mortality increased with BMI among offspring of overweight and obese women. The BMI-related risk of infant mortality was primarily confined to term infants (>37 weeks), and more prominent for neonatal than for postneonatal deaths (infant deaths within and after the first 28 days of life, respectively).2 Risks of asphyxia-related neonatal complications, including meconium aspiration, neonatal seizures, and low Apgar scores (0-3) at five and ten minutes also increased with BMI in offspring of overweight and obese women.3 Weight gain between first and second pregnancies was associated with a dose-dependent increase in risks of preeclampsia, gestational hypertension, gestational diabetes, stillbirth, infant mortality, and asphyxia-related neonatal complications.4-6 The effect of weight gain on risks were primarily obtained or restricted to mothers and offspring of mothers with normal BMI (<25) in the first pregnancy. **Conclusions:** Primary preventive efforts, aimed at reducing the prevalence of overweight and obesity is a global concern. Reduced prevalence of overweight and obesity in girls and women of reproductive ages might reduce the prevalence of obesity-related pregnancy complications, preterm birth, asphyxia-related neonatal morbidity, stillbirth and infant mortality.
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Trainee Thematic Presentations

TO 27

MATERNAL PRE-PREGNANCY BODY MASS INDEX AND GESTATIONAL WEIGHT GAIN: INTERPROVINCIAL VARIATION AND IMPACT ON BIRTHWEIGHT

Dzakpasu S, Woolcott C, Chapinal N, Guo M, Murphy P, Grabovac M, McDonald SD.

Introduction: More than half of women exceeded the 2009 national guidelines for weight gain during pregnancy, and approximately one fifth of women gain below. Both excess and inadequate gestational weight gain (GWG) significantly increase maternal and infant risks. **Objective:** 1) To describe provincial variation in maternal pre-pregnancy body mass index (BMI) and gestational weight gain (GWG); 2) To estimate the impact of maternal BMI and GWG on two key perinatal indicators, small-for-gestational age (SGA) and large-for-gestational age (LGA). **Methods:** Four provinces with a perinatal database were included in this study, namely British Columbia, Ontario, Nova Scotia and Newfoundland.

Multiple, concurrent retrospective studies were conducted to compare provincial variation. Women were included if they were >18 years, gave birth from 22+0 to 42+6 weeks' gestation, to a live singleton from April 2013 to March 2014. Gestational weight gain was categorized as below, within or above the Institute of Medicine recommendations. The outcomes were SGA (<10th percentile) and LGA (>90th percentile) relative to a Canadian reference of birthweight for gestational age and sex. Adjusted odds ratios were calculated using logistic regression models. To estimate the contribution of pre-pregnancy BMI and GWG to SGA and LGA, population attributable fractions (PAF) were calculated. **Results:** In British Columbia, Ontario, Nova Scotia, and Newfoundland, the prevalence of overweight was 21.1%, 24.0%, 23.7%, and 25.2%, and the prevalence of obesity was 14.1%, 18.1%, 24.2%, and 28.0%, respectively. The prevalence of GWG above the guidelines was 53.8%, 49.9%, 57.6% and 60.5%, in British Columbia, Ontario, Nova Scotia, and Newfoundland, respectively. A higher proportion of LGA was estimated to be attributable to excess GWG (PAF: 29.3% – 32.1% depending on the province) than to pre-pregnancy overweight (PAF: 6.5% -11.1%) or obesity (PAF: 8.9% - 17.2%). Similarly, the contribution of GWG below the guidelines to SGA was considerably higher than underweight BMI, and depending on province, PAFs varied from 9.2% - 10.6% and 4.0% - 6.2%, respectively. **Conclusion:** In the first interprovincial comparison with recent Canadian data, increasing proportions of women from west to east begin pregnancy with excess weight or gain too much weight during pregnancy. Excess GWG was a far larger contributor to LGA than either overweight or obese BMI. Similarly, the contribution of inadequate GWG to SGA exceeded that of underweight BMI. GWG is a potentially-modifiable, important determinant of key adverse perinatal outcomes across Canada, making it an important focus for public health.

TO 28

LABOR OUTCOMES AFTER SUCCESSFUL EXTERNAL CEPHALIC VERSION COMPARED TO SPONTANEOUS CEPHALIC VERSION

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Introduction: Previously, birth outcomes for pregnancies after a successful external cephalic version (ECV) from breech to cephalic presentation have been compared to spontaneously cephalic pregnancies that were not known to be breech after 33 weeks gestation. In order to analyze birth outcomes after a successful ECV procedure, a more appropriate comparison group are those pregnancies where the fetus is known to be breech in the third trimester and turns spontaneously to a cephalic presentation. **Objective:** To compare obstetrical outcomes for women with a cephalic presentation at birth resulting from a successful external cephalic version (ECV) to those resulting from spontaneous cephalic version (SCV) from breech presentation in the third trimester. **Methods:** We performed a secondary analysis on Early ECV Trial data. Study participants were in breech presentation between 34-36 weeks gestation and cephalic at birth. We compared the incidence of intrapartum interventions among those with a successful ECV and those with no ECV and a SCV. A generalized linear mixed model was used to determine odds ratios for our primary outcomes. We controlled for parity, maternal body mass index at enrolment, previous cesarean and enrolment centre. **Results:** No differences were found following ECV compared to SCV in incidence of cesarean (96/557 and 76/374, aOR 0.89, 95% CI 0.63 – 1.26), instrumental birth (68/557 and 29/373, aOR 1.55, 95% CI 0.96 – 2.50) or spontaneous birth (393/557 and 268/373, aOR 0.92, 95% CI 0.68 – 1.24). Multiparae with successful ECV were half as likely to require a cesarean compared to those with SCV and no ECV (28/313 and 42/258, aOR 0.45, 95% CI 0.26 – 0.80). **Conclusion:** This is the first study to compare birth outcomes of breech pregnancies that convert to cephalic presentation by means of SCV to those that have an ECV. Women with a cephalic presenting fetus at birth due to a successful ECV are not at greater risk of obstetric interventions at birth when compared to women with fetuses who spontaneously turn to a cephalic presentation in the third trimester.

TO 29

NEONATAL ABSTINENCE SYNDROME: A HEALTH ECONOMIC PERSPECTIVE

Timothy Disher[a,b], RN, BScN, PhD(student), Louis Beaubien[a], PhD, CPA, Marsha Campbell-Yeo[a,b], NNP-BC, PhD

Introduction: When neonates with neonatal abstinence syndrome (NAS) require pharmacological treatment, there are a variety of treatments to choose from. Head-to-head comparisons of pharmacological agents are abundant in the literature with some including measures of cost, but a decision analysis considering all possible options is absent. Further, while measurement of effectiveness in terms quality adjusted life years is preferred in Canadian guidelines their use in neonates is likely inappropriate **Objective:** To create a normative decision model to guide selection of first-line pharmacological agents for neonatal abstinence syndrome, based on the current evidence. **Methods:** We used information from existing published primary trials, and publically available estimates of costs to develop a cost-effectiveness decision analytic model to compare the cost-effectiveness morphine, methadone, buprenorphine, morphine + clonidine, phenobarbital alone, phenobarbital + morphine, and clonidine alone as first line pharmacological treatments for NAS. The analysis took the perspective of the Canadian health care system, and effectiveness was measured in days of exposure to potentially neurotoxic drug avoided. **Results:** Under the base-case scenario, morphine + clonidine has an incremental cost-effectiveness ratio (ICER) of 824.16 per day of exposure to a potentially neurotoxic drug avoided compared to buprenorphine monotherapy. All other choices were dominated. Results are sensitive to the length of home treatment with adjunct therapy, and the efficacy of buprenorphine. **Conclusion:** Morphine monotherapy is unlikely to be a cost-effective treatment for neonatal abstinence syndrome. Morphine with clonidine as first-line treatment is cost-effective and should be implemented more broadly.

TO 30

MATERNAL OBESITY AND HEALTH CARE UTILIZATION FOR MENTAL HEALTH CONDITIONS IN THE OFFSPRING

Alexa Grudzinski, Leslie-Anne Campbell, Linda Dodds, Christy G. Woolcott, Bryan Maguire, Stefan Kuhle

Introduction: Maternal obesity has recently been linked to various adverse infant neurodevelopmental outcomes. Several mechanisms to explain the association have been postulated, including an adverse intrauterine environment, postnatal influences, and genetic predisposition. Similar mechanisms could lead to a relationship between maternal obesity and offspring mental health, but this association warrants further investigation. **Objective:** To examine the relationship between pre-pregnancy maternal weight status and offspring physician visits for any mental health condition, as well as the specific subcategories of internalizing disorders, conduct disorders, and attention deficit hyperactivity disorder (ADHD). **Methods:** We conducted a population-based retrospective cohort study of singleton infants born between the years of 1989 and 1993 using a linkage of the Nova Scotia Atlee Perinatal Database and administrative health data. Offspring were followed from birth to age 18 years. Maternal weight status, as reported at the first prenatal visit, was categorized to approximate the WHO body mass index cutoffs. The number of physician visits for any mental health condition, internalizing disorders, conduct disorders, and ADHD were determined with the corresponding ICD diagnosis codes. Offspring physician visits from age 0-18 years were assessed and stratified by age ranges 0-5, 6-12, and 13-18 years. Compound Poisson regression adjusting for maternal smoking and sociodemographics was used to model the association. **Results:** In total, 35,090 mother-offspring pairs were included in the cohort. Within the first 18 years of life, offspring of mothers with obesity had significantly more physician visits for any mental health condition (adjusted incidence rate ratio [IRR] 1.30, 95%CI 1.22-1.37), internalizing disorders (IRR 1.18, 95%CI 1.10-1.25), conduct disorders (IRR 1.25, 95%CI 1.12-1.40), and ADHD (IRR 1.44, 95%CI 1.27-1.63) compared to mothers of normal weight. The highest IRRs were observed in the 0-5 and 6-12 years groups for ADHD, and in the 13-18 years group for conduct disorders. There was a dose-response relationship between weight status and offspring physician visits for all-type mental health conditions and ADHD but not for internalizing and conduct disorders. **Conclusion:** Offspring of mothers with obesity have more physician visits for mental health conditions in the first 18 years of life than children of normal weight mothers. Whether this finding is due to a higher risk for the development of mental health conditions in this group or is explained by residual confounding by health care accessibility needs to be further investigated in future research.

PAEDIATRIC STEM CELLS

TO 31 Invited Speaker

STEM CELL-DERIVED ALVEOLAR-LIKE MACROPHAGES FOR PULMONARY CELL THERAPY

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Embryonic stem (ES) cell and induced pluripotent stem (iPS) cell technology has made it possible in recent years to generate a variety of tissues and cells. This includes hematopoietic cells. Previously, it was thought that alveolar macrophages (AMs) – the primary hematopoietic cell of the airways – originated from adult circulating monocytes; however, new studies have shown these cells arise from early embryonic and fetal development and, thus, the phenotype and lifespan of alveolar macrophages differ from monocyte-derived macrophages. We hypothesized that to better represent the early developmental origin of AMs, we could use ES and iPS cells to generate AM-like cells. We used primitive hematopoiesis to derive primitive macrophages from rodent (mouse and rat) pluripotent stem cells that we conditioned to be like AMs. We confirmed that the cells express AM-like markers (e.g., CD11c and SiglecF) and that they are independent of the transcription factor myb –indicative that they are of a primitive origin. Additionally, we observed that unlike monocyte-derived macrophages, the macrophages we generated are highly proliferative in the presence of GM-CSF and M-CSF. We exploited this to obtain cell numbers for preclinical experimentation in rodent airway disease models. For example, when we delivered these stem cell-derived AMs to the airways of adenosine deaminase deficient mice – which are devoid of functional AMs – the mice lived and displayed oxygenation levels similar to their healthy littermates; whereas the untreated deficient mice displayed poor oxygenation levels and died of respiratory failure. We have also observed that the stem cell-derived AMs internalize various common pathogenic bacteria – including E. coli, S. aureus, and P. aeruginosa. We confirmed that the stem cell-derived AMs display bactericidal effects to all of the above bacterial species in vitro. Moreover, in a rodent model of E. coli-derived pulmonary sepsis, we confirmed that by direct intratracheal delivery these macrophages internalize live E. coli and reduce the number of airway neutrophils. The AMs also suppress RSV infection in vitro. Noting the therapeutic value of these functional macrophages, we also sought to modify the cells using lentiviral gene transfers to confer upon the macrophages a constitutive expression of the anti-inflammatory cytokine interleukin (IL-)10 and the protease inhibitor alpha-1 antitrypsin (A1AT). These advances in therapeutically scalable and functionally active stem cell-derived alveolar-like macrophages for pulmonary disease treatments represent a novel non-pharmacological approach to address the unmet needs of a variety of chronic airway diseases where innate immunity is insufficient or compromised; such as chronic obstructive pulmonary disease, cystic fibrosis and bronchopulmonary dysplasia.

Trainee Thematic Presentations

TO 32

REMOTE ORGAN INJURY: NEURAL PROGENITOR CELL FUNCTION IS IMPAIRED IN A NEONATAL MOUSE MODEL OF CHRONIC LUNG DISEASE LEADING TO ADVERSE NEURODEVELOPMENT

Marissa Lithopoulos[1,2,3], Arul Vadivel[1,2,3], Diane Lagace[2], Jing Wang[1,2], Ruth Slack[2], Bernard Thébaud[1,2,3]
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Introduction: One of the most common complications of preterm birth is bronchopulmonary dysplasia (BPD), a chronic lung disease caused by oxygen therapy, which is characterized by an arrest in lung growth. BPD is an independent risk factor for adverse neurodevelopment. Neural progenitor cells (NPCs)—cells crucial for brain development—have yet to be examined in BPD. **Objective:** To determine whether NPC function is perturbed in a BPD mouse model, contributing to adverse neurodevelopment **Methods:** Newborn C57BL/6 mice were exposed to room air or 80% O2 (BPD model) until postnatal day 14. NPC niches (subventricular zone (SVZ) and hippocampus) were then assessed for structural damage (cresyl staining) and immature brain cell lineage formation. NPCs were also isolated from the SVZ and hippocampus and functionally assessed via neurosphere assays (n=5/group). A portion of the mice (n=11 for controls;

n=9 for hyperoxia-exposed mice) were housed in room air until 4.5 months of age. Fear conditioning tests (tone-shock association) were then conducted to assess learning and memory (linked to postnatal neurogenesis). **Results:** Cresyl staining of the SVZ and hippocampus, revealed a sparse corpus callosum, as well as neuronal disorganization in the brains of hyperoxia-exposed mice compared to room air control mice. Production of the 3 major brain lineages (astrocytes, oligodendrocytes, and neurons) was greatly reduced in the SVZ of hyperoxia-exposed mice compared to room air control mice. Furthermore, NPCs isolated from the SVZ of hyperoxia-exposed mice formed significantly fewer primary ($p<0.01$) and secondary ($p<0.0001$) neurospheres than those isolated from control mice. Hyperoxia-exposed mice also experienced deficits in associative learning and memory, i.e., during fear conditioning tests, they formed a weaker association between the tone and the adverse stimulus (shock), freezing for significantly less time upon hearing the tone ($p<0.001$), compared to control mice. **Conclusion:** Decreased in vitro self-renewal and in vivo production of immature brain lineages demonstrate impairments in the functional capabilities of hyperoxia-exposed NPCs. Structural damage to the SVZ and hippocampus indicates injury to the NPC niche after hyperoxia exposure. Furthermore, the learning and memory deficits exhibited by hyperoxia-exposed mice indicate a significant reduction in postnatal neurogenesis. These results provide insight into potential mechanisms of BPD-associated adverse neurodevelopment. This study will help to develop future treatments to improve the lives of preterm infants.

TO 33

MESENCHYMAL STROMAL CELLS IN BRONCHOPULMONARY DYSPLASIA: SYSTEMATIC REVIEW AND META-ANALYSIS OF PRECLINICAL STUDIES.

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Introduction: Preclinical evidence suggests that mesenchymal stromal cells (MSC) improve neonatal lung structure, function and inflammation in experimental models of Bronchopulmonary dysplasia (BPD). **Objective:** To date, there has been no systematic review and meta-analysis on the therapeutic potential of MSC in experimental BPD. **Methods:** We searched MEDLINE, Embase, Pubmed, Web of Science and conference proceedings for controlled comparative studies of preclinical neonatal animal models that received MSCs or cell free MSC-derived conditioned media. Study selection was according to PRISMA guidelines, data analysis by random effects models and 'Risk of bias' by using modified Cochrane Risk of Bias tool for animal studies. **Results:** Out of 990 citations, 26 met inclusion criteria. All used neonatal rodents exposed to hyperoxia to model BPD. Eighteen studies reported on the primary outcome, lung alveolarization. MSCs had a significantly large treatment effect on alveolarization [Standardized mean difference (SMD) of -1.330, 95% Confidence interval (CI) (-1.724, -0.94) (I2 69%)], irrespective of timing of treatment and assessment, source, dose or route of administration. MSCs also had a significantly large effect on lung inflammation, pulmonary hypertension [SMD -1.18, 95% CI (-2.09, -0.27) (I2 82%)], lung fibrosis [SMD -2.54, 95% CI (-3.95, -1.13)(I2 80%)], lung angiogenesis [SMD -1.53, 95% CI (-1.94, -1.16)(I2 46%)], lung apoptosis [SMD -6.86, 95% CI (-11.06, -2.67) (I2 93%)], and oxidative stress [SMD -5.82, 95% CI (-7.44, -4.2) (I2 0%)] and survival [Odd Ratio 0.88, 95% CI (-0.33, 2.37), $P<0.001$) (I2 76%)] Similarly, MSC-derived conditioned media significantly improved alveolarization [SMD of -2.07, 95% CI (-2.74, -1.33) (I2 57%)], lung angiogenesis [SMD -3.17, 95% CI (-4.72, -1.62)(I2 83%)] and pulmonary artery remodelling [SMD -2.16, 95% CI (-3.98, -0.33) (I2 86.75%)]. None of the studies met all the criteria for low risk of bias across 11 domains. In general, we found high heterogeneity and incomplete reporting in the primary studies with potential publication bias for our primary outcome. **Conclusion:** MSC therapy in preclinical hyperoxic models of BPD in rodents significantly improved lung injury. There is a need to explore this effect in larger animal models/other species. Overall, we noted incomplete reporting in the primary studies suggesting a need to implement reporting standards such as the ARRIVE guidelines.

TO 34

PROTECTIVE EFFECT OF HUMAN UMBILICAL CORD MESENCHYMAL STROMAL CELL-DERIVED EXOSOMES ON MULTIFACTORIAL LUNG INJURY IN NEONATAL MICE

Lannae Strueby[1], Megan O'Reilly[2], Marius Moebius[2], Farah Eaton[2], Moses Fung[2], Colin Suen[3], Jennifer Collins[3], Dylan Burger[3], Bernard Thébaud[3,4]
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Introduction: Bronchopulmonary dysplasia (BPD) is a frequent complication of prematurity, with a multifactorial pathogenesis. Inflammation, supplemental oxygen, and mechanical ventilation are key contributors to the development of BPD. BPD is associated with long-term health consequences including cerebral palsy, cognitive delay, and pulmonary hypertension. Mesenchymal stromal cell (MSC)-based therapies represent a promising approach to treating BPD. MSCs prevent oxygen-induced lung injury in rodent models of BPD via paracrine effects. The paracrine effect of human umbilical cord-derived MSCs on neonatal ventilation-induced lung injury is unexplored. **Objective:** To determine if human umbilical cord MSC-derived exosomes and conditioned media (CDM) attenuate lung damage in a neonatal mouse model of BPD combining inflammation, ventilation-induced lung injury, and supplemental oxygen. **Methods:** Neonatal mice (C57Bl/6) were exposed to inflammation, supplement oxygen and mechanical ventilation to create a clinically more relevant mouse model of BPD. Mice were ventilated at postnatal day 9-10 for 8 hours with a tidal volume of 10µl/g, 180 breaths/minute and 40% oxygen. Inflammation was induced by intra-peritoneal administration of lipopolysaccharide (LPS) 48 hours prior to ventilation. Age matched unventilated mice that did not receive LPS were controls. Treatment groups received intra-tracheal MSC-CDM (3µl/g) or MSC exosomes (0.005mcg/g) immediately preceding ventilation. **Results:** Ventilated mice that received LPS exhibited alveolar simplification and reduced vascular density compared to controls, as demonstrated by a greater mean linear intercept (MLI), and reduced number of vessels/high power field ($p<0.05$). Treatment with MSC-CDM significantly attenuated structural lung injury and improved vascular density compared to untreated, ventilated mice ($p<0.05$). Neonatal mice treated with MSC exosomes also exhibited significant attenuation of structural lung injury and improved vascular density, as demonstrated by a reduced MLI and greater number of vessels/high power field ($p<0.05$). **Conclusion:** MSC-based therapies, including CDM and exosomes, attenuate alveolar simplification and improve vascular density in a multifactorial neonatal mouse model of BPD. Exploiting the beneficial paracrine effects of MSCs may aid in the development of new therapies for the prevention/treatment of BPD. ACKNOWLEDGMENTS: Sandra Schmirler Foundation, Women and Children's Health Research Institute, CIHR, Stem Cell Network

TO 35

ENDOTHELIAL PROGENITOR CELL-DERIVED EXOSOMES FOR NEONATAL PULMONARY HYPERTENSION

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Introduction: Pulmonary hypertension (PH) is an increasingly recognized complication that doubles the risk of death in severe neonatal lung diseases such as Congenital Diaphragmatic Hernia (CDH) and Bronchopulmonary Dysplasia (BPD). CDH and BPD are characterised by lung vascular hypoplasia. Evidence suggests that angiogenic factors promote alveolar growth and regeneration. Accordingly, we showed that endothelial colony forming cells (ECFCs), a subset of vascular progenitor cells with self-renewal and de novo angiogenic potential, exist in the developing lung, are perturbed in experimental lung injury. Furthermore, exogenous human umbilical cord blood-ECFCs promote lung growth and attenuate PH in nude rats with Monocrotaline (MCT) induced PH through a paracrine effect. Increasing evidence suggest that extracellular vesicles, including exosomes, mediate cellular communication of stem cells. **Objective:** ECFCs mediate their therapeutic benefit through the release of exosomes. **Methods:** In the experimental group Sprague-Dawley (SD) rat pups were injected with MCT on postnatal day 6 (P6) to induce PH. The treatment group received 10 million human umbilical cord blood-derived ECFCs/kg or an equivalent dose of exosomes (4.5µg exosome/animal) intravenously on P7. In the control group some animals received similar cell and exosome treatment without the MCT injection. At P21 the

animals were sacrificed and the heart and lungs were harvested and processed for various endpoints. **Results:** MCT impaired lung growth characterized by fewer and larger alveoli and caused PH characterized by right ventricular hypertrophy (RVH) and pulmonary artery remodelling with increased medial wall thickening (MWT). Exosome treatment significantly decreased alveolar enlargement (as quantified by the mean linear intercept, $P<0.0001$), while ECFC treatment did not show any significant decrease. Exosome treatment significantly decreased MWT ($P<0.001$), while ECFC treatment did not. **Conclusion:** MCT injection induced lung hypoplasia and characteristics of PH such as RVH and vascular remodelling, confirming a robust animal model. Exosomes were able to reduce lung hypoplasia and attenuate features of PH. Thus, the previously seen therapeutic potential of ECFCs may be mediated through exosomes as similar therapeutic effects were seen. Exosomes open new allogeneic ECFC-based therapeutic options for PH.

NURSING AND MIDWIFERY

TO 36 Invited Speaker

WOMEN AT-RISK FOR PTSD SYMPTOMS FOLLOWING CHILDBIRTH: A PROSPECTIVE COHORT STUDY

Nancy Feeley RN PhD
McGill University

The purpose of this prospective cohort study was to examine posttraumatic stress (PTSD) symptoms over time, and the relationship between PTSD symptoms and maternal interactive behavior in four groups of postpartum women. We followed two groups of women at-risk for PTSD (mothers of low birthweight infants and those having an emergency caesarean birth) and two groups not at-risk (vaginal birth and planned caesarean) to 26 weeks postpartum. At 5 and 8 weeks postpartum, women who had a low birthweight infant reported significantly more PTSD symptoms than all other groups. At 26 weeks, they continued to report greater symptoms than women who had a vaginal or planned caesarean birth. The emergency cesarean birth group had significantly greater symptoms compared to women having a vaginal birth without forceps or vacuum at 26 weeks. For all groups, PTSD symptoms decreased significantly from 5 to 8, and 8 to 26 weeks; and there was no difference between groups. Women with elevated PTSD symptoms at 26 weeks were significantly more intrusive in interactions with their infants.

Trainee Thematic Presentations

TO 37

THE ETHICS OF FAMILY INTEGRATED CARE IN NEONATOLOGY

Martin Reichherzer, Annie Janvier on behalf of the PAF group
("Partenariat Famille", CHU Sainte-Justine)

Introduction: The philosophy of care in the NICU has changed in the last decades: from patient-centered, to family centered to more recently, family-integrated care (FIC) where parents are increasingly involved. **Objective:** Examine the perspective of all stakeholders regarding FIC in a large tertiary NICU. **Methods:** A questionnaire, co-constructed by providers and parents, included a wide variety of FIC items. For each item, 2 questions were asked: 1. In the NICU, AT THE PRESENT TIME, can parents (item), if they wish to?"; 2. "IDEALLY, should parents be able to (item)?" Participants were providers and parents taking care of sick neonates: residents, fellows, neonatologists, nurses and other professionals. For three months, parents in the NICU for > 1month were recruited, and parents who came for follow-up > 1yr after NICU discharge **Results:** 331 participants (73% resp rate); 92 parents For many basic care items, >90% answered Family integrated care occurred in the NICU and should be standard of care: giving the bath, diaper change, kangaroo care, etc. For more medical items, >80% of physicians wished for more parental involvement, generally more than other groups, including parents, who were heterogeneous in their answers. For items related to parental presence during procedures, physicians were more likely to wish involvement than other groups, including parents. Parents were generally satisfied with their involvement, except for access to chart and written information, planning the discharge, giving oral medication and tube feeds. Those items were not always adequately identified as priorities by providers. While many nurses embraced FIC, others were resistant to change. "They are not there to be nurses, they are there to be parents", "it is my chart, not their chart", "Parents do not pay the professional orders, this is my job". Many parents report feeling guilty and being harmed by suggestions for more FIC "Every day, a nice nurse would ask me if I would come for more kangaroo in the evening. I had 2 other small children at home and an exhausted husband. So I ended up every night either crying at home missing my baby, or crying in the NICU missing my other kids. Family integrated care occurs at home too. I wish they understood […] sometimes just asking us hurts." **Conclusion:** Physicians fully embrace FIC, sometimes even more than parents. Other providers, whose daily routine is significantly affected by FIC, can be more critical. Changes need to respect the reality of each NICU, with implementation priorities identified by parents. Gradual changes and a flexible philosophy of care will ensure FIC is not perceived a "Family Imposed Care".

TO 38

VULNERABLE WOMEN REPORT HIGH LEVELS OF SATISFACTION WITH GROUP PRENATAL CARE

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Introduction: Even in countries with publicly funded healthcare systems, socially vulnerable women, including immigrants and women with lower household income, are less likely to have adequate prenatal care or to attend perinatal education classes. Centering Pregnancy (CP) is a model of group prenatal care, which combines assessment, education and support. Understanding the satisfaction with this model in vulnerable populations can help to determine if it is an appropriate model of care for this group. **Objective:** Compare the satisfaction with group prenatal care among vulnerable women compared to individual care. **Methods:** All women participating in CP at a community-based health centre in urban Alberta between January 2015 and August 2016 were eligible to participate. Women were asked a series of questions on satisfaction with their prenatal care approximately 2 weeks after their baby was born. A convenience sample of women who had recently given birth and had received individual prenatal care at a low risk maternity clinic were giving a similar questionnaire. Demographic and patient satisfaction responses were compared using chi-square, fisher's exact and t-tests. **Results:** Forty-five women accessing CP and 92 women accessing individual care agreed to participate. Women in the CP group were younger, more likely to be single and more likely to be having their first baby than women in individual care. Thirty-one percent of women in the CP group listed English as a second language, and 46% listed their household income below 33000. Most women in both groups indicated they had received sufficient information on pregnancy-related topics(>70%). Compared to individual care, women in CP were significantly more likely to report that they had received enough information on exercise during pregnancy (92% vs 66%, p = 0.002), breastfeeding (95% vs. 70%, p=0.002) and baby care (95% vs. 67%, p=0.001). Compared to individual care, women in the CP group were more likely to report that they had enough information to make decisions (100% vs. 88%, p=0.30), that they were prepared for their birth experience (95% vs. 75% p=0.020) and that their prenatal care providers were interested in how the pregnancy was affecting them (100% vs. 73%, p <0.001). All women in the CP group noted that they would recommend the program to a friend and 85% said they planned to keep in touch with someone from the group. **Conclusion:** Group prenatal care provides high levels of satisfaction among vulnerable populations. Prenatal care providers should consider group prenatal care as an option for women who may be socially vulnerable.

TO 39

PARENTAL NEEDS RATING BY PARENTS AND NURSES: ASSOCIATION WITH ILLNESS SEVERITY

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Introduction: Unmet psychosocial needs of parents with preterm infants significantly impact their ability to effectively adjust to their parenting role as well as the family and infant health outcomes. Unfortunately, parental needs are not always met by healthcare providers. Nurses in the neonatal intensive care unit (NICU) routinely provide care to parents and infants based on their perception of the importance of a need. Understanding how parents and nurses perceive and prioritize parental needs in relation to the infant's illness severity is important in identifying and developing strategic measures to equip nurses with the knowledge and skills needed to assess, recognize and meet the needs of parents. **Objective:** To explore parents' and nurses' perception of the important needs and met needs of parents with infants born before 32 weeks gestation as well as explore the association between parental needs and illness severity in the first 10 days of admission to the NICU. **Methods:** A single site, cross-sectional, descriptive-correlational study was conducted in a level III, non-surgical NICU. Prospective participants were approached by the researcher and provided information about the study. Eligible and consenting individuals were given a study package which contained a study information letter, consent form, demographic form, modified Needs Met and NICU Family Needs Inventories. **Results:** In total, 24 parents (10 fathers, 14 mothers), 14 infants and 16 nurses participated in the study. The results showed no statistically significant difference in how parents and nurses reported parental needs in terms of importance. Statistically significant differences were observed in the perception of needs that are considered met. Differences were observed between the ratings of the top ten needs that were identified by parents and nurses. No correlation between parental needs and

illness severity was detected. **Conclusion:** These results provide nurses and other healthcare providers with insight into areas of care where parents require additional support and interventions to meet their psychosocial needs. Knowing the needs of parents is an essential step to understanding how to respond to those needs. Collaborating with individual parents to identify their specific needs and tailoring interventions to support those needs is congruent with the principles of family-centered care.

TO 40

THE EFFECT OF METHOD OF DELIVERY AND PSYCHOSOCIAL FACTORS ON POSTPARTUM SEXUAL SATISFACTION.

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Introduction: Female sexual dysfunction is a common postnatal morbidity. Perineal birth trauma is hypothesized to be a major factor adversely affecting women's postnatal sexual health. Recently, attention has turned to the protective role that Cesarean section (C-section) may play in preventing perineal birth trauma. At the same time, there is growing opinion that the quality of women's postnatal sexual health is not solely related to method of delivery. **Objective:** The aim of this study was: 1) to determine whether method of delivery is a predictor of sexual satisfaction at 6 months and 12 months postpartum; 2) to develop a predictive model to understand what factors best predict sexual satisfaction at 6 months and 12 months postpartum. **Methods:** The current study undertook a secondary data analysis of The Ontario Mother and Infant Study (TOMIS) III which recruited 2560 postpartum women from across Ontario, Canada. Participants completed a self-report questionnaire in hospital and structured telephone interviews 6 weeks, 6 months and 12 months postpartum. Interview questions measured factors such as overall health, mental health, breastfeeding status, pelvic floor trauma and sexual satisfaction. A predictive model of sexual satisfaction at 6 months and 12 months postpartum was developed. Associations were assessed using linear regression analyses. **Results:** Most women were sexually satisfied at 6 months (91.7%) and 12 months (92.1%). Predictors for sexual satisfaction at 6 months and 12 months were mental health and perceived social support. At 6 months, age, primiparas, born in Canada, currently breastfeeding and being at risk of postpartum depression were predictors of lower sexual satisfaction. At 12 months postpartum, results were similar to those at 6 months with the exception of age and method of delivery. Age was no longer associated with sexual satisfaction. C-sections were found to be associated with lower sexual satisfaction at 12 months but not at 6 months. Contrary to our expectations, C-sections were found to have a negative association with postpartum sexual satisfaction. **Conclusion:** Our findings do not support the hypothesis that C-section delivery provides a protective benefit to women's sexual satisfaction. The impact of common postpartum factors on sexual satisfaction is complex. Understanding the multidimensional nature of postpartum sexual satisfaction is necessary to better counsel women on delivery method and postpartum sexual health.

DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE

TO 41 Invited Speaker

THE SPERM EPIGENOME IS IMPLICATED IN FERTILITY AND OFFSPRING DEVELOPMENT

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Generally, men are not aware that their lifestyle including diet, BMI, alcohol use, smoking, age and toxicant exposure can not only impact their fertility, but also the health of their children. Promising research in epigenomics and paternal inheritance indicates that the sperm epigenome is predictive of reproductive outcomes. Studies in humans and animal models show that a father's age, fertility status and his environment (diet, BMI, and toxicants) can lead to altered health outcomes of his offspring including increased risk of birth defects, metabolic disorders and complex diseases. More recently our research and that of others has linked environmental exposures to alterations in the sperm epigenome that were associated with developmental defects and disease offspring. Our promising preliminary studies assessing the epigenome at the chromatin level of idiopathic infertile men in comparison to fertile men has revealed unique alterations in H3K4 methylation levels specifically at genes implicated in spermatogenesis and embryo development.

Trainee Thematic Presentations

TO 42

PREDICTIVE MODELLING OF BEHAVIOR THROUGH GENE EXPRESSION

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Introduction: Prenatal exposure to excess glucocorticoids increases risk for psychiatric disease. We have demonstrated that antenatal synthetic glucocorticoids (sGC) program gene transcription in the hypothalamic paraventricular nucleus (PVN), with strongest effects in females. Understanding the relationship between gene expression and phenotype allows for predictive modelling, which has broad implications for the use of gene profiles in disease detection. Here, we hypothesized that transcriptional programming of the PVN is correlated to behavioral outcomes and can be used in predictive modelling. **Objective:** Here, we hypothesized that transcriptional programming of the PVN is correlated to behavioral outcomes and can be used in predictive modelling. **Methods:** Pregnant guinea pigs received 3 courses of betamethasone (Beta;1mg/kg) or saline (C) in late gestation. Total locomotor activity in open-field (OFA) was measured in female offspring on postnatal day 24 and brains collected at day 40. PVN was micro-punched (C;n=5, Beta;n=5);RNA extracted for RNA-seq; data analyzed using standard bioinformatics. Principal component analysis (PCA), which uses the underlying variance of a dataset to show how factors are related, was carried out on normalized expression profiles of significantly up-regulated genes, and OFA scores. Relationships were analyzed by linear regression. Multiple regression combined gene profiles to predict OFA, linear regression determined the correlation of predicted and observed OFA. **Results:** PCA showed OFA is associated with expression of Greb1l (estrogen receptor signaling), Prlr (prolactin receptor), & Trim66 (transcriptional regulator). Linear regression revealed the correlation to be significant (Greb1l: R2=0.71, p=0.002, Prlr: R2=0.51, p=0.019, Trim66: R2=0.58, p=0.01), and significant correlation between predicted and observed OFA (R2=0.80, p=0.015). **Conclusion:** This is the first evidence of a correlation between stress-activated locomotor behavior and gene expression in the PVN following prenatal sGC. Interestingly, this association focused on a subset of genes involved in regulation of sex-hormone signaling. These findings provide insight into the potential mechanisms of antenatal sGC and how these molecular events relate to behavior. Furthermore, we demonstrated that predictive modelling using gene expression accurately predicts stress-activated locomotor behavior, providing proof of principal for the use of gene expression modelling in disease prediction, detection, and prevention.

TO 43

PRENATAL IRON DEFICIENCY CAUSES FETAL KIDNEY HYPOXIA AND SEX-DEPENDENT UPREGULATION OF CYTOCHROME C OXIDASE

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Introduction: Iron deficiency (ID) is the most prevalent nutritional deficiency worldwide, and affects populations across the socioeconomic spectrum. The incidence of ID anemia in pregnant women is of chief concern, with estimated rates of 50-80% in developing countries, and 30% in western countries. Our group and others have shown that prenatal ID causes intrauterine growth restriction, to which the kidney is particularly vulnerable, although the precise mechanisms underlying the altered developmental and growth trajectories are unknown. **Objective:** Here, we sought to determine whether prenatal ID causes fetal kidney hypoxia, cell death, and mitochondrial dysfunction, and whether such outcomes are sex-specific. **Methods:** Six and 12-week old female rats (severe and moderate ID groups, respectively) were fed either a low iron (3 mg/kg diet) or iron-replete (35 mg/kg diet) diet throughout pregnancy. Dams were treated with pimonidazole on gestational day (GD)20 to assess tissue hypoxia. Pregnant dams and fetuses were euthanized on GD21, and hematological indices of iron status were assessed. TUNEL was performed on fetal kidneys to assess apoptosis, and kidney morphology was assessed in stained tissue sections. Finally, high-resolution respirometry was used to assess mitochondrial function in fetal kidney homogenates. **Results:** Maternal iron restriction resulted in 17% ($P<0.01$) and 48% reductions ($P<0.001$) in maternal hemoglobin (Hb) in the moderate (M-ID) and severe (S-ID) groups on GD21, respectively. While maternal plasma transferrin and ferritin levels were not altered in M-ID, S-ID maternal plasma ferritin decreased 75% ($P<0.01$) and plasma transferrin increased 25% ($P<0.05$). M- and S-ID resulted in 39% and 65% decreases in fetal Hb (both $P<0.001$), which was accompanied by asymmetric fetal growth restriction, an effect more pronounced in the S-ID group. Evidence of hypoxia was present in kidneys of both M- and S-ID fetuses (both $P<0.01$). Female fetal kidneys in both M- and S-ID groups exhibited upregulation of cytochrome c oxidase activity versus controls (both $P<0.05$), whereas males did not. Interestingly, S-ID male kidneys exhibited increased apoptosis compared to controls ($P=0.01$), whereas females did not ($P=0.86$). No differences in glomerular size or density were observed in male or female S-ID fetuses on GD21. **Conclusion:** Both moderate and severe ID cause hypoxia and sex dependent upregulation of cytochrome c oxidase in fetal kidneys. Interestingly, fetal kidneys of ID females which upregulate cytochrome c oxidase do not become apoptotic like their male counterparts, which may provide insight into the sex-specific programming of hypertension and renal dysfunction by prenatal ID.

TO 44

MATERNAL NUTRIENT RESTRICTION (MNR) IN GUINEA PIGS LEADS TO FETAL GROWTH RESTRICTED (FGR) OFFSPRING WITH DIFFERENTIAL RATES OF ORGAN CATCH-UP GROWTH

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Introduction: FGR and early post-natal catch-up growth have been linked to later life adverse health outcomes, but there has been little study of organ specific catch-up growth. **Objective:** To determine if moderate MNR in guinea pigs leading to asymmetric FGR results in neonatal catch-up growth and the extent to which this is organ-specific with implications for later life disease risk. **Methods:** Guinea pig sows were fed ad libitum (Control) or 70% of the control diet pre-pregnancy increased to 90% at mid-pregnancy (MNR), with animals delivering near or at term. Control newborns >95g (appropriate for gestational age or AGA, N=18) and MNR newborns <85g (FGR, N=18) were followed until necropsy at ~25 days post-natal age. Body and organ fractional growth rates (FRs) (the weight change per day as a percent of the weight at birth) were calculated from the body and organ weights at neonatal necropsy along with their birth weights and estimated organ weights at birth using organ/body weight percentages for similar fetal groups necropsied near term. Results are presented as group means±SEM. **Results:** While FGR-MNR newborn weights were decreased 35% at 71±2g vs the AGA-Control newborns at 110±2g ($p<.001$), at neonatal necropsy FGR-MNR weights were only decreased

16% at 259±10g vs the AGA-Controls at 309±7g (p<.001) and indicating catch-up growth. Whole body FRs were increased 36% in the FGR-MNR neonates at 9.8±0.4%/day vs the AGA-Controls at 7.2±0.2%/day (p<.001) as a further indication of this catch-up growth. Brain AGA-Control FRs were much lower at ~0.47%/day consistent with guinea pigs as prenatal brain developers, but these still increased ~30% in the FGR-MNRs indicating catch-up growth. Heart AGA-Control FRs were comparable to whole body values at ~7.7%/day and indicating similar growth trajectories, but were decreased ~6% in the FGR-MNRs indicating no catch-up growth and an uncoupling of heart growth from body growth. While liver AGA-Control FRs were slightly lower than whole body values at ~ 6.2%/day, these were increased ~ 70% in the FGR-MNRs indicating marked catch-up growth. **Conclusion:** Moderate MNR in guinea pigs results in FGR offspring with neonatal catch-up growth as seen with other FGR animal models and in humans. However, there are different rates of organ catch-up growth which will involve developmental timing and organ specific signalling activity with implications for later life disease in these organ systems.

TO 45

PRENATAL BISPHENOL A EXPOSURE IS ASSOCIATED WITH SEXUALLY DIMORPHIC CHANGES IN HYPOTHALAMIC-PITUITARY-ADRENAL AXIS FUNCTION IN INFANTS.

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Introduction: Animal models show that prenatal bisphenol A (BPA) exposure leads to sexually dimorphic disruption of the neuroendocrine system in offspring, including the hypothalamic-pituitary-adrenal (HPA) neuroendocrine system, but human data are lacking. In humans, prenatal BPA exposure is associated with sex-specific behavioural problems in children, and HPA axis dysregulation may be a biological mechanism. **Objective:** We examined sex differences in associations between prenatal maternal urinary BPA concentration and HPA axis function in 3 month old infants. **Methods:** Mother-infant pairs (n = 132) were part of the Alberta Pregnancy Outcomes and Nutrition study, a longitudinal birth cohort recruited (2010–2012) during pregnancy. Maternal spot urine samples collected during the 2nd trimester were analyzed for total BPA and creatinine. Infant HPA axis function was assessed via cortisol from saliva samples collected prior to (baseline) and after (reactivity) a blood draw. Linear growth curve models were used to characterize changes in infant cortisol as a function of prenatal BPA exposure. **Results:** Higher maternal BPA was associated with increased baseline cortisol among female infants (β = 0.13 log µg/dL; 95% CI: 0.01, 0.26), but decreased baseline cortisol among male infants (β = -0.22 log µg/dL; 95% CI: -0.39, -0.05). In contrast, higher BPA was associated with increased cortisol reactivity in male infants (β = .31 log µg/dL; 95% CI: 0.05, 0.57) but decreased cortisol reactivity in female infants (β = -0.16 log µg/dL; 95% CI: -0.36, 0.04). Models adjusting for creatinine yielded similar results. **Conclusion:** Prenatal BPA exposure is associated with sex-specific changes in infant HPA axis function. The biological plausibility of these findings is supported by their consistency with evidence in rodent models. Furthermore, these data support the hypotheses that sexually dimorphic changes in children's behaviour following prenatal BPA exposure are mediated by sexually dimorphic changes in HPA axis function.

MATERNAL FETAL MEDICINE II: FETAL MEDICINE

TO 46 Invited Speaker

FETAL CIRCULATORY PHYSIOLOGY AND BRAIN DEVELOPMENT IN CHD AND IUGR

Mike Seed
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Intrauterine growth restriction (IUGR) has been linked to adverse neurodevelopmental outcomes and animal models of chronic IUGR reveal delayed myelination and reduced synaptogenesis in fetuses exposed to chronic hypoxemia. Similarly, congenital heart disease (CHD) is associated with poor neurodevelopmental outcomes and although postnatal factors such as hemodynamic instability and cardiac surgery likely play an important role, recent evidence indicates that the abnormal brain development typical of CHD has its origins in the prenatal period. In order to investigate the hypothesis that IUGR and CHD are associated with impaired in utero cerebral oxygen delivery as a potential driver of fetal brain dysmaturation, we developed MRI techniques for measuring the oxygen content and blood flow in fetal vessels. Using metric optimized gating, we have been able to achieve high resolution cardiovascular imaging despite the absence of the usual electrocardiographic trigger. Magnetic resonance relaxometry has provided the means for measuring the oxygen content (oxygen saturation and hematocrit) of fetal blood. Our approach has enabled novel measures of placental function (fetal oxygen delivery) and fetal metabolism (oxygen consumption). We combined this approach with quantitative MRI measures of brain maturation including diffusion tensor imaging, brain volumetry and magnetic resonance spectroscopy. Despite "brain-sparing" circulatory adaptations to fetal hypoxia, we found reductions in cerebral oxygen delivery associated with impaired brain growth and development and reduced cerebral metabolism in both IUGR and CHD fetuses, which correlated with evidence of early neurodevelopmental delay. Future directions for our group will include longer term follow-up of these patients and attempts to assess the relative importance of postnatal influences on brain development and genetic causes of neurodevelopmental delay.

Trainee Thematic Presentations

TO 47

MIDTRIMESTER INTRA-AMNIOTIC INFLAMMATION AND DEVELOPMENT OF ABNORMAL GROSS MOTOR SKILLS IN INFANTS

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Introduction: "Silent" or "subclinical" intra-amniotic inflammation (IAI) at midtrimester amniocentesis is associated with microbial invasion of the amniotic cavity (MIAC), spontaneous preterm birth (sPTB), with combination of both (PTB & MIAC) being a major risk factor for neurodevelopmental disorder. However, in most cases of midtrimester IAI, women deliver at term without evidences of MIAC, and this raises the question about the significance of subclinical IAI not associated with preterm delivery. **Objective:** To determine if midtrimester IAI in asymptomatic women is a risk factor for abnormal neurodevelopment of the children. **Methods:** This was a prospective study of asymptomatic women undergoing midtrimester amniocentesis for clinical indications. Amniotic fluid samples were tested for IL-6 and MMP-8 concentrations that were reported as multiple of medians (MoM) after log transformation and adjustment for

gestational age. Infant neurodevelopment was evaluated at 18 months for five development areas (communication, gross motor skills, fine motor skills, problem solving, personal-social skills) using the Ages and Stages Questionnaire (ASQ) 2nd edition. Non-parametric statistics, ROC curves, and multivariable regression analyses were used. **Results:** Among 709 infants, those with abnormal gross motor skills at 18 months had higher amniotic fluid concentrations of MMP-8 ($p<0.05$) and IL-6 ($p=0.05$) than those with normal motor skills. Values of logMMP-8 >1.09 MoM (RR: 2.33; 95%CI: 1.24 - 4.36) and logIL-6 >1.10 MoM (RR: 2.66; 95%CI: 1.43 - 4.95) were associated with a greater than two-fold risk of abnormal infant gross motor skills. This important association remained significant after adjustment for birthweight, gestational age at delivery and infant's corrected age at ASQ. Additionally, after exclusion of all births < 37 weeks, similar results were obtained (high IL-6: RR: 2.08; 95%CI: 1.06 - 4.12; $p=0.03$). Moreover, we observed a dose-response effect: 1) severe intra-amniotic inflammation (logIL-6 target="1"> 1.125 MoM) was associated with an increased risk of severe adverse neurological outcome (failure of at least four of all five ASQ categories, see figure) (aRR: 4.57; 95%CI: 1.01– 20.79); and 2) very severe intra-amniotic inflammation (logIL-6>1.50 MoM) was associated with failure of all five ASQ categories ($p<0.05$). **Conclusion:** Midtrimester subclinical intra-amniotic inflammation is a major risk factor for neurodevelopmental disorders, particularly gross motor skills development, even in infants born at term. These observations have major implications for the understanding of neurodevelopmental disorders and the effect of "silent" chronic intra-amniotic inflammation on infant outcome. Future research should focus on the origin and prevention of early intra-amniotic inflammation.

TO 48

3D WATER-FAT MRI OF FETAL FAT DEVELOPMENT

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Introduction: Fetal adipose tissue volume and its development are reflective of the energy balance within the fetus, and may be altered due to maternal health (e.g. gestational diabetes) or pregnancy complications (e.g. fetal growth restriction or macrosomia). Imaging techniques such as ultrasound (US) and magnetic resonance imaging (MRI) may provide a suitable method to study the fetal adipose tissue in utero. Previous MRI and US studies have investigated fetal adipose tissue volumes, but have failed to measure the lipid content of the adipocytes. It may be possible to detect the development of fetal adipose tissue with 3D water-fat MRI, a technique sensitive to the lipid content of tissues. Pre-adipocytes are primarily water based cells with low lipid content that develop into mature adipocytes filled with large lipid vesicles, which have much higher lipid content. 3D water-fat MRI provides a fat fraction (FF) that quantifies the proportion of MRI signal received from lipid. **Objective:** To apply a novel technique (3D water-fat MRI) to assess fetal fat development throughout gestation **Methods:** Women with singleton pregnancies and gestational ages between 28 and 38 weeks underwent a fetal MRI in a wide-bore 1.5T MRI (GE Optima 450w). Fat-only and water-only images were acquired axial to the fetal abdomen and used to generate FF images. The fetal subcutaneous adipose tissue (FSAT) was segmented from where the arm meets the thorax to where the leg meets the abdomen. The lipid volume (LV) and mean FF was measured within the segmented volume for each fetus. Fetal LV and FF were correlated to maternal pre-pregnancy BMI, MRI EFW percentile and gestational age. **Results:** 23 women were recruited to the study (BMI 19.2–52.5 kg/m2). 2 FF images sets were corrupted by motion and could not be analyzed. No correlation was found between maternal pre-pregnancy BMI and FF or LV ($R2=0.03$ and $R2=0.05$ respectively), or between EFW percentile and FF or LV ($R2=0.07$ and $R2=0.1$ respectively). A significant positive correlation was found between gestational age and FF ($R2=0.42$, $P=0.002$) and between gestational age and LV ($R2=0.40$, $P=0.002$), indicating that FSAT is depositing lipid within adipocytes in this gestational age window. **Conclusion:** 3D water-fat MRI can be used to non-invasively study the development of fetal adipose tissue in mid- to late gestation. The gestational age window studied is an important time for adipose tissue development, during which adipocytes are rapidly filling with lipid, as shown by a strong correlation between gestational age and FF. The FF of mature adult white adipose tissue is 90%, while the average FF reached at gestational ages 36-37 weeks was 26.8%. Thus, it is likely that within the gestational age window examined, the FSAT has not reached full maturity, representing a crucial developmental stage.

TO 49

ANTENATAL MANAGEMENT OF FETAL/NEONATAL ALLOIMMUNE THROMBOCYTOPENIA: SHOULD WE COMPLETELY

ABANDON INVASIVE PROCEDURES?

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Introduction: Fetal/neonatal alloimmune thrombocytopenia (F/NAIT) is the most common causes of severe thrombocytopenia in newborns with a 20% risk of severe intracranial hemorrhage (ICH). No consensus regarding antenatal treatment strategies (maternal intravenous immunoglobulin therapy (IVIG) and in utero platelet transfusions (PLT IUT)) to prevent recurrence in subsequent pregnancies is available. A noninvasive approach in lieu of fetal invasive procedures to avoid FBS-related adverse outcomes was recently proposed. **Objective:** To retrospectively review the management and neonatal outcomes of pregnancies with a previous F/NAIT analyzing the risk due to fetal invasive procedures, the characteristics of responders (R) vs non-responders (N-R) to medical treatment and the rate of CS in relation to the expected rate of CS if invasive techniques were abandoned. **Methods:** Pregnancies with a previous F/NAIT followed in the FMU of MSH (1993-2016) were included. Demographic data, maternal alloantibody type, clinical management of the current pregnancy, mode of delivery, neonatal outcome and index case characteristics were collected. **Results:** 47 pregnancies were included. The FBS related adverse outcomes was 1.6% (2/119). 43 patients were medically treated and divided in R(n=21) and N-R (n=22): No differences were found in maternal age, parity, blood group type, category of risk in the two groups. HPA1a Ab was detected in all NR and at a significantly lower rate in R. The index case was significantly more thrombocytopenic at birth in NR compared with R (median PLT x109/L R=20; IQR 8-43 vs. N-R=9.5; IQR 5-17.5, $p<0.01$). No significant differences were found in the commencement of the treatment, rate of women treated with IVIG, dosage, duration of treatment and gestational age at the first FBS. PLT at birth were significantly lower in N-R compared with R (Median PLT x 109/L: R= 226; IQR 135-250 vs N-R = 103; IQR 69-120, $p<0.001$). Post-natal treatment was performed at a significantly higher rate in N-R (42% vs 9% $p<0.02$) as compared to R. No cases of ICH were diagnosed in utero or in the neonatal period. The CS rate was 32.5% (24% for R and 42% for N-R). The expected CS rate in case of no fetal blood sampling would have been 47.5% (43% in R and 53% in N-R). **Conclusion:** Medical treatment with IVIG is associated with a different response in a group of patients homogeneously selected and treated. The lack of predictors in determining a priori the non responders urges caution in completely abandoning fetal invasive procedures especially in third level centers given the low FBS related adverse outcomes and with the view towards limiting unnecessary caesarean deliveries.

TO 50

PLACENTAL MICRORNA EXPRESSION IN PREGNANCIES COMPLICATED BY INTRAUTERINE GROWTH RESTRICTION AND PRE-ECLAMPSIA

Zain Awamleh[1], Victor Han[1].
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Introduction: Placenta is the major regulator of the intrauterine environment and transports O2 and nutrients from the mother to the fetus and CO2 and waste from the fetus to the mother. Normal development of the placenta is critical to ensure proper fetal growth in utero and abnormalities affect both maternal and fetal health. Preeclampsia (PE) and intrauterine growth restriction (IUGR) are two of the most common pregnancy related complications resulting from abnormal placental development. Placental microRNAs (miRNAs) have recently been investigated as potential biomarkers for these complications, but they are also believed to play a role in placental growth and development by influencing gene expression. In depth validation and characterization of placental miRNAs is therefore required to fully understand their role in placental development and function. **Objective:** To determine miRNA and mRNA expression in human placenta obtained from patients with intrauterine growth restriction and/or pre-eclampsia, and to compare with those from gestational age matched controls. **Methods:** RNA was isolated from placental tissues obtained from patients diagnosed with pre-eclampsia and/or intrauterine growth restriction in early gestation. A full clinical profile for each patient was obtained. miRNA and mRNA sequencing was completed at the Genome Quebec Innovation Centre, using the Illumina Hiseq2000. Stringent differential expression analysis was completed for both miRNA and mRNA expression data, in each of the patient groups (PE only, IUGR only, PE+IUGR). Real-time PCR was used for validation of the differentially expressed miRNAs. Finally, correlation analysis was used to identify miRNAs of interest that inversely

correlate with mRNA expression. **Results:** A total of 20 placental samples were collected for each patient group. miRNA expression analysis revealed disease specific miRNAs, as well as miRNAs that are common to all three patient groups. A total of six miRNAs were validated using real-time PCR in all diseased groups, as well as an additional three miRNAs that are specific to patients with pre-eclampsia. Differential gene expression analysis also revealed a number of genes that are aberrantly expressed in all diseased groups, while some are disease specific. To identify which of these genes are influenced by placental miRNAs, correlation analysis was used, revealing significant inverse correlations between miRNA and mRNA expression. **Conclusion:** This study identifies and successfully validates a number of miRNAs associated with PE and/or IUGR and the potential impact of those miRNAs on mRNA expression. Validation of miRNA-mRNA interactions will reveal the potential role of miRNAs in placental development, function or disease.

NEONATALOGY I: RESPIRATION/VENTILATION/CARDIOLOGY

TO 51 Invited Speaker

NOVEL PULMONARY IMAGING BIOMARKERS OF CHRONIC LUNG DISEASE

Grace Parraga PhD
Professor & Graduate Chair, Department of Medical Biophysics
Scientist & Faculty Scholar, Robarts Research Institute
Western University

Recent imaging research and engineering developments have accelerated the acquisition of high-resolution pulmonary images using novel methods such as hyperpolarized 3He and 129Xe functional MRI and ultrashort echo time anatomical MRI. I summarize recent approaches to derive measurements of lung structure and function in lung disease and suggest a pathway forward towards clinical translation and utility.
Learning objectives:

1. Describe limitations of current tools to diagnose and monitor lung disease
2. Summarize novel functional imaging tools and their use in asthma, CF and BPD
3. Provide evidence of how these new tools may be used to provide better patient outcomes.

Trainee Thematic Presentations

TO 52

ALVEOLAR EPITHELIAL CELL THERAPY RESCUES THE LUNG PHENOTYPE IN A MOUSE MODEL OF SURFACTANT PROTEIN C DEFICIENCY

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Introduction: Pulmonary surfactant protein C (SP-C) is synthesized by Alveolar epithelial cells type II (AEC-II) as a precursor and is processed to form the functional secreted protein. Mutations in the SP-C gene (Sftpc) are inherited as an autosomal dominant or sporadic trait and lead to a misfolded protein and subsequent cellular stress in AEC-II. The application of fresh AEC-II therapy and human induced pluripotent stem cell (hiPSCs)-derived AEC-II to rescue a lung genetic disease has never been investigated. **Objective:** In this study, we hypothesized that naïve and hiPSC-derived AEC-II therapy can rescue the phenotypic and pathological consequences of Sftpc gene knock-out in SP-C deficient mice (sftpc-/-). **Methods:** Wild type AEC-II for transplantation were isolated from wild type 4-6 weeks old 129J mice. We also established an efficient method to differentiate hiPSCs into a homogenous population of AEC-II. Both cell types were labelled with a membrane-specific fluorescent dye and were intratracheally administered as single cells to one-year-old sftpc-/- mice. Cyclosporine A (CSA) was administered to mice that received human cells to prevent immune rejection. Mice were treated with two doses of AEC-II during a period of 14 days and 2.5 months. **Results:** Both naïve and hiPSC-derived AEC-II engrafted into the distal lung, improved lung function and structure in sftpc-/- mice. AEC-II therapy increased the exercise capacity and improved lung mechanical properties. Our results showed that both AEC-II were retained in the distal lung, engrafted into alveolar structure and attenuated lung structural injuries for 2.5 months. **Conclusion:** AEC-II therapy exerts short-term and mid-term therapeutic benefit in this experimental model and may offer new therapeutic options for lung genetic disorders that affect alveolar epithelial cells.

TO 53

WITHDRAWN

TO 54

INTERMITTENT HYPOXIA DURING RECOVERY FROM NEONATAL HYPEROXIC LUNG INJURY CAUSES LONG-TERM IMPAIRMENT OF ALVEOLAR DEVELOPMENT: A NEW RAT MODEL OF BRONCHOPULMONARY DYSPLASIA (BPD)

Anastasiya Mankouski[1,2], Crystal Kantores[2], Mathew J Wong[2,4], Julijana Ivanovska[2], Amish Jain[3,4], Richard L Auten[1], Robert P Jankov[2,3,4]

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Introduction: BPD is a chronic lung injury characterized by impaired alveologenesis that may persist into adulthood. Rat models of BPD using varying degrees of hyperoxia to produce injury either cause early mortality or spontaneously recover following removal of the inciting stimulus, thus limiting clinical relevance. **Objective:** We sought to refine an established rat model induced by exposure to 60% O2 from birth by following hyperoxia with intermittent hypoxia (IH). **Methods:** Rats exposed from birth to air or 60% O2 until postnatal day (PND) 14 were recovered in air with or without IH (FiO2 = 0.10 for 10 min every 6 hours) until PND 28. **Results:** Animals exposed to 60% O2 and recovered in air had no evidence of abnormal lung morphology on PND 28 or PND 80 (young adulthood). In contrast, 60% O2-exposed animals recovered in IH had persistently increased mean chord length, more dysmorphic septal crests and fewer peripheral arteries. Recovery in IH also increased pulmonary vascular resistance, Fulton index and arterial medial wall thickness. IH-mediated abnormalities in lung structure (but not pulmonary hypertension) persisted when re-examined on PND 80, accompanied by increased pulmonary vascular reactivity and decreased exercise tolerance. Increased mean chord length secondary to IH was prevented by treatment with a peroxynitrite decomposition catalyst, FeTPPS (30 mg/kg/d, PNDs 14-28). Treatment with FeTPPS also led to fewer inflammatory cells (neutrophils and macrophages) in the IH-exposed lung. **Conclusion:** IH during recovery from hyperoxia-induced injury prevented recovery of alveologenesis and led to changes in lung and pulmonary vascular function that lasted into adulthood, thus more closely mimicking contemporary BPD.

TO 55

IMPACT OF PARENTERAL LIPID EMULSION SMOFLIPID AND INTRALIPID ON HEPATIC REDOX POTENTIAL OF GLUTATHIONE AND DNA METHYLATION IN NEWBORN GUINEA PIG.

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Introduction: Infants born <30 weeks of gestation suffer from major oxidative stress causes by their treatments: oxygen supplement generating in vivo H2O2, and divers peroxides contaminating their parenteral nutrition (PN). This oxidative stress in early life is suspected to be an important inducer of several health complications observed in adults; epigenetic modifications are suspected. High FiO2, PN, as well as peroxides, induce an oxidation of the redox potential of glutathione, a main regulator of the activity of methylation. Indeed, peroxides as well as the oxidized redox potential reduce the activity of the methionine adenosyltransferase, leading to a lower generation of S-adenosylmethionine (SAM), the substrate for DNA methylation. The recent proposition to change the lipid emulsion of PN from Intralipid (low n-3 fatty acids) to SMOFLipid (high n-3 fatty acids) is questionable. Indeed, n-3 fatty acids are more prone to oxidation and to peroxides generation. Compared to Intralipid (IL), SMOFLipid (SMOF) is suspected to induce greater oxidative stress and lower DNA methylation. **Objective:** To compare the oxidative property of SMOF and IL by measuring redox potential of glutathione, and to correlate the DNA methylation values with the redox values. **Methods:** At three day of life, guinea pigs received PN (dextrose, amino acids, vitamins, electrolytes) compounded with SMOF (n=15) or IL (n=16) through a jugular vein catheter. Four animals without manipulation served as control. After 4 days of infusion, redox potential of glutathione (mV, by the Nernst equation using the GSH and GSSG concentrations measured by capillary electrophoresis) and global DNA methylation (U = nmol of 5MedCyt / µg DNA; commercial kit) were determined in liver.

Statistics: ANOVA and Pearson correlation; $p<0.05$) **Results:** The mean (±sem) redox potential was higher in SMOF compared to IL (-207±1 vs. -213±2 mV, $p<0.02$), both were more oxidized than control (-224±1 mV). The level of methylated DNA was lower in SMOF compared to IL 0.17±0.02 vs. 0.32±0.05 nmol/ ug DNA, $p<0.01$). The correlation between DNA methylation and redox potential was linear ($y = a•x + b$: -0.012U•mV-1•x – 2.34U; $r2 = 0.49$, $p<0.01$); with more oxidized redox potential, the DNA methylation was lower. **Conclusion:** Our data from newborn guinea pig support the concept that oxidative stress in early life may alter the health of adult following epigenetic modification. Future studies will point out genes as well as metabolisms that are altered. In light of these results, the clinician must assess the risks versus the benefits of using SMOFLipid, rather than Intralipid, in preterm under PN.

PLACENTAL AND FETAL PHYSIOLOGY

TO 56 Invited Speaker

CAN HEPARIN PREVENT SEVERE PREECLAMPSIA?

Dr. John Kingdom, MD
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Lunenfeld Tanenbaum Research Institute
Mount Sinai Hospital
Chair, Department of Obstetrics & Gynaecology
University of Toronto

Severe early-onset pre-eclampsia (sPE) is typically associated with IUGR and abnormal Doppler studies, and causes significant maternal and perinatal ill-health. It is a very different disease from near-term pre-eclampsia (tPE), where the placenta is normally-perfused and structurally-normal, and fetal growth is normal. A major difference between these types of pre-eclampsia lie is the early maternal cardio-vascular adaption to pregnancy. In the pre-clinical phase of sPE, women have poor weight gain and low cardiac output that masks their elevated systemic vascular resistance. Low placental secretion of placenta growth factor (PlGF) may contribute to this pathophysiology. In this phase, the placenta is communicating an anti-angiogenic response to the mother, who eventually decompensates with multi-organic ischemia-reperfusion injury and severe hypertension. Low molecular weight heparin (LMWH) is a complex macromolecule, whose anti-thrombin-3 binding sites confer anticoagulant properties. LMWH appears to reduce the risk of sPE, yet not via it's anticoagulant actions. LMWH promotes the secretion of placenta growth factor (PlGF) by both placental vili and endothelial cells, effects which we have recently demonstrated in-vivo in high-risk pregnant women, 30% of whom subsequently developed sPE.* We have extended this work to separate the soluble from larger and smaller micro-particle fractions, released by the syncytiotrophoblast into maternal blood, using an explant system+. The small (40-120nm) exosome vesicle (EV) fraction (with low sFlt-1/PlGF ratio, <50) enters target endothelial cells, but seems to exert no deleterious effects (on angiogenesis, inflammatory gene induction, leukocyte activation) , even when 10x concentrated, in comparison with the soluble fraction, where the residual sFlt-1/PlGF ratio is high (>100). LMWH blocks EV entry into HUVEC from healthy placental villi; EVs derived from sPE placental villi will not enter endothelial cells, yet do enter control breast cancer cells. Presently our data support a purely endocrine role for LMWH to reduce the risk or severity of sPE via augmentation of PlGF bio-availability, in an attempt to restore normal maternal hemodynamics. Though the theory of micro-particle-mediated vascular injury is an attractive concept in pre-eclampsia research, to date our findings suggest that systemic vascular dysfunction largely resides in the soluble placental angiogenic imbalance, initiated by abnormal development of the villous compartment of the placental villi.

Trainee Thematic Presentations

TO 57

COMPARING MICORNA EXPRESSION IN PLACENTAS FROM ACTIVE VS. INACTIVE MOTHERS: AN EXPLORATORY STUDY

Denize KM[1], Holcik M[2], Harvey ALJ[1], Brett, KE[1]. Mohammad, S.[1], Adamo KB[1]
[1]University of Ottawa, [2]Children's Hospital of Eastern Ontario

Introduction: Healthy development of the placenta is essential for proper in utero growth and development. Studies show that physical activity (PA) during pregnancy can positively impact maternal-fetal health. The mechanisms behind these phenomena remain to be elucidated. Recent studies have considered differences in gene expression, including the miRNAome as potential contributors. Research to date has focused on altered miRNA expression in placenta from pregnancy-related disease states such as preeclampsia. However, no studies have examined the miRNAome in healthy placenta, exposed to different levels of PA. **Objective:** Knowing that miRNAs are involved in skeletal muscle health, and are dysregulated in diseases such as cancer, the aim of this initial study was to compare miRNA expression in placentas from active and inactive mothers during pregnancy, as defined by the Canadian Physical Activity Guidelines (>150

moderate-vigorous physical activity per week). **Methods:** This study capitalized on a global transcriptome analyses performed using placenta RNA extracted from 'Active Mom' and 'MOM trial' participants. We used the 5 most active and 5 least active women for this analysis. Global gene expression profiling was conducted using a GeneChip® exon wide examination, containing 67528 probes including 22829 non-coding genes. Differences between groups were evaluated using a 1-way ANOVA. Absolute fold change greater than 2 and a p-value less than .05 were used to identify differentially expressed genes. **Results:** In total, 49 non-coding genes were differentially expressed: 6 up-regulated and 43 down-regulated in active vs. inactive mothers. Two miRNAs were identified to be differentially expressed in mothers who were active during pregnancy. Active mothers had a 2.5 fold decrease in miR-584w and a 2.1 fold decrease in miR-644a ($p < 0.05$). **Conclusion:** Understanding how miRNA interact with mRNA to alter protein expression enables a greater understanding of how the environment can influence genetic phenotypes. Although epidemiological data has repeatedly shown the benefits of PA for maternal-fetal health, the mechanisms behind these are unknown. This study found altered miRNA expression from placentas of active vs. inactive mothers. It has been postulated that the miR-548 family and miR-644a play a role in modulating mRNA and protein expression in metabolic pathways and common cell-signalling pathways required for optimal cellular health. These findings provide support for future studies to continue to examine miRNAs role in the placenta, and how lifestyle factors such as PA can influence signalling pathways and physiological processes involved in placenta development or nutrient transport.

TO 58

MATERNAL CIRCULATING PLGF LEVELS IN RELATION TO LEPTIN AND ADIPONECTIN CONCENTRATIONS IN INFANTS BORN SMALL-FOR-GESTATIONAL-AGE

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Introduction: Maternal circulating placenta growth factor (PlGF) is a biomarker of placental function and fetal growth. Mothers with low circulating PlGF levels are more likely to deliver small-for-gestational-age (SGA) infants who are at increased risk of diabetes in adulthood. Leptin and adiponectin are important hormones in regulating insulin sensitivity. **Objective:** It is unknown whether maternal PlGF levels are associated with leptin and adiponectin concentrations in infants born SGA. The present study aimed to address this question. **Methods:** This was a nested case-control study in a prospective pregnancy cohort - the Integrated Research Network of Perinatology in Quebec (n=2366). Maternal plasma PlGF at the 3nd trimester (32-35 weeks) of gestation and cord plasma leptin and adiponectin were measured. The study included 162 SGA (birth weight <10th percentile) and 162 AGA (25th -75th percentiles) singleton infants matched for ethnicity, smoking status and gestational age. **Results:** SGA newborns had significantly lower maternal PlGF and cord plasma leptin concentrations than AGA (all $P<0.0001$) infants. Overall, maternal plasma PlGF concentrations were positively correlated to birth weight ($r=0.35$, $P<0.0001$) and cord plasma leptin ($r=0.14$, $P=0.0266$) concentrations, but not correlated with adiponectin concentrations. Interestingly, there were differential correlations between maternal PlGF and cord leptin concentrations in SGA ($r=0.20$, $P=0.0329$) and AGA ($r=-0.08$, $P=0.3456$) infants. Among SGA neonates, those with low maternal PlGF concentrations (<25th percentile) had lower cord blood leptin concentrations (median: 6128.00 vs. 8335.00 pg/ml, $P=0.0108$). **Conclusion:** Maternal PlGF may be a prenatal biomarker of fetal adipose tissue/fat content in SGA infants.

TO 59

MEASUREMENT OF PLACENTAL OXYGENATION IN A GUINEA PIG MODEL OF INTRAUTERINE GROWTH RESTRICTION

K Sinclair, L Friesen-Waldner, T Wade, C Vander Tuin, B de Vrijer, T Regnault, and C McKenzie

Introduction: Intrauterine growth restriction (IUGR) affects up to 10% of all pregnancies and is a leading cause of perinatal morbidity and mortality. IUGR resulting from placental insufficiency is often associated with fetal hypoxia. Oxygen supply through the placenta is the major driver for fetal growth and the ability to measure placental oxygenation

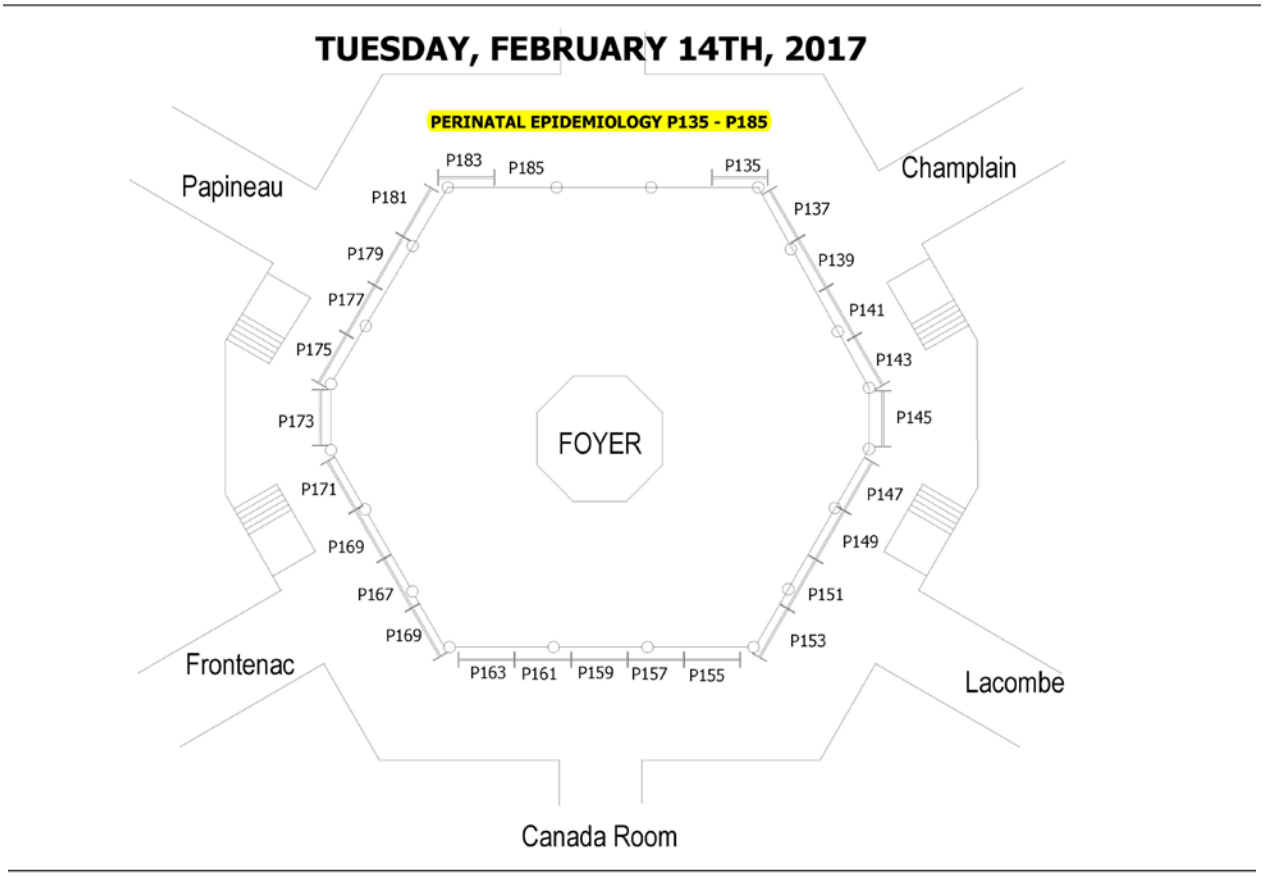
can give us valuable information regarding the status of fetal development. MRI is emerging as a valuable technique to study oxygenation of tissue and blood vessels in vivo. In MRI experiments, the presence of deoxyhemoglobin causes more rapid signal decay than oxyhemoglobin. Taking advantage of this fact, oxygenation status can be probed by examining the rate of signal decay, governed by the decay constant T2*. **Objective:** To use MRI to examine the placental oxygenation status in a guinea pig model of IUGR, in which an increased brain to liver volume ratio (BLVR) indicates redistribution of fetal blood flow in response to fetal hypoxia. **Methods:** To induce IUGR, vessel occluders were placed bilaterally on the uterine arteries at 35 days gestation (term ~68 days, N = 4, 14 fetuses). Sham surgeries were performed to produce a control group (N = 4, 18 fetuses). At ~60 days gestational age, sows were anaesthetized and scanned at 3T. A T2* mapping sequence was performed with the maternal guinea pig breathing air with an oxygen concentration of 20%. The animal was then switched to 100% oxygen and the imaging was repeated after 10 minutes. T2* maps were calculated by fitting the multi-echo images to an exponential decay function. ROIs were drawn on the T2* maps to obtain values for each placenta. T2* values were also calculated in the maternal kidneys to ensure validity of the technique. **Results:** Fetuses in the surgical group were defined as IUGR if they had a BLVR >0.7. Only fetuses in mothers that responded to the inhaled oxygen concentration change based on a T2* increase in the maternal kidney were analyzed. Thus our study population consisted of 7 IUGR fetuses and 11 control fetuses. In the placentae, there was a difference in T2* change from 20% to 100% inhaled oxygen observed between control and IUGR fetuses ($P < .05$). Further, a negative correlation was observed between T2* change and BLVR ($r = -.53$). **Conclusion:** These data suggest that fetoplacental oxygen demand in control pregnancies is sensitive to, and increases with maternal oxygenation, a response that has been curtailed in the situation of IUGR, likely due to decreased oxygen transfer capacity. Further we have demonstrated the utility of using MRI to detect changes in maternal and placental oxygenation in response to increased oxygen availability through measurement of the decay constant T2*.

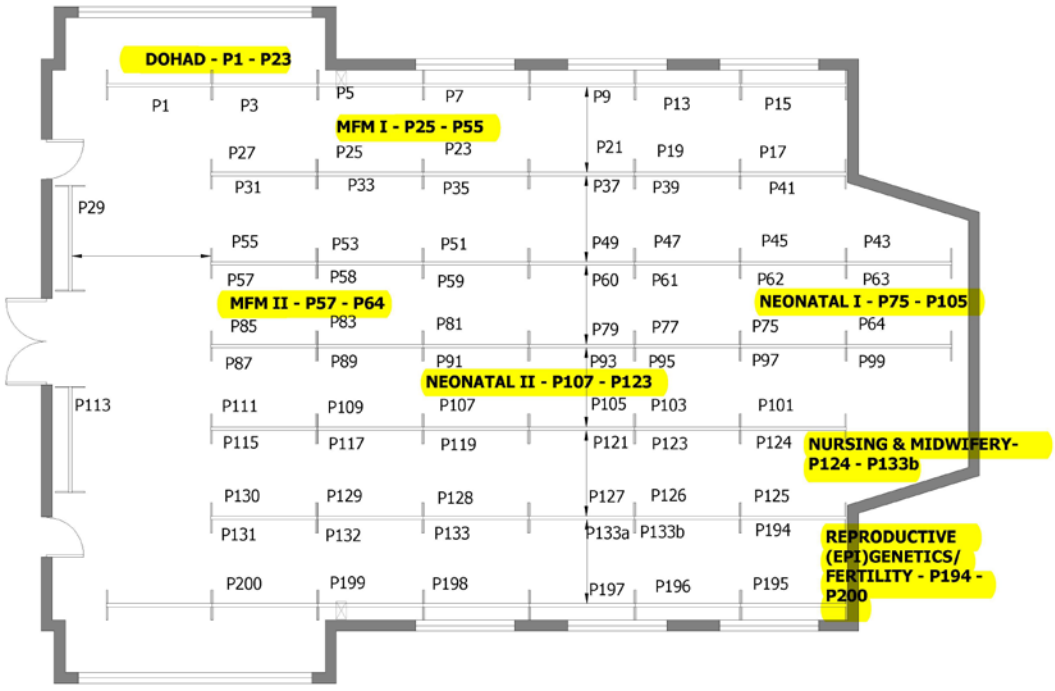
TO 60

WITHDRAWN

Poster Display Maps

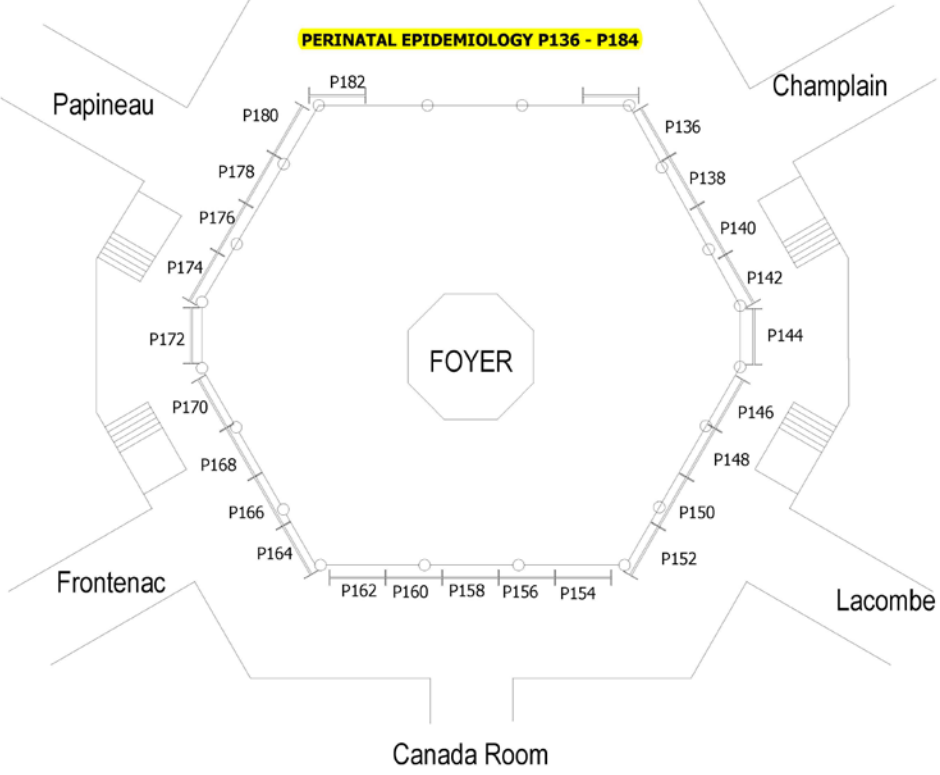
Tuesday

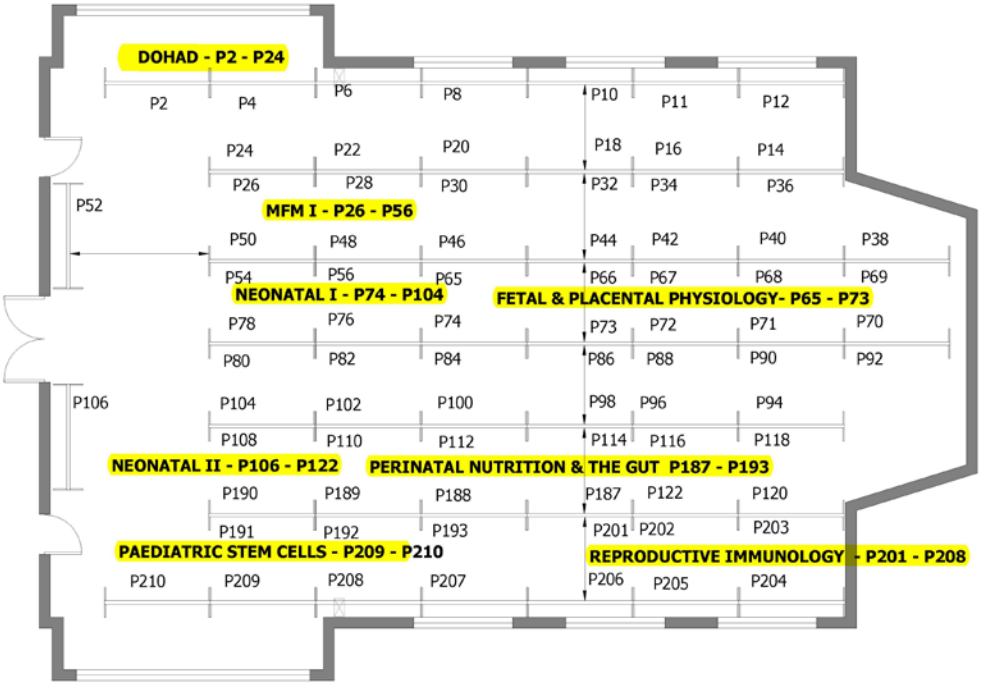




POSTER ALLOCATION FOR TUESDAY, FEBRUARY 14TH, 2017

WEDNESDAY, FEBRUARY 15TH, 2017





POSTER ALLOCATION FOR WEDNESDAY, FEBRUARY 15TH, 2017

POSTER ABSTRACTS

THEME: Developmental Origins of Health and Disease

P1

TISSUE-SPECIFIC EXPRESSION CHANGES ASSOCIATED WITH AN ALTERED ADULT METABOLISM IN A MOUSE MODEL OF IUGR

Bethany Radford and Victor Han
Western University, London Ontario

Introduction: Intrauterine Growth Restriction is a pregnancy condition where the fetus fails to grow to its full potential. As adults, this population has an increased risk for diabetes mellitus type II. Our lab has established a mouse model of IUGR using 30% total calorie nutrient-restriction, where a proportion of male offspring develop glucose intolerance at 6 months. **Objective:** To understand metabolic alterations and associated expression changes in response to fetal nutrient restriction in liver, skeletal muscle and adipose tissue in adult males that may be associated or cause glucose intolerance. **Methods:** Pregnant females were randomly assigned to an ad libitum fed or the nutrient-restricted groups at E6.5. At birth, litters with 13 +/- 2 pups culled or fostered to obtain a litter size of 13 and placed on a standard chow or HFHS diet. Serum total cholesterol, GIP, GLP-1, ghrelin, insulin, C-peptide, glucagon, leptin, PAI-1 and resistin were measured at one and six months. At 6 months, serum triglyceride and cholesterol, and liver cholesterol were also measured. Glucose tolerance testing, pyruvate challenge, and hepatic portal vein insulin challenge were performed. Additionally, at one and six months, RNA was extracted from the left lateral and right medial lobe of the liver and quadriceps femoris for RNAseq. **Results:** At 6 months, decreased insulin signalling was observed in standard chow-fed offspring liver and adipose tissue, as well as an increased serum resistin and PAI-1. 20-30% of the nutrient-restricted offspring became glucose intolerant, and had elevated serum insulin, resistin and leptin. No changes in serum or liver total cholesterol, serum triglycerides, hepatic glucose output, random blood glucose and body mass were detected in all nutrient-restricted or intolerant offspring relative to controls. Despite the metabolic changes in the male nutrient-restricted and intolerant offspring, no genes were differentially expressed (p-value < 0.1, fold change target="1">1.3) in the liver or skeletal muscle at 6 months. **Conclusion:** Moderate changes in metabolism were detected in male nutrient-restricted offspring in the absence of differential expression in liver and skeletal muscle. Small fold changes in in many genes of a pathway may result in metabolic changes; investigation into differential expression at the pathways level may indicate expression changes in these tissues. Additionally, changes in adipose tissue may contribute to glucose tolerance, serum markers and insulin signalling alterations.

P3

ENDOTHELIUM-DEPENDENT RELAXATION IS IMPAIRED IN 12 MONTH OLD FEMALE OFFSPRING FROM AGED DAMS

Christy-Lynn M. Cooke, Alison S. Care, Jude S. Morton, Sandra T. Davidge

Introduction: The age at which women deliver their first child has been increasing over recent years. Advanced maternal age (≥35 years) is associated with increased maternal and perinatal morbidity and mortality. Although evidence suggests that the risk of adult onset cardiovascular disease is increased in children born from compromised pregnancies, little is known about the impact of advanced maternal age on developmental programming of vascular function in the offspring. We previously demonstrated that 4 month old male, but not female rats from aged dams had increased susceptibility to cardiovascular disease via impaired cardiac and vascular function. Aging may be considered a 'second-hit' on the cardiovascular system, which could uncover an abnormal phenotype in a susceptible population, such as female offspring born from dams of advanced age. **Objective:** We hypothesize that 12 month old female offspring from aged dams will have impaired vascular function compared to 12 month old offspring born from young dams. **Methods:** Aged female Sprague Dawley rats (9 months) and young controls (4 months) were mated with young males. Mesenteric artery vascular reactivity was assessed using wire myography at 12 months of age (N=4 per group). **Results:** Fetuses from aged dams had a lower body weight at gestational day 20 [young dam (YD): 3.78 ± 0.1 g vs. aged dam (AD): 3.19 ± 0.2 g; *P<0.05], but body weight was not different in female offspring at 12 months of age [YD: 469 ± 22 g vs. AD: 533 ± 35 g; not significant (NS)].Vasoconstriction to phenylephrine (PE) was not different between groups (PE pEC50: YD: 5.7 ± 0.09 vs. AD: 5.5 ± 0.02; NS). Female offspring from aged dams had reduced endothelium-dependent

(methacholine; MCh) relaxation (MCh pEC50: YD: 8.3 ± 0.25 vs. AD: 7.4 ± 0.13; *P<0.05). The effect of nitric oxide synthase inhibition (incubation with L-NAME; NOS inhibitor) was not different between groups in female offspring. However, inhibition of endothelium-derived hyperpolarisation (EDH) [incubation with apamin and TRAM-34 (A/T)] significantly affected maximal relaxation to MCh in offspring from young but not aged dams (MCh Emax: YD control: 100 ± 1.0% vs. A/T: 64.9 ± 4.2%, *P<0.05; AD control: 97 ± 2.6% vs. A/T: 70.5 ± 14%, P =0.1). **Conclusion:** Endothelium-dependent relaxation was impaired in 12 month old female offspring, which may be related to reduced EDH-dependent vasodilation in offspring from aged versus young dams. These data demonstrate that female offspring born from dams of advanced maternal age may be programmed in utero for an increased risk of cardiovascular disease as they themselves age.

P5

EXPOSURE TO GESTATIONAL AND PRE-GESTATIONAL DIABETES IMPAIRS CARDIAC RELAXATION IN ADOLESCENTS WITH TYPE 2 DIABETES

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Introduction: At least 1 in 20 Canadian children was exposed to type 2 diabetes (T2D) or gestational diabetes (GDM) in utero. **Objective:** We wanted to determine if this exposure predisposes adolescents with T2D to cardiomyopathy **Methods:** We compared echocardiograms between Indigenous adolescents with T2D stratified by maternal-reported T2D (n=46), GDM (n=23) or normoglycemia (n=50). Outcomes were cardiac diastolic and systolic function as well as markers of size. **Results:** No differences were observed for confounders such as sex (62 vs 43 vs 71% female), age (14.8±2.7 vs 14.8±2.6 vs 15.2±2.3 years), duration of diabetes (2.5, [interquartile range]: [1.5-4.4] vs 1.7 [0.7-3.8] vs 2.2 [1.1-3.7]years), adiposity (29±10 vs 31±10 vs 34±11%) or 24-hour blood pressure (45 [22-68] vs 45 [32-59] vs 37 [21-65]%), respectively. We observed impaired relaxation left ventricular (LV) (early-to-late transmitral blood velocity: 1.59 [1.38-1.84] vs 2.14 [1.65-2.35] vs 1.78 [1.43-2.10]; p=0.03) and smaller LV adjusted mass (72 [63-68] vs 71 [64-74] vs 82 [70-92]g; p=0.04) in those exposed to T2D and GDM compared to normoglycemia. No LV hypertrophy was observed (eg. posterior wall thickness: 9.3 [8.4-10.4] vs 9.0 [8.0-10.4] vs 9.8 [8.8-10.7]mm; p=0.3) and systolic function was reduced only in GDM-exposed adolescents (ejection fraction: 62.3 [57.0-65.0]%) compared to those exposed to T2D (64.3 [62.3-67.7]%) or normoglycemia (64.0 [60.7-65.7]%; p=0.02). **Conclusion:** Adolescents with T2D exposed in utero to T2D or GDM exhibited impaired LV relaxation and smaller LV size in the absence of hypertrophy or altered systolic function. Thus, in utero exposure to GDM or T2D may predispose adolescents with T2D to early cardiomyopathy.

P7

DNA METHYLATION MEDIATES THE EFFECT OF MATERNAL COGNITIVE APPRAISAL OF A DISASTER IN PREGNANCY ON HER CHILD'S C-PEPTIDE SECRETION AT AGE OF 13½ YEARS: PROJECT ICE STORM

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Introduction: Animal and human studies suggest that prenatal exposure to stress is associated with adverse health outcomes, such as Type 2 diabetes, hyperglycemia, and insulin resistance in offspring. Epigenetic modification, such as DNA methylation, is considered one possible underlying mechanism. The 1998 Quebec ice storm provides a unique opportunity to study an independent prenatal stressor on child outcomes. We have already shown that higher prenatal maternal hardship from the ice storm predicts higher insulin secretion in the children at age 13½. **Objective:** The objectives of this study are to determine 1) the extent to which prenatal exposure to disaster-related objective hardship influences children's C-peptide secretion and the extent to which maternal cognitive appraisal influences children's insulin and C-peptide secretion at age 13½; and 2) whether DNA methylation of diabetes-related genes mediates the effects of prenatal stress on insulin and C-peptide secretion. **Methods:** Project Ice Storm mothers were pregnant during

the January 1998 ice storm, and completed questionnaires about their stress in June 1998. Their children's (n = 32) insulin and C-peptide secretion in response to an oral glucose tolerance test were assessed in blood at 13½ years. DNA methylation levels of selected type 1 and 2 diabetes-related genes were chosen based upon the genes association with objective hardship and/or cognitive appraisal levels. Bootstrapping analyses were performed to determine the mediation effect of DNA methylation. **Results:** We found that children whose mothers experienced higher objective hardship exhibited higher C-peptide secretion. Cognitive appraisal was not directly associated with either insulin or C-peptide secretion. Next, DNA methylation of type 1 and 2 diabetes-related genes had a positive mediation effect of objective hardship on both insulin and C-peptide secretion: higher objective hardship predicted both higher insulin and C-peptide secretion through DNA methylation. Negative mediation effects of cognitive appraisal were observed on both outcomes: negative (versus neutral/positive) cognitive appraisal predicted both higher insulin and C-peptide secretion through DNA methylation. However, only one gene LTA remained a significant mediator of cognitive appraisal on C-peptide secretion after the conservative Bonferroni multiple corrections. **Conclusion:** Our findings suggest that DNA methylation could act as an intervening variable between prenatal stress and metabolic outcomes, highlighting the importance of epigenetic mechanisms in response to environmental factors.

P9

LONG TERM CARDIAC STRUCTURE CORRELATES WITH ADVERSE PERINATAL COMPLICATIONS IN YOUNG ADULTS BORN PRETERM.

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Introduction: Studies support a direct association between preterm birth and increased risk of cardiovascular diseases. Increased left and right ventricular mass and impaired systolic and diastolic function have been reported in young adults born very preterm (≈30.3 weeks) (1,2). Deleterious perinatal conditions, as in extreme preterm birth, could differently impact on myocardial tissue. **Objective:** To assess and correlate left ventricle (LV) structure with perinatal complications in young adults born extremely preterm versus term. **Methods:** Eighty young adults born extremely preterm (27±1 weeks, 980±225g) were recruited along with term-born controls (39±3 weeks, 3237±640g) matched for age (23±2 yrs), sex (55% female) and socio-economic status. Neonatal and maternal data were collected. 24h ambulatory blood pressure and echocardiographic measurements of LV function, mass, and dimensions were taken. T-test was used for comparisons across groups. **Results:** Young adults born extremely preterm presented with increased systolic (119 ± 9 vs 116 ± 8 mmHg, P<0.05) and diastolic (68 ± 5 vs 66 ± 6 mmHg, P<0.05) blood pressures. Preterms exhibited reduced septal thickness (6.7 ± 0.9 vs 7.0 ± 1.0 mm, P<0.05), and trend of reduced LV posterior wall thickness (6.7 ± 0.9 vs 7.6 ± 1.2 mm, P=0.06) and LV mass index (66 ± 13 vs 71 ± 16 g/m2, P=0.06). Preterms exhibited decreased LV internal dimension (4.6 ± 0.4 vs 4.8 ± 0.5 mm, P<0.05) and corrected end-systolic volume (21 ± 5 vs 23 ± 6 ml/m2, P<0.01). Extremely preterm adults born from mothers with hypertensive complications exhibited greater reduction in corrected end-diastolic (54 ± 7 vs 60 ± 12 ml/m2, P<0.05) and systolic (19 ± 4 vs 23 ± 6 ml/m2, P<0.05) volumes. Preterms with bronchopulmonary dysplasia (O2 use at 36 weeks gestational age) exhibited greater reduction in septal thickness (6.5 ± 0.8 vs 7.0 ± 1.0 mm, P<0.05). **Conclusion:** Young adults born extremely preterm exhibit alterations in left ventricle geometry and size compared to term-born individuals. Maternal hypertensive complications and bronchopulmonary dysplasia in individuals born extremely preterm further contribute to long-term decreased left ventricle mass. REFERENCES: 1. Lewandowski AJ et al. Circulation. 2013;127:197-206. 2. Lewandowski AJ et al. Circulation. 2013;128:713-20.

P13

EXPOSURE TO ADVERSE CHILDHOOD EXPERIENCES AND MATERNAL UTILIZATION OF PARENTING SUPPORT

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Introduction: There is growing evidence to support an association between adverse childhood experiences (ACEs) and

lifelong implications including poor physical and mental health. The health repercussions of ACEs may affect parenting behaviours leading to poor early childhood environments or the multigenerational transmission of ACEs. It has been proposed, however, that the effects and pervasiveness of ACEs can be lessened through community-wide services that support healthy parenting through relevant and accessible interventions. **Objective:** To describe the pattern of parenting support utilization among mothers exposed to ACEs in Calgary, Alberta. **Methods:** This is a secondary analysis of data from the All Our Babies Study (AOB), a prospective community-based pregnancy cohort, situated in Calgary, Alberta, Canada (n=3388). Detailed information was collected via questionnaires during the perinatal period (22-24 and 32-36 weeks gestation), and during early childhood (4, 12, 24 and 36 months post-partum). A history of ACEs was operationalized as reporting >3 adverse experiences on an 11-item Adverse Childhood Experiences Checklist. Two distinct types of parenting support were examined: 1) primary support aimed at promoting the understanding and enablement of positive parenting interactions, and 2) secondary support aimed at providing an integral environment for promoting optimal family functioning. Multivariable logistic regression modeling was used to examine the association between parenting support utilization and maternal exposure to ACEs. **Results:** Of the 1994 mothers included in this study, 27.4% reported a history of ACEs. Women were highly engaged with their communities as 89.9% and 80.2% reported utilizing primary and secondary parenting support, respectively. No significant barriers to primary parenting support were identified. Barriers to secondary parenting support included social and practical barriers, and a history of ACEs. **Conclusion:** Our study shows that women in Calgary, Alberta are engaged with their communities and generally seek parenting support. Intrinsic differences between the types of parenting support, including cost and convenience, resulted in differing barriers. By recognizing the social and practical barriers to secondary parenting support, we can improve the accessibility of these programs. Moreover, the association of ACEs and parenting support utilization, highlights the importance of creating relevant support such as mutual aid and trauma-informed services.

P15

MODERATING EFFECTS OF MATERNAL EMOTIONAL AVAILABILITY ON LANGUAGE DEVELOPMENT IN TODDLERS OF MOTHERS EXPOSED TO A NATURAL DISASTER IN PREGNANCY: THE QF2011 QUEENSLAND FLOOD STUDY

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Introduction: Prenatal maternal stress (PNMS) is linked to less than optimal developmental outcomes in toddlers. Maternal emotional availability (EA) is associated with better cognitive and language abilities. It is less clear whether early care-giving relationships can moderate this impact. **Objective:** To determine if maternal EA moderates the relationship between PNMS and toddler language abilities. **Methods:** Data were available 128 families. Measures of PNMS were collected within one year of the 2011 Queensland floods. EA (sensitivity and structuring) when thee toddlers where 16 months based on video recorded mother-child play interactions. The toddlers' cognitive (Bayley Scales) and language (maternal checklist) abilities were assessed at 30 months. Moderation analyses were used to determine whether EA moderated the relationship between PNMS and toddler outcomes. **Results:** PNMS was not directly associated the toddlers' cognitive and language abilities at 30 months. Overall, high maternal structuring and sensitivity were associated with better vocabularies in the toddlers. However, toddlers of high structuring mothers exposed to high levels of overall subjective stress and peritraumatic distress spoke more words relative to toddlers of low structuring mothers exposed to high levels of overall subjective stress and to a lesser extent high peritraumatic distress. Toddlers of low structuring mothers exposed to high levels of PTSD-like symptoms, and to a lesser extent peritraumatic distress, spoke fewer words relative to toddlers of high structuring mother exposed to high level of PTSD-like symptoms, and to a lesser extent peritraumatic distress. **Conclusion:** The current study highlights the importance of EA for language development in young children, especially maternal structuring. It suggests that toddlers exposed to higher levels of PNMS at the time of the event may benefit from high maternal structuring in their language development. Moreover, the results also suggest that exposure to enduring subjective stress (i.e., PTSD-like symptoms) may be detrimental to language development in the face of low maternal structuring. EA did not moderate the relationship between PNMS and cognitive abilities.

P17

CEREBELLAR VOLUME MEDIATES THE ASSOCIATION BETWEEN PRENATAL MATERNAL STRESS AND MOTOR PERFORMANCE IN ADOLESCENT BOYS: PROJECT ICE STORM

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Introduction: There is new interest in determining which factors influence the morphological development of the cerebellum and its related behaviors. While prenatal maternal stress (PNMS) reduces the cerebellar volume in laboratory animals, ethical constraints have limited human research. However, natural disasters expose pregnant women to varying levels of stress in quasi-random fashion. **Objective:** First, to determine whether disaster-related PNMS is associated with differences in cerebellar gray matter volume (CGV), and whether this relationship is moderated by fetal sex and/or by the timing of the PNMS exposure in gestation. Second, to investigate whether CGV mediated the association between PNMS and motor performance in young adolescents. **Methods:** Measures of PNMS (objective hardship, subjective distress, and cognitive appraisal) were obtained from mothers shortly after the 1998 Quebec Ice Storm; the women were either pregnant during the storm or became pregnant within 3 months. When the children were 11½ years old, structural MRI scans were conducted. Cerebellum segmentation was done on T1-weighted images, using the Multiple Automatically Generated Templates (MAGeT) pipeline, for 57 right-handed offspring, and corrected for total intracranial volume. Indices of balance and bilateral coordination (N=51) were obtained when the youth were 13½ years of age. **Results:** In boys only, high objective PNMS predicted smaller CGV if they were exposed to the ice storm during preconception, but predicted larger CGV if exposed at the 9th week of gestation or later. Moreover, CGV mediated the association between objective PNMS and motor functioning at 13½ years in late-exposed boys: higher objective stress was associated with larger CGVs, which were associated with poorer motor performance. **Conclusion:** The results demonstrate that CGV mediates the relationship between objective PNMS and motor functioning in adolescence, that boys appear to be more vulnerable than girls to these effects, and that these associations depend on the timing of the stressor in gestation. This is the first demonstration in humans that prenatal exposure to a sudden-onset, independent stressor influences development of the cerebellum, which then predicts two aspects of motor development. The results also implicate the women's objective exposure to the disaster (example: days without power) rather than their psychological distress from the event.

P19

CHARACTERIZATION OF BRAINSTEM PHENYLETHANOLAMINE N-METHYLTRANSFERASE GENE IN FETAL PROGRAMMING OF HYPERTENSION

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Introduction: The prenatal environment can be a significant determinant of long-term health outcomes. An adverse fetal milieu such as undernourishment or exposure to environmental insults can have long-term developmental consequences impacting adult health, a phenomenon known as fetal programming; conditions in utero can be linked to diseases like hypertension, diabetes and other pathophysiological conditions in adulthood. Fetal programming of adult diseases can be mediated by glucocorticoids (GCs); either endogenous (eg. maternal stress), or exogenous (eg. synthetic GCs administered to aid in the development of premature babies). GCs regulate catecholamine biosynthesis which are critical for blood pressure homeostasis, with elevated levels leading to hypertension. **Objective:** To understand how stress experienced during fetal life could be an antecedent for the development of hypertension. Our focus is the regulation of phenylethanolamine N-methyltransferase (PNMT), the terminal enzyme in the catecholamine biosynthetic pathway. PNMT is directly responsible for adrenaline synthesis, and has been linked to hypertension. **Methods:** Pregnant Wistar-Kyoto (WKY) dams were injected with 10, 50 or 100µg/kg/day of the synthetic GC dexamethasone

(DEX) in the third trimester. Blood pressure and weights of the offspring were measured from week 3-18, at which point the animals were sacrificed and tissues collected. Total RNA was extracted from the adrenergic neurons C1, C2 and C3 of the brainstem, and the expression of PNMT and its regulatory transcription factors analyzed by qRT-PCR. **Results:** The current study demonstrates that rats that were subjected to prenatal DEX exposure suffer from elevated blood pressure in adulthood. The systolic, diastolic and mean arterial pressures were significantly elevated, and correlated with the DEX dose. In addition, results from qRT-PCR show that PNMT mRNA levels were upregulated, in a dose dependent manner, in all 3 adrenergic neurons of DEX exposed rats, compared to the saline group. Furthermore, analyses of transcriptional regulators of the PNMT gene show alterations in Sp1, EGR-1, and GR mRNA. The results suggest that prenatal GC exposure increases brainstem PNMT gene expression via altered transcriptional regulatory mechanisms. **Conclusion:** The study emphasizes that the tightly regulated catecholamine biosynthesis can be disarrayed by in utero insults, resulting in elevated catecholamines and subsequent hypertension in adulthood.

P21

MATERNAL METABOLIC COMPLICATIONS IN PREGNANCY AND OFFSPRING BEHAVIOUR PROBLEMS AT TWO YEARS OF AGE

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Introduction: Many studies have now reported on associations between fetal exposure to maternal metabolic complications in pregnancy, such as pre-pregnancy obesity, excessive gestational weight gain and gestational diabetes mellitus, and offspring behavioural problems later in life. However, it is unclear whether these associations are causal or due to confounding variables such as maternal gestational diet. **Objective:** To examine if maternal pre-pregnancy adiposity, gestational weight gain (GWG), and/or gestational diabetes mellitus (GDM) are associated with symptoms of psychological problems in offspring at 2 years of age, or if these links were due to confounding variables. **Methods:** Data from 815 children born to women enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) cohort were used to examine associations between maternal body mass index (BMI), GWG, GDM, and externalizing and internalizing scale scores on the Child Behaviour Checklist (CBCL) 1½-5 at 2 years of age. Associations were examined before and after adjustment for maternal gestational diet quality, postpartum depression (PPD), smoking, breastfeeding duration, and socioeconomic status (SES). **Results:** Pre-pregnancy BMI and GDM, but not GWG associated with greater externalizing and internalizing problems in offspring. However, associations were no longer statistically significant following adjustment for confounders. Exploratory post-hoc analyses found that unhealthy gestational diet accounted for the most unique variance in externalizing problems (semi-partial rdiet=-0.19, $p<0.01$) while PPD and SES also accounted for associations in externalizing (semi-partial rPPD=0.14, $p<0.05$, rses=-0.14, $p<0.05$) as well as internalizing problems (semi-partial rPPD=0.18, $p<0.01$, rses=-0.13, $p<0.05$). **Conclusion:** Pre-pregnancy body mass index and GDM were not associated with offspring behavioural problems after adjustment for confounders. It was found that gestational diet quality confounds associations between metabolic complications in pregnancy and offspring behavioural problems. Since the size of the effect of gestational diet was similar in magnitude to more well-known, potent risk factors for offspring behaviour problems: postpartum depression and socioeconomic status, future research should consider the impact of unhealthy prenatal diets on offspring neurodevelopment.

P23

IS THERE AN ASSOCIATION BETWEEN GESTATIONAL WEIGHT GAIN AND INFANT PHYSICAL ACTIVITY?

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Introduction: Maternal weight-related factors have been associated with developmental programming of offspring PA in animal models. However, more research on human infants is required. **Objective:** The purpose of this study was to investigate the association of gestational weight gain (GWG) and change in total daily physical activity (PA) of infants from 3 to 6 and 12 months of age. **Methods:** Eight boys and five girls who participated in the maternal obesity management (MOM) trial were included in this study. PA counts were measured over 24 hours using Actiwatch

accelerometers. GWG was calculated as the difference between weight measured at delivery from antenatal record and self-reported pre-pregnancy weight. Data was analyzed using linear mixed models. **Results:** The association between the GWG and offspring PA was significantly different at 12 mo compared to the 3 mo (b = -9.6 counts/min, 95% CI = -18.4 –-0.8, p=0.033). No significant difference in association was found between the 3 mo and 6 mo (b = -0.6 counts/min, 95% CI = -5.7 –4.5, p=0.831). At 12 mo, greater GWG was inversely associated with offspring PA (b = 7.0 counts/min, 95% CI = -14.3 – 0.2, p = 0.057, whereas at 3 months no association was found (b = 1.3 count/min, 95% CI = -4.2 –6.8, p = 0.620). **Conclusion:** Lower GWG is associated with an upwards change in infant's PA from early to late infancy. Our findings suggest that lower maternal gestational weight gain may play a role in developmental programming of greater engagement in PA during late infancy.

THEME: Maternal and Fetal Medicine I – Maternal Medicine

P27

THE EFFECT OF OBSERVATION ON SKILL ACQUISITION IN OBSTETRIC SIMULATION BASED ULTRASOUND TRAINING

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Introduction: Simulation based medical education is now well integrated into the curricula of many medical specialties, as it is understood to be a highly effective albeit resource dependent form of clinical skill development. Recent studies have used the ScanTrainer™ to study the effect of simulation on ultrasound training. It has been demonstrated that dyad practice improves the efficiency of simulation-based training and is non-inferior to individual practice in terms of skills transfer, and that simulation-based ultrasound training during the initial part of residency followed by clinical training of new residents in Obstetrics and Gynecology had a sustained impact on clinical performance. **Objective:** Our objective was to elaborate on these findings by investigating the differential benefit of observation prior to active scanning versus isolated active scanning using an ultrasound simulator both at initial exposure and at retention, 2 to 3 weeks after initial exposure, in the same cohort of ultrasound naive students. **Methods:** In a randomized study, 43 ultrasound naïve university students (N = 33) were recruited. Participants were randomized into dyads, with one member of each pair designated as the Active Scanner (AS) (N=21) and the other as the Observer Scanner (OS) (N=22). The AS completed the training and assessment portion of a ScanTrainer module which the OS initially observed; once complete, the OS performed the same tasks. The participants (N=40) were re-assessed individually 2-3 weeks following the initial exposure, using the previously utilized module in addition to a novel module.
Summative assessments, number of attempts, and time to completion of each module as provided by the Scan Trainer™ provided the basis of evaluation. **Results:** 43 participants completed the simulation based dyad testing and 40 of these completed the retention assessment. There was no significant difference found between the active and observer scanner scores, number of attempts, or time to completion of the initial module. There were significant differences in performance scores between the initial and retention assessments in both the active scanner and observer scanner groups. **Conclusion:** There is demonstrable improvement in performance amongst ultrasound naïve students with simulation based practice, however dyad practice does not improve performance.

P29

MECHANISMS OF UTERINE CONTRACTION: A POSSIBLE ROLE FOR REGULATOR OF G-PROTEIN SIGNALING 2

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Introduction: Oxytocin and prostaglandins (PGF2 and PGE2) are used to augment/induce labour. These pathways are also targeted to treat preterm labour, but with limited effectiveness. Developing superior approaches requires further study of the mechanisms that govern myometrial smooth muscle (MSM) function in labour. Oxytocin and PGF2 act at the OXTR and PTGFR G-protein coupled receptors (GPCRs), respectively. Following ligand binding, OXTR and PTGFR activate a Gq protein to initiate contractile signaling pathways. Regulators of G-protein signaling (RGS) have been identified, and include the RGS2 that selectively turns off Gq signals. Drugs that activate Gs-coupled GPCRs, alone and in combination with corticosteroids, upregulate RGS2 resulting in reduced Gq-mediated contraction.
RGS2 is expressed in the pregnant MSM and we hypothesise that it plays a relaxatory role. The MSM also expresses Gs-coupled receptors associated with pro-quiescent functions that might induce RGS2. Among these are the PGE2 PTGER receptors, two of which signal via Gs. PGE2-induced RGS2 expression may be synergistically enhanced by corticosteroids in the MSM, such as dexamethasone (DEX), used in preterm labour to hasten fetal maturation. If RGS2 in the MSM attenuates OXTR and PTGER signals, manipulating RGS2 expression could be a novel approach to reduce multiple contractile pathways in preterm labour. **Objective:** To investigate the pathways by which RGS2 is regulated in MSM, we tested the hypothesis that RGS2 expression is induced by PGE2 and DEX in the human MSM, and that this prevents Gq-mediated contraction. Additionally, we sought to determine RGS2 expression patterns in myometrial tissue. **Methods:** Myometrial biopsies were obtained with consent, from women undergoing C-section. Biopsies were used to isolate primary MSM cells. Cells were used to test the effects of PGE2 (1M) alone or in combination with DEX (1M) on RGS2

gene/protein expression, and contractile responses to oxytocin (300nM). Myometrial biopsies were also collected for gene expression analysis by RT-PCR and western blotting. **Results:** In MSM cells, RGS2 RNA and protein was inducible by PGE2 with DEX at several time points. Increased RGS2 expression dampened contractile responses following treatment with oxytocin in MSM cells. In term myometrial tissues, there were no significant changes in RGS2 expression (n=11 labour, n=8 non-labour). However, at preterm, RGS2 expression was lower ($p>0.05$) in labour (n=12) than in non-labour (n=9). **Conclusion:** Expression of RGS2 in MSM is associated with pro-quiescent signaling, and may be manipulated, in vitro, to modify MSM function.

P31

THE PREGNANCY CARE EXPERIENCE OF WOMEN WITH PHYSICAL DISABILITIES: QUALITATIVE INTERVIEWS TO IMPROVE PATIENT CARE

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Introduction: Women with physical disabilities confront special maternity care issues. There is limited data on maternity care needs for this group of women. We aim to develop a prenatal clinic for women with physical disabilities; however, prior to this undertaking, an understanding of the current care experience is necessary. **Objective:** To explore the experience of pregnant women with physical disabilities and to identify barriers though personal interviews. This information will be used to inform the creation of a specialized prenatal clinic for women with disabilities and improve maternity care. **Methods:** Three interviews were conducted with women with physical disabilities attending a Maternal-fetal-medicine prenatal clinic at Sunnybrook Health Science Center. These 1 hour face-to-face semi-structured interviews were audio recorded, transcribed, and analyzed. Pregnant women were asked to describe their experience with pregnancy, childbirth, and the neonatal period and to identify gaps and barriers to quality services. **Results:** Women reported three broad positive themes: positive staff attitudes, compassionate care and interprofessional collaboration. However, three majors barriers were encountered including lack of suitable equipment and access to health and parent education information. **Conclusion:** A Maternal-fetal-medicine prenatal clinic for women with a disability has the potential to offer specialized care. However, this specialized antenatal clinic requires access to suitable equipment, provision of sensitive antenatal classes and specific parent information. This information is vital to the development and improvement of this specialized clinic. Further studies and collaboration with stakeholders are required to develop policy and practice recommendations to improve the current service.

P33

CARDIOVASCULAR DISEASE RISK PERCEPTION BEFORE AND AFTER COUNSELLING FOR PREGNANCY-RELATED CARDIOVASCULAR RISK INDICATORS

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Introduction: The development of pregnancy-related cardiovascular risk indicators (ie. preeclampsia, gestational hypertension, gestational diabetes, significant placental abruption, intrauterine growth restriction, and/or idiopathic preterm birth) predict an increased risk for cardiovascular disease (CVD). At Kingston General Hospital, these patients are referred for standardized postpartum follow-up through the Maternal Health Clinic (MHC). **Objective:** The objective of this study was to assess whether this intervention is associated with improved accuracy of patients' perceived CVD risk and/or healthy lifestyle changes. **Methods:** Patients were invited to complete a questionnaire regarding their perceived risk for CVD prior to the MHC assessment and again after 3 months. Participants rated their lifetime CVD risk according to American Heart Association (AHA) Lifetime CVD Risk categories and as an absolute risk. The 3-month follow-up questionnaire also assessed for lifestyle changes. Participants' Lifetime CVD Risk scores, calculated as part of the MHC assessment, were compared to their perceived CVD risk. **Results:** Prior to the MHC assessment, 13 of 36 participants underestimated their AHA risk category. 14/36 accurately estimated and 9/36 overestimated their risk category. This distribution did not change significantly after 3 months ($p=0.388$). Most participants (34/36) underestimated their absolute CVD risk prior to the MHC, while 2/36 accurately estimated and 0/36 overestimated their absolute risk. This distribution was significantly different after 3 months ($p=0.0001$). Fewer participants underestimated (22/36) and more accurately estimated (14/22) their absolute risk. None overestimated their absolute risk. 29/36

participants endorsed healthier eating since the MHC and 30/36 participants endorsed increased physical activity. 11/36 said they had seen a nurse or doctor to discuss preventive health. **Conclusion:** The MHC intervention significantly improves the accuracy of patients' perceived absolute lifetime CVD risk. Most patients report adopting healthy lifestyle changes in the 3 months after the MHC. Whether more accurate risk perception, and whether the lifestyle changes described lead to decreased CVD morbidity requires further investigation.

P35

CHANGES IN MANAGEMENT OF PRE-ECLAMPSIA BETWEEN TWO TIME PERIODS AT THE BC WOMEN'S HOSPITAL, VANCOUVER

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Introduction: The fullPIERS model, which predicts adverse maternal outcomes in women with pre-eclampsia, was developed in 2010 in a cohort of 2023 women in high-resourced settings.. The model was internally validated and had a good discrimination with an area under the receiver-operating characteristic curve of 0.88 (95%CI 0.84-0.92). Re-evaluating the model performance in the same setting at a later time (temporal validation) is necessary to ensure its clinical utility. Before temporally validating the model, it is useful to examine any changes in population characteristics and clinical management over time as these will give useful information on the potential performance of the model. **Objective:** To compare changes in risk of pre-eclampsia, adverse maternal and neonatal outcomes and management in one of the development settings (British Columbia (BC) Women's Hospital, Vancouver), between the time period prior to the fullPIERS model development (development data) and after the model development (temporal data). **Methods:** Our study population included 1071 women admitted to the BC Women's hospital from 2003 to 2010 included in the model development, and 545 women admitted with pre-eclampsia in the same centre from 2012 to 2014. The demographic characteristics, management of pre-eclampsia and rates of adverse outcomes of the development and temporal data were compared using $\chi 2$ and Mann Whitney test statistics. **Results:** The women in the temporal cohort were more likely to be older, multiparous and had a later onset of pre-eclampsia compared with the development cohort (Table 1). The rate of adverse maternal outcomes within 48 h of admission in the temporal data was 4.2% similar to the development data (4.7%). There were no significant differences in the rates of adverse perinatal outcomes. Regarding the treatment and management of pre-eclampsia, the rate of administration of antihypertensive medication and MgSO4 did not differ between the two groups. However, women in the temporal data were more likely to have a shorter admission-to-delivery interval compared with the development cohort. **Conclusion:** Overall, there was no significant change in the management of pre-eclampsia and outcome rate in the hospital over the time periods studied. However, there were some significant differences in the demographics and signs of the women between the development and temporal data. Therefore, it is important to investigate if and how these changes could affect the fullPIERS model performance on temporal validation.

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LLABORATORY BIAS FOR PROTEINURIA AND ALBUMINURIA IN HYPERTENSIVE PREGNANCIES

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Introduction: Accurate measurement of proteinuria in the hypertensive disorders of pregnancy (10% of pregnancies) is key for the diagnosis of preeclampsia (2-5%) and its clinical management. Methods currently used for determining proteinuria in pregnancy suffer important limitations. Laboratory measurement of proteinuria itself is suboptimal due to analytic considerations and albuminuria may be a better alternative. **Objective:** To compare the analytic variation and bias of protein:creatinine (PC) and albumine:creatinine (AC) ratios in urinary samples of hypertensive pregnant women. **Methods:** Urinary samples from 27 hypertensive women collected at ≥ 20 weeks' gestation were analysed for AC and

PC in one batch at four hospital laboratories. Analyzers/reagents for urinary protein were as follow: Sherbrooke (Roche – Modular P – benzethonium), Drummondville (Ortho – Vitros 5600 – pyrocatecol-molybdate), Memphremagog (Beckman – Dxc600i – M-TP pyrogallol red) and BC Women's and Children (Ortho – Vitros 5600 – randox pyrogallol red). Coefficient of variation (CV) ranged from 1.4% to 6.7% for urinary protein while only 2.0% to 2.8% for albumin and 0.7% to 1.9% for creatinine. **Results:** The median and range for the mean PC and AC values for the four laboratories were respectively 37 [9-739] and 12 [1-506] mmg/mmol. At higher levels, AC values were within ±15% whereas they were closer to ±30% for PC values. When looking at absolute differences, bias between laboratories was more pronounced for proteinuria (up to 45 mg/mmol) than for albuminuria (mostly within 10 mg/mmol) (see Figure). **Conclusion:** Analytic variation appears to be higher for proteinuria compared to albuminuria in women investigated for hypertension during pregnancy. This variation between laboratories has the potential to impact on the diagnosis of preeclampsia and could further lead to misclassification.

P39

USE OF FOOT-TO-FOOT BIOELECTRICAL IMPEDANCE ANALYSIS TO ASSESS BODY COMPOSITION IN LACTATING WOMEN.

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Introduction: Body composition analysis has not been validated in lactating women. There are many dynamic physiological factors that can affect measurements. Bioelectrical impedance analysis (BIA) is a rapid, simple, non-invasive body composition test that is an appropriate alternative to dual-energy x-ray absorptiometry (DXA) in non-lactating adults. **Objective:** To evaluate the validity of using a standard foot-to-foot BIA model to assess body composition in lactating women compared to DXA. **Methods:** Data from a randomized controlled trial (clinicaltrials.gov: NCT02563015) in greater Montreal provided for detailed body composition assessments at <4 wk (baseline) and 3 mo postpartum in lactating women. Body composition was measured after a 2 h fast using a foot-to-foot BIA (TANITA Body Composition Analyzer, TBF-310 model) and whole body DXA (Hologic Discovery, APEX software version 13.3:3) at both time-points. Fat mass (FM), fat free mass (FFM; FFM corresponds to lean mass + bone mineral content) and percent fat (% fat) were compared between DXA and BIA using a mixed model ANOVA (SAS, version 9.3), Bland-Altman plots and Pearson correlations. **Results:** Women (n=35; 20 white, 15 non-white) age 32.2 ± 5.2 y, had BIA and DXA measures at baseline (mean body mass index (BMI): 27.3 ± 4.9 kg/m2), and 18 were measured again at 3 mo (mean BMI: 26.4 ± 4.9 kg/m2). At baseline and 3 mo, there was a positive correlation between BIA and DXA for all body composition measurements (Baseline: FM: r=0.96, % fat: r=0.83, FFM: r=0.92, p<0.001; 3 mo: FM: r=0.89, % fat: r=0.71, FFM: r=0.62, p<0.01). At baseline, measurement of FM was higher on BIA than DXA (BIA: 26.4 ± 9.7 kg, DXA: 25.1 ± 7.8 kg, p=0.02) and the Bland-Altman plot showed a bias of 1.3 ± 3.1. Percent fat was also higher on BIA than DXA (BIA: 35.9 ± 6.9%, DXA: 34.3 ± 5.4%, p=0.02) and had a bias of 1.6 ± 3.9. Measurement of FFM was lower on BIA than DXA (BIA: 44.8 ± 3.6 kg, DXA: 47.2 ± 6.6 kg, p<0.001) and had a bias of -2.4 ± 3.5. Three mo weight, FM, % fat and FFM did not significantly change from baseline (p>0.05). The Bland-Altman plots of 3 mo changes in body composition corresponded to those at baseline. **Conclusion:** These results demonstrate that foot-to-foot BIA overestimates mean FM and % fat and underestimates mean FFM when compared to DXA. The Bland-Altman plots suggest body composition or size affects the differences between measurement techniques, making it more appropriate for use in groups of women vs. individuals. As baseline and 3 mo body composition did not differ significantly, a longer time frame would be needed to investigate how DXA and BIA capture changes in maternal body composition across lactation.

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CORM-A1 TREATMENT LEADS TO INCREASED BLOOD CARBOXYHEMOGLOBIN IN PREGNANT CD-1 MICE

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Introduction: Pre-eclampsia (PE) is a disorder affecting 5-7% of pregnancies, characterized by new-onset hypertension and proteinuria. While the etiology of PE is unknown, it is widely accepted that it is a result of impaired placental

perfusion, which results in hypoxia and oxidative damage in the placenta. At low doses, carbon monoxide (CO) has been shown to reduce inflammation, apoptosis, and increase vasodilation and angiogenesis in placental vessels. Carbon Monoxide Releasing Molecules (CORMs) are a class of pharmaceutical compounds composed of transition metal carbonyl complexes. CORM-A1 (sodium boranocarbonate) can be delivered to pregnant mice to increase carboxyhemoglobin (%COHb) levels in vivo, making it a possible alternative to inhaled gas for the study of CO as a therapeutic for PE. **Objective:** This study aims to a) Quantify the increase in CO in blood %COHb following intermittent dosing with CORM-A1, at various dosing schedules and concentrations in pregnant mice, b) Determine fetal, litter and histological effect of CORM-A1 on dams, and c) Determine any changes in systolic blood pressure in an sFlt-1 model of preeclampsia, following administration of CORM-A1 during pregnancy. **Methods:** Female CD-1 mice (Charles River, USA) (5-7 weeks) were mated. Dams were treated with various doses of CORM-A1 (Sigma Aldrich, USA) by IP injection on E10.5 or daily E10.5-12.5. Blood was collected at specific intervals post-CORM injection via a submandibular bleed. Hemoglobin was measured using a Hemocue (Radiometer) and blood %COHb was measured using a head-space gas chromatograph CO analyzer (Peak Laboratories, USA). Data are presented as mean±SD. Analysis was performed by one-way ANOVA with post-hoc Dunn's test with significance of $p<0.05$. **Results:** Blood %COHb increased from 0.68%±0.09% at baseline (n=6) to 3.52%±0.81% at 15min post-CORM-A1 treatment (5mg/kg dose)(n=3). %COHb was significantly elevated at 15min post-injection, followed by a decline at each 15min interval post-injection back to baseline levels. Higher doses of CORM-A1 (10mg/kg E10-12) showed an increase in number of fetal resorptions compared to controls. There was no observable difference between treatment groups in maternal gestational weight gain, fetal or placental weight at E17.5. **Conclusion:** Preliminary data indicates that a dose of 5mg/kg CORM-A1 increases %COHb at 15 minutes post-treatment. A more complete understanding of the mechanism by which CORM-A1 is acting on the placenta and fetus is required before CORM-A1 can be tested as CO-donor therapeutic in PE.

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DECORIN-MEDIATED FOS REGULATION IN TROPHOBLAST MIGRATION: IMPLICATIONS FOR PRE-ECLAMPSIA

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Introduction: Inadequate trophoblast migration, endovascular differentiation (ED) and uterine arterial remodeling, leading to compromised flow of maternal blood to the placenta, are implicated in the origin of preeclampsia (PE) & fetal growth restriction (FGR). We have shown that Decorin (DCN), a decidua-derived proteoglycan restrains trophoblast migration, ED and uterine arterial remodeling, and that DCN is overproduced by the decidua in PE-associated placentas. Furthermore, an elevation of maternal plasma DCN during the 2nd trimester was shown to predict PE. However, the molecular mechanisms in DCN action on the trophoblast are unclear. **Objective:** In order to identify DCN target genes/miRNAs regulating trophoblast functions, differential gene/microRNA microarrays were conducted with wild-type vs DCN-transfected first trimester trophoblast HTR-8/SVneo cells. **Methods:** Target genes and miRNAs were validated with real time qPCR. Of the numerous target genes up-regulated by DCN, we identified FOS, a key transcription factor reported to inhibit trophoblast migration. **Results:** In "scratch" or "wound" assays of live trophoblast cells in monolayers collected in the act of migration at 2 h exhibited 9 fold upregulation of FOS in DCN-transfected cells compared to mock-transfected cells, indicating the role of FOS in DCN-mediated anti-migratory action. FOS protein upregulation was confirmed by Western blot. Micro(mi)RNA microarray identified down-regulation of 13 miRNAs in DCN-transfected cells, validated by qPCR, all theoretically targeting FOS. To identify which of them played a role in migration, we compared their expression levels between unwounded mock/DCN transfected cells and those extracted at 1-6 h after wounding. From this analysis, we identified miR383 as the key miRNA to be upregulated and thus taking part in migration. Furthermore, in wound assays we found miR383 downregulation in DCN-treated cells, and FOS upregulation in DCN overexpressing cells compared to controls. **Conclusion:** DCN down-regulates a key microRNA miR383 in trophoblast cells, which targets an anti-migratory transcription factor FOS that may be linked with PE. Future studies: (1) Overexpress miR383 in DCN transfected cells to check whether this can reverse the anti-migratory effects of FOS. (2)To validate FOS regulation by DCN in situ, measure trophoblast migration from undisrupted chorionic villi plated on matrigel. (3)Compare expression levels of FOS and miR383 in PE/FGR vs control placentas. We expect respective up- and

down regulation of FOS and miR383 in PE/FGR placentas. (Supported by CHRI-TRF to PKL, GE & BDV and a CHRI fellowship to PN).

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RATE OF STILLBIRTH AND POST-DELIVERY DEATH IN SINGLETON PREGNANCIES BY PRE-PREGNANCY BODY MASS INDEX

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Introduction: In high-income countries, maternal overweight and obesity were found to be one of the highest ranking modifiable risk factors for stillbirth. With an increasing prevalence of overweight and obesity in the maternal population, further investigation on the timing (gestational age) of significant increase in rate of stillbirth and neonatal death is warranted. **Objective:** The objective of this study was to examine the relationship of pre-pregnancy BMI to (1) the rate of stillbirth, (2) the rate of post-delivery death and, (3) the combination of stillbirth and post-delivery death by gestational age, with the goal of finding the optimal gestational age for delivery for each pre-pregnancy BMI category. **Methods:** This was a descriptive, retrospective cohort study of 268,306 singleton gestations from 2009 to 2013 obtained from the Better Outcomes Registry & Network (BORN) database from the province of Ontario. Rates of death with provided by gestational age, for each BMI category and also stratified by parity (nulli- and multiparous). **Results:** The rates of both stillbirth and post-delivery death were generally higher in underweight, overweight and obese categories relative to normal weight. In addition, rate of death was generally higher in nulliparous pregnancies. Overall, the rate of death was generally highest in Class II obesity. Notably, the rate of death from Class II to Class III obesity dropped significantly. It was not possible to detect a specific gestational age at which rate of death significantly increases in a particular BMI group, due to high amounts of missing data. **Conclusion:** Similar to findings of systematic reviews, rates of death were higher in non-normal BMI classes. It may be possible that Class II obesity is a neglected group as their rates of death were much higher than the Class III group. The drop of rates of death from Class II to Class III obesity can therefore likely be explained by the more aggressive surveillance and management by delivery at earlier gestational ages in the latter group. Future goals include utilizing a larger sample to acquire adequate number of events for statistical analysis. Finally, preventative goals at aiming to reduce pre-pregnancy BMI are to be continuously encouraged and prioritized.

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FIRST-LINE ANTIHYPERTENSIVE TREATMENT FOR SEVERE HYPERTENSION IN PREGNANCY: A BAYESIAN NETWORK META-ANALYSIS

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Introduction: It is estimated that hypertensive disorders of pregnancy complicate 5-10% of pregnancies worldwide and account for 18% of maternal deaths. Severe hypertension in pregnancy is associated with an increased risk of maternal and neonatal mortality and morbidity. General consensus supports immediate intervention with guidelines recommending IV hydralazine, IV labetalol, and oral nifedipine as first-line treatments. While all three are effective, there is a lack of sufficient evidence regarding their comparative safety and efficacy. **Objective:** To conduct a systematic review and network meta-analysis (NMA) to determine the comparative effectiveness and safety of hydralazine, labetalol, and nifedipine for severe hypertension in pregnancy. **Methods:** A systematic search of Medline, Embase, and CENTRAL up to October 20, 2015 was conducted. Screening, data abstraction, and quality assessment was done by two independent reviewers. To estimate relative effects from all available evidence, a Bayesian NMA with vague priors was conducted using both a fixed and random effects model. In October 2015, this NMA was registered on PROSPERO (CRD42015025839). **Results:** Of the 995 publications identified, 10 RCTs consisting of a total of 943 women met our

selection criteria. For successful treatment of hypertension, the fixed effects model showed nifedipine to be superior to both labetalol (OR 2.65 [95% CrI 1.13-6.56]) and hydralazine (OR 3.66 [95% CrI 1.63-8.76]). Similarly, composite maternal side effects favored nifedipine to hydralazine (OR 0.48 [95% CrI 0.27-0.81]) and labetalol (OR 0.61 [95% CrI 0.33-1.09]), but the difference with labetalol was not significant. Rates of caesarean section were comparable across all treatments, however, the results were inconclusive due to wide credible intervals. The trends for the random effects model were similar to that of the fixed effects, however, none showed significance. Labetalol and hydralazine were comparable across both models but the results were inconclusive due to wide credible intervals. There was insufficient evidence to quantitatively summarize other outcomes of interest.< /p target="1"> **Conclusion:** This study suggests a trend favoring oral nifedipine for the management of severe hypertension in pregnancy. The results remain inconclusive as they are informed by a small number of trials, each with a relatively small sample size. Future trials should investigate the effectiveness of nifedipine compared to labetalol/hydralazine using a larger sample size.

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HEALTH PROVIDER OPINIONS ON APPROPRIATE POSTPARTUM VENOUS THROMBOEMBOLISM PROPHYLAXIS: A QUALITY IMPROVEMENT STUDY.

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Introduction: Venous thromboembolism (VTE) is a relatively uncommon but important cause of maternal morbidity and mortality in the peripartum period. There is currently a lack of consensus amongst international guidelines regarding both an appropriate absolute risk threshold that should prompt postpartum prophylaxis as well as the ideal duration of treatment. Whereas the 2014 Society of Obstetricians and Gynaecologists of Canada (SOGC) guideline recommends a 1% absolute risk threshold, the 2015 guideline from the Royal College of Obstetricians and Gynaecologists in the UK suggests prophylaxis for patients with a risk as low as 0.2%, and recent guidelines from the American College of Chest Physicians and the Anticoagulation Forum suggest a cut-off as high as 3% in some or all postpartum patients. As a result, the use of thromboprophylaxis in the postpartum period is not standardized at our institution. **Objective:** To evaluate the opinions of care providers regarding VTE risk factors and overall absolute risk levels that should prompt consideration of postpartum VTE prophylaxis. **Methods:** Electronic survey of obstetric and thrombosis specialists at McMaster University Medical Centre regarding appropriate risk thresholds (expressed as absolute risks and number needed to treat), duration of treatment, and specific risk factors for postpartum VTE as described in the 2014 SOGC guideline “Venous Thromboembolism and Antithrombotic Therapy in Pregnancy”. Data for individual risk factors was collected using a 5-point Likert scale and compared to risk estimates from the existing literature. **Results:** Our survey had a 44% (16/36) response rate. The majority of respondents selected 3% as the threshold to trigger postpartum VTE prophylaxis. The most commonly selected duration of treatment was six weeks. There was a high degree of consistency between respondents’ perception of risk for individual risk factors and the pooled risk estimates available from the existing literature. **Conclusion:** Obstetricians and Thrombosis Specialists at McMaster who responded to our survey feel that a 3% absolute risk cut-off should be used to consider if individual patients should be prescribed postpartum VTE prophylaxis. There was general agreement between survey respondents and the published literature regarding the degree of risk attributable to individual risk factors. This information will be used to design a “chart prompt” checklist that will ask healthcare providers to consider individual patient risk factors for postpartum VTE, score these risk factors, and advise prophylaxis for those with an estimated VTE risk of 3% or more.

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SLEEP DURATION AND SERUM LEPTIN CONCENTRATIONS THROUGHOUT PREGNANCY IN HEALTHY LEAN AND OVERWEIGHT/OBESE WOMEN

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Introduction: Pre-gravid overweight and excess gestational weight gain occur in > 50% of Canadian pregnant women and both conditions predispose to sleep disordered breathing (SDB), which is associated with sleep apnea, decreased blood oxygenation, interrupted sleep and daytime drowsiness. Short sleep duration is known to modulate glucose

metabolism and secretion of appetite regulatory hormones such as leptin. Both short sleep duration in pregnancy and hyperleptinemia have been associated with risk of gestational diabetes and preeclampsia. Little is known about the mechanisms for these associations and there have been no studies to date evaluating leptin status and sleep duration throughout pregnancy. **Objective:** To determine if serum leptin concentrations are associated with sleep duration in pregnancy in healthy lean and overweight/obese women. **Methods:** Healthy pregnant women were recruited into The Be Healthy in Pregnancy (B-HIP) Study in Hamilton, Ontario between 12-17 wk gestation and followed throughout pregnancy. Women were categorized by pre-pregnancy BMI: lean (BMI < 25 kg/m2) and overweight/obese (BMI ≥25 kg/m2). Sleep data were collected from Sensewear™ Armbands (BodyMedia, Pittsburg) worn by participants for three days at 12-17 wk (n=122), 26-28 wk (n=103) and 36-38 wk (n=92) gestation. Sleep duration was classified into 4 categories: ≤6, 7, 8 and ≥ 9 hr. Fasted serum leptin was measured at 12-17 (n=58) and 36-38 wk (n=59) using Magnetic Luminex Assay® (R&D Systems Inc., Minneapolis). ANOVA followed by Tukey's post-hoc analysis were performed to evaluate the association between sleep categories and serum leptin concentration (Stata® 11.0, Texas). **Results:** In early pregnancy (12-17 wk) there was no association between sleep duration and serum leptin. However, in late pregnancy (36-38 wk) women with short sleep duration had significantly elevated serum leptin (p=0.004). Women reporting < 6 hr sleep had higher mean serum leptin compared to those with 7 hr sleep (42.68 vs 23.83 ng/ml, p=0.03) or 8 hr sleep (42.68 vs 23.09 ng/ml, p=0.01). Neither lean nor overweight/obese demonstrated changes in sleep duration across pregnancy; however, overweight/obese women slept less than lean women at 26-28 weeks (p=0.06) and significantly less at 36-38 weeks (p=0.02). **Conclusion:** Short sleep duration, and to a lesser extend long sleep duration, were associated with elevated circulating leptin in the third trimester of pregnancy, particularly in overweight/obese women. How short sleep duration and elevated leptin contribute to adverse pregnancy outcomes requires further investigation. (Funded by CIHR)

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MATERNAL LEPTIN STATUS THROUGHOUT PREGNANCY AND 6-MONTHS POST-PARTUM

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Introduction: Leptin, known as a satiety hormone produced in white adipose tissue that circulates in proportion to body fat, rises during pregnancy and may play a role in placentation and maternal-fetal exchange processes regulating growth and development. The relationship between leptin status and maternal adiposity in pregnancy have not been fully explored. **Objective:** To determine i) the pattern of change in maternal leptin status throughout pregnancy and recovery period up to 6 mo post-partum and ii) the impact of pre-pregnancy BMI on pattern of change. **Methods:** Data were obtained from a subset (n=66) of women enrolled in the Be Healthy in Pregnancy (BHIP) Study. Pre-pregnancy BMI, calculated as weight measured at baseline (12-17 wk gestation) and self-reported weight gain, was categorized as: lean (BMI < 25 kg/m2) and overweight/obese (BMI ≥25 kg/m2). Maternal blood samples were collected at baseline, end of pregnancy (36-38 wk), and 6 mo post-partum, and analyzed for serum leptin using Luminex pre-coated human leptin enzyme-linked immunosorbent assay (R&D Systems, Minneapolis MN). **Results:** In this group of women, 54.5% had normal BMI and 45.5% had overweight/obese BMI. By two-way ANOVA, serum leptin changed significantly (p<0.001) over the 3 time points and was higher (p<0.001) in overweight compared to normal BMI groups at both end of pregnancy (p<0.005) and 6 mo post-partum (p<0.005). The key change was in the decline in leptin status from the end of pregnancy to 6 mo post-partum for both normal BMI (21.7 vs 6.2 ng/ml, p<0.05) and overweight BMI (40.8 vs 22.2 ng/mL, p<0.005) groups. **Conclusion:** Pattern of change in leptin concentration is significantly different between normal weight and overweight/obese BMI groups both during and post-pregnancy. The influence of maternal leptin status in pregnancy on growth and body composition of the offspring in early life will be investigated. (Funded by CIHR)

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OPERA: OPTIMAL PREGNANCY ENVIRONMENT RISK ASSESSMENT – AN INITIATIVE OF THE WORLDWIDE UNIVERSITIES NETWORK.

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Introduction: Introduction. OPERA is an international, interdisciplinary program of women's health researchers, care providers, foundations and international agencies dedicated to discovering and disseminating inexpensive and accessible tools to diagnose those women at risk for preterm birth and other adverse pregnancy outcomes as early as possible in pregnancy and to promoting effective interventions to mitigate these risks. **Purpose**. Initial efforts will focus on risk diagnosis in existing cohorts of pregnant, vulnerable women in any jurisdiction who are victims of natural disasters or conflict, are migrants, are living in megacities or are in generational cohorts (e.g. F2's from the Dutch Hunger Winter, World War II, or migrants). New cohorts will be created as required. Evidence will be developed to: 1) determine how to assess risk for preterm birth and other adverse pregnancy outcomes simply, inexpensively and as early as possible in pregnancy, 2) identify the women in the highest (20%) at-risk group (with 80% precision), and 3) share this information with other studies, care-providers and interested parties. **Supports.** OPERA is not a funding organization but instead: 1) provides support in terms of special skills, study design, data evaluation and sharing, guidance, advocacy, website services (pending); 2) informs about best practices and 3) communicates discoveries and achievements to partners and target audiences. **International meetings.** 1st International OPERA Meeting, San Francisco March 23-24, 2015. Thirty-eight leading investigators, international organizations, funders and trainees representing a variety of expertise with populations of vulnerable women or an understanding of evaluating risk for adverse pregnancy outcomes shared their expertise and provided future direction: see www.operamtg.org. OPERA China Workshop, Chongqing November 12, 2016. Representatives from 8 Chinese universities and 3 foreign universities plus WUN met to describe OPERA cohorts and projects. Several large Chinese pregnancy cohorts are eager to participate in OPERA. The Born in Guangzhou Cohort is already using its data to predict preterm birth risk and the Chongqing Birth Cohort is predicting preeclampsia risk. 2nd International OPERA Meeting, Mexico City March 12-13, 2016, will be organized along a 'workshop' format providing practical advice for topics including management organizations for cohorts, funding cohorts long-term, methods for studying F2 cohorts, using algorithms to predict risk, types of data useful for risk prediction, etc.

THEME: Maternal and Fetal Medicine 2 – Fetal Medicine

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INCIDENCE, RISK FACTORS AND OUTCOMES OF PULMONARY HYPERTENSION IN PRETERM INFANTS WITH BRONCHOPULMONARY DYSPLASIA: A SINGLE CENTRE EXPERIENCE

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Introduction: Pulmonary hypertension (PH) is a known complication of bronchopulmonary dysplasia (BPD). At our centre, all patients with BPD are screened for PH but its exact incidence and impact on clinical outcomes remains unclear. **Objective:** Objectives: To determine the incidence of and risk factors for PH in preterm infants with moderate-severe BPD and to compare short-term outcomes in BPD patients with PH and without PH. **Methods:** This was a single centre cohort study of preterm infants < 32 weeks GA born between August 2013 and July 2015 with moderate-severe BPD at 36 weeks postmenstrual age. Patients were categorized into BPD+PH (exposure) and BPD alone (control). PH was defined as right ventricular systolic pressure (RVSP) target="1"> 40 mmHg or septum flattening in absence of RVSP. Cases of a) RVSP between 30-40 mmHg with normal/unknown septum status and b) RVSP < 40 mmHg with flat septum were defined as “possible PH” (classified as exposure). Predictors of BPD+PH were sought using logistic regression analyses. Outcomes included mortality, growth parameters and NICU resource utilization. Sensitivity analyses were conducted for all outcomes by re-categorizing “possible PH” cases from exposure to control group. A p value of < 0.05 was considered significant. **Results:** Among 92 BPD patients in study period, 87 had echocardiograms completed of whom 24 (28%) had PH. Baseline characteristics were similar in the two groups with the exception of GA and number of surfactant doses (Table). On multiple logistic regression, after correcting for GA and sex, lack of receipt of antenatal corticosteroids was identified as a significant risk factor for PH (adjusted OR 5.3, 95% CI 1.1-25.1, p = 0.039). There were no significant differences in any outcomes (Table). Similar results were obtained with sensitivity analyses. **Conclusion:** Almost 1 in 3 patients with BPD was identified as having (or possibly having) PH at our centre, with lack of antenatal corticosteroid administration identified as a significant risk factor. No significant differences in outcomes were noted. However, larger prospective studies and long term outcome evaluations are required prior to definitive recommendations regarding screening.

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PRE-GRAVID PREDICTORS OF NEW ONSET HYPERTENSION IN PREGNANCY– RESULTS FROM A PRE-CONCEPTION COHORT STUDY IN CHINA

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Introduction: Although new onset hypertension in pregnancy occurs and is first diagnosed during pregnancy, it may be originated prior to pregnancy. To our knowledge, no study has assessed pre-gravid risk factors of new onset hypertension in pregnancy in a prospective design to characterize the risk factors enabling systematic evaluation of all participants from pre-gravid to across gestation **Objective:** To prospectively identify pre-gravid predictors of new onset hypertension in pregnancy. **Methods:** This was a prospective, pre-conception cohort study, which recruited women who attended clinics for pre-marriage health assessment at the time of marriage registration at the catchment area of Liuyang Maternal and Infant Hospital and who were planning to have a baby in the next 6 months between February 2009 and December 2012. At recruitment, participants were asked to attend a baseline assessment that consisted of interviewer-administered questionnaires (pertaining to demographics, lifestyle, and medical history), physical examination, and the drawing of venous blood samples for biochemical analyses. Once pregnant, participants received obstetrical care through clinical services at Liuyang Maternal and Infant Hospital. Blood pressure measurements during gestation and the diagnosis of medical complications in pregnancy were obtained through this clinical care. Data collected at delivery included infant sex, gestational age, and birth weight. Baseline characteristics between those

participants who were included in the final analysis and those who were excluded because of missing important outcome or exposure data were compared, maternal and infant characteristics of the participants who were included in the analysis were described, and the association between pre-gravid factors and new onset hypertension in pregnancy was analysed. Cubic spline analyses were conducted to assess the best fit of the continuously distributed exposure variables, and the optimal cut-off points were then applied in the multiple logistic regression models. **Results:** This was a young and homogeneous population, with mean (SD) age of 25.6 (3.1) years, 85% nulliparous, mean (SD) body mass index 20.2 (2.5), and incidence of new onset hypertension in pregnancy 6.2%. In crude analysis, elevated blood pressure, body mass index, waist circumference, and triglyceride levels measured at pre-conception visit were associated with increased risk of new onset hypertension in pregnancy. After simultaneously adjustment for all pre-gravid factors, elevated body mass index (≥ 21.48kg/m2) and blood pressure (either systolic blood pressure ≥121 mmHg or diastolic blood pressure ≥80 mmHg) were associated with increased risk of new onset hypertension in pregnancy. **Conclusion:** Moderately elevated body mass index and blood pressure may be the most important pre-gravid predictor of new onset hypertension in pregnancy in low risk women

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PREDICTION OF FETAL GROWTH ABNORMALITIES PRE-PREGNANCY AND IN THE 2ND TRIMESTER

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Introduction: While there is increasing interest in predicting pregnancies at risk for adverse outcome, few studies have had the ability to adequately assess population-based risks for obstetrical and perinatal outcomes. Also, existing prediction models have been based on conventional regression methods, which may not perform as well as machine learning techniques. **Objective:** To use logistic regression and machine learning methods to identify predictors of fetal growth abnormalities and compare their diagnostic properties in a large population-based sample of infants from the Canadian province of Nova Scotia. **Methods:** The current study uses data of all births between 2009 and 2014 in the Nova Scotia Atlee Perinatal Database. The primary outcomes were SGA and LGA, defined as a birth weight <10th or >90th percentile for gestational age and sex. Up to 25 demographic and clinical characteristics at pre-pregnancy and at 26 weeks were used as predictors. We developed separate models for SGA and LGA, stratified by nulliparous and multiparous women. We used logistic regression, elastic net, classification trees, random forest, gradient boosting, and neural networks to build the models. Data were split 3:1 into training and test sets. Ten-fold cross validation in the training data was used to develop the prediction models. The area under the curve (AUC) for predictions in the test data was used to compare the models. Relative importance of predictors was compared qualitatively between methods. **Results:** For 30,705 out of 49,604 pregnancies complete information on all variables was available. 7.9% and 13.5% of births were SGA and LGA, respectively. Predictions were poor to fair for both SGA and LGA (AUC 60-75%). The predictions improved in the order Nullipara/Pre-Pregnancy, Nullipara/26 weeks, Multipara/Pre-Pregnancy, Multipara/26 weeks. None of the prediction methods offered any advantages over the others in terms of AUC. Smoking, a previous low birth weight infant, and gestational weight gain were consistently identified as strong predictors for SGA, while pre-pregnancy body mass index, gestational weight gain, and a previous infant > 4080g were the strongest predictors for LGA. **Conclusion:** There is limited value in predicting SGA or LGA birth from demographic and clinical characteristics. Knowledge of pregnancy history has the greatest impact on prediction accuracy. In this setting, machine learning methods did not offer any advantage over logistic regression, indicating that the relationship between predictors and outcomes is likely linear and there are no interactions.

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ZIKA VIRUS INFECTION IN PREGNANCY: A ONE CENTRE EXPERIENCE.

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Introduction: In the current context of a Zika virus (ZIKV) epidemic in South America and the Caribbean, a causal link

between congenital ZIKV infection and fetal abnormalities has been shown. Current data are very limited, particularly on mother-to-child transmission of the virus and its pathogenicity in the context of congenital infection. **Objective:** To study mother-to-child transmission of ZIKV and its fetal and neonatal consequences. **Methods:** Women with positive ZIKV tests during pregnancy were prospectively enrolled at Centre hospitalier universitaire Sainte-Justine. Our reference clinic is the only multidisciplinary team with expertise in congenital infections in Quebec, and includes maternofetal medicine specialists, pediatricians, pathologists and microbiologists. ZIKV testing was performed at the Canadian National Microbiology Laboratory. Clinical management of pregnant women and children followed current national guidelines. **Results:** In total, 98 women screened for ZIKV (IgM serology) were assessed at our center following travel to a high risk area or sexual contact with an at-risk partner. Five had positive IgM serology and confirmatory test (plaque-reduction neutralization test) – all were infected around the time of conception or during the first trimester of pregnancy. One decided to terminate the pregnancy at 20 weeks. Neuropathological examination showed microglial activation associated with macrophages in the white matter and germinal zones. There was no necrotic foci, nor calcification. In one case, amniocentesis was performed at 22 weeks and the amniotic fluid was positive for ZIKV by PCR. The woman delivered at term without complication. The baby is 4 month old now and has a normal development, including head growth. Postnatal imaging, hearing tests and eye examination were normal. The initial lumbar puncture came back positive for ZIKV, but control at 2 month was negative. Placenta, urine and infant serum were negative. Another woman delivered at term – her 1 month old newborn did not present any symptoms of congenital ZIKV infection and all his samples were PCR negative. Two pregnancies are still ongoing, for which so far monthly prenatal ultrasound follow-up is normal. **Conclusion:** Managing ZIKV-infected pregnant women in the current context of restrained access to tests and limited knowledge is particularly challenging. Our experience illustrates that some infants congenitally infected with ZIKV could have a normal outcome. It calls for careful counseling of pregnant women with ZIKV infection as little is known about outcome of infected infant in utero when imaging is normal.

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FETAL GROWTH RESTRICTION IN UNITED ARAB EMIRATES: A GENETIC PERSPECTIVE.

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Introduction: There are published reports in the West about the association between FGR and congenital malformations but the same was not studied in a population with high Consanguinity rate (60%) as the UAE. Hence, we aim to investigate and document this association. **Objective:** The objective of the study is to identify the genetic association with fetal growth restriction (FGR) in a population with a high consanguinity rate. Moreover, the study aims to report the mode of delivery and perinatal outcome of fetuses diagnosed with genetic syndrome and to provide a comprehensive and detailed antenatal counseling for parents. **Methods:** A Retrospective chart review was performed in a tertiary referral center over a period of 3 years from 1st January 2008 to December 2010 for pregnant ladies with a confirmed postnatal diagnosis of fetal growth restriction. The data of 158 cases referred to our fetal medicine unit were analyzed. Of the 158 patients, 8 were found to have normal fetal growth (5.1%), 8(%) lost follow up, and 17 were found to have normal postnatal growth (10.7%). Therefore, a total of 125 patients were included in the study. **Results:** In total, 125 pregnant patients were evaluated. Of the 125 patients, 106 were Emirati (84.8%), 9 from GCC (7.2%), and the remaining 10 were non GCC (8 %). Intrauterine growth restriction (IUGR) was the most common indication for referral, accounting for almost ½ of the referrals. We found that the referral for fetal abnormalities was significantly higher in genetic condition (P=0.005). Maternal age (>35 years) was more significantly associated with genetic condition (P=0.03).The mean Gestational age at delivery was (M= 36.75, SD =3.24) weeks. The mean weight of the newborn in grams is (M = 1974, SD= 636.5). 74.4 percent of the newborns weights were below the third percentile. Genetic Syndrome is present in (31/ 125) 24.8 %. We found a higher risk of skeletal abnormalities in offspring's affected with a genetic condition (P=0.002). However, Gastrointestinal tract anomalies are highly associated to offspring not affected by genetic condition (P=0.008). There is no difference in mode of delivery between the two groups, genetic versus non genetic. Survival of offspring with genetic condition is 29 percent, a criteria that is crucial for parental counselling **Conclusion:** This study describes that the degree of IUGR is not different between genetic and non-genetic group. However, FGR associated with genetic conditions are highly correlated with skeletal anomalies. Survival of offspring with genetic conditions is 29 percent in our series, which may be relevant to prenatal counseling.

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CMV-SPECIFIC HYPERIMMUNOGLOBULINS IN PREGNANCY: TOLERANCE AND PREGNANCY OUTCOME

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Introduction: There is no consensus on the use of CMV-specific hyperimmunoglobulins (CSHIG) in suspected congenital CMV infections during pregnancy. Since 2005, observational studies have shown a significant decrease of occurrence, and severity of congenital disease when CSHIG were both used as treatment and as prophylaxis, with rates as low as 0-13 % of sequelae, but the only randomized control trial to date showed a non-significant trend toward less congenital infection when used as prophylaxis. **Objective:** Analyse the tolerance and pregnancy outcome, especially rate of positive PCR and symptoms at birth, after treatment with monthly intravenous CSHIG **Methods:** Retrospective cohort including all pregnant women who were given CSHIG (150 mg/kg) since 2008. Patients were offered CSHIG once maternal infection was confirmed. Congenital CMV infection was confirmed with PCR in blood, urine, saliva and/or spinal fluid within 2 weeks after birth. **Results:** A total of 16 women were included, and received 1-4 doses at a median GA of 26.9 weeks (minimum 21.1 – maximum 36.6); 4 reported mild symptoms during or shortly after administration, such as nausea, vomiting, shivers or abdominal pain. No women presented with preterm labor or preeclampsia. 11/16 women were given CSHIG as treatment: 5 women with fetal ultrasound anomalies and a positive amniocentesis, 5 women with fetal ultrasound anomalies, but who declined amniocentesis, 1 women with normal ultrasounds but a positive amniocentesis. Two women opted for pregnancy termination, 1 fetal demise was noted at 27 weeks. All the remaining live birth cases had positive PCR at birth, and 2 were asymptomatic. In 5/16 women CSHIG was initiated as prophylaxis: 4 women with normal ultrasounds and a negative amniocentesis, 1 woman with normal ultrasound but who declined amniocentesis. Three newborn had negative PCR at birth, one pregnancy is still ongoing, one is lost to follow-up. **Conclusion:** In our practice CSHIG appeared to be safe, however we could not demonstrate its effectiveness to prevent CMV in utero transmission and severe sequelae secondary to CMV congenital infection.

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THE IMPACT OF PRETERM BIRTH AND BRONCHOPULMONARY DYSPLASIA ON GAS EXCHANGE DURING EXERCISE

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Introduction: Despite increased risk of adverse long-term cardiovascular and respiratory function in young adults born preterm (PT) with and without bronchopulmonary dysplasia (BPD), studies examining the effect of PT birth on aerobic exercise capacity have yielded contradictory results. There is also limited data on underlying mechanisms for impaired exercise capacity. **Objective:** This study aimed to compare aerobic exercise capacity including gas exchange kinetics during between young adults born PT with BPD, without BPD and term-born (T) controls. **Methods:** Sixty-five young adults born PT (< 29 weeks) and 65 T controls underwent pulmonary function tests and cardiopulmonary exercise testing. PT born participants with and without BPD (O_2 use at 36 weeks gestational age) were further divided. Peak O_2 consumption (VO_2) was measured. Time to reach ventilatory threshold (VT) was assessed as a proxy of onset of anaerobic metabolism. We also calculated two additional indices of cardiopulmonary function: O_2 uptake in relation to work rate increment ($\Delta VO_2/\Delta Watt$) and the O_2 uptake efficiency slope (OUES). The latter is physiologically determined by development of metabolic acidosis and physiologic dead space. The ventilatory efficiency slope (VE/VCO_2 slope) was derived to examined the ventilatory response to increase in CO_2 production and is typically impaired with reduced pulmonary perfusion. Comparisons across groups were performed using ANOVA and Student's t-test. **Results:** At rest, PT with and without BPD displayed airflow limitation compared to T. PT-born participants reached VT more rapidly than T controls suggesting earlier onset of anaerobic metabolism. At peak effort, PT displayed lower pulmonary ventilation and lower absolute, predicted, and relative to lean body mass VO_2. In addition, they achieved a lower exercise load compared to T and lower $\Delta VO_2/\Delta Watt$. Furthermore, OUES was reduced in PT vs. T However, ventilatory response to CO_2 was similar across groups. **Conclusion:** Young adults born PT displayed impaired aerobic exercise capacity

compared to T controls. Two mechanisms may be involved: (1) increased physiologic dead space due to airflow limitation leading to increased ventilatory effort, (2) impaired perfusion to the skeletal muscles leading to earlier onset of lactic acidosis which also stimulates ventilation. Therefore, for a given ventilatory effort, oxygen uptake will be reduced. Interventions targeting these mechanisms need to be elaborated.

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THE EFFECT OF MATERNAL STRESS AND ANXIETY ON PREGNANCY AND THE INFANT

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Introduction: Pregnancy is considered to be one of the most stressful events in women's lives. Previous research has suggested that adverse outcomes in pregnancy including Pre-term birth (<37 weeks gestation) and low birth weight (<2500g) may be related to stress or anxiety disorders during pregnancy. Stress may weaken the immune system, leading to an increased susceptibility to infection and potentially pre-term birth. Anxiety may interrupt normal hypothalamus-hypophysis-adrenal function and restrict maternal blood flow through the placenta which could have implications for fetal growth and ultimately birthweight. **Objective:** To assess the association between maternal stress and anxiety in pregnancy with child birthweight and gestational age at birth. **Methods:** We conducted a prospective cohort study involving 283 women recruited from the Maternal Fetal Medicine and low risk Obstetrics clinics at the Ottawa hospital between June 2010 and June 2011. The sample was then restricted to singleton births, accurate gestational dating, comprehension of written English, and a gestational age <36 at recruitment. A total of 96 women met these criteria and had completed a demographic questionnaire and validated instruments which assessed maternal stress (Perceived Stress Scale) and anxious attachment (Experiences in Close Relationships Scale). Statistical analyses were performed using hierarchical linear regression (ANOVA) models. **Results:** Mean gestational age at delivery was 38.8 weeks (S.D. +/- 2.3), as very few delivered premature. The mean Anxious Attachment Score was 18.0 (out of 42, SD of +/- 6.8), and the mean Perceived Stress Score was 19.8 (out of 40, SD +/- 2.6. The majority (of the participants were Caucasian (72.3%), with 66.7% being married, 88.6% being non-smokers and 55.1% having an income of 80,000+ (19.6% with income <%50,000). The ANOVA model indicated the association between stress and anxious attachment and pre-term delivery was $F(2,93)= 0.396$, $p=0.674$ with a variance of 0.8% ($R2=0.008$). **Conclusion:** These findings indicated that perceived stress and anxiety did not appear to correlate with preterm delivery in this sample. Additional analyses will consider low SES groups and gestational age at the time of study enrollment.

THEME: Neonatology I – Respiration/Ventilation/Cardiology

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CURRENT PRACTICES OF ANTISEPTIC AGENT USE IN CANADIAN NEONATAL INTENSIVE CARE UNITS

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Introduction: Neonatal sepsis is associated with an increase in mortality, morbidity, and length of hospitalization. Skin antiseptics reduce nosocomial infections but may cause adverse effects. There is a paucity of evidence to support the preferential use of any antiseptic in the Neonatal Intensive Care Unit (NICU). **Objective:** The purposes of this survey were to assess the degree of variability in the use of skin antiseptic agents in Canadian NICUs, explore different experiences related to the pros and cons of the agents used and identify if their use was regulated by institution-specific guidelines. **Methods:** A clinical representative of each of the 124 level 2 and level 3 Canadian NICUs was contacted via email to participate in an anonymous survey link (OPINIO) regarding the use of antiseptic agents. Both French and English versions of the survey were available. **Results:** One hundred and two respondents (82.2%), representing all Canadian provinces, completed the survey (Figure1). Most of the responders were nurse practitioners and educators (70.3%) with 5-20 years of experience (66.7%). Level 3 and level 2 units were evenly represented. Chlorhexidine with/without alcohol was the most antiseptic used (93.1%) with the highest reported local adverse effects (Table1). Specific guidelines for antiseptic use were available in 57% of the units. Only 23% of responders indicated that health care providers in their unit were aware of the side effects of antiseptics used and 57% were either not or only partially satisfied with the antiseptic agents used in their unit. **Conclusion:** There is significant heterogeneity in the use of antiseptic agents in Canadian NICUs and many centres have no guidelines. Local adverse effects are reported most commonly with chlorhexidine which is the most often used agent. More studies are needed to guide the practice and improve the safety in this vulnerable population.

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THE OUTCOME AND PREDICTORS OF INHALED NITRIC OXIDE (INO) THERAPY ON PRETERM NEONATES WITH SEVERE HYPOXEMIC RESPIRATORY FAILURE (HRF) RESCUED WITH HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV)

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Introduction: Despite being an experimental therapy in preterm neonates, the use of INO has increased as a rescue therapy when HFOV and other conventional therapies fail. **Objective:** To determine the effect of INO as a rescue therapy and the predictors of survival in very preterm neonates with HRF. **Methods:** We retrospectively reviewed all very preterm neonates (<33 weeks gestation with birth weight <1500g) who required HFOV and INO from Mar 2009-Apr 2014 at the Royal Alexandra Hospital (RAH) Neonatal Intensive Care Unit (NICU). We collected demographic and clinical parameters, dosages, duration and response to INO, survival to NICU discharge and major complications. Neurodevelopmental outcome was also assessed at 18-24 months of corrected age. **Results:** During the study period, 1168 very preterm neonates were admitted to the RAH; 155 (13%) had HRF treated with HFOV, of which 47 (30%) received INO. There were 24 survivors (S) and 23 non-survivors (NS) who did not differ in baseline characteristics including oxygenation indices (OI) (median of 30.7 for S vs. 29.5 for NS) (table I, II). However, there was a significantly greater decrease in OI of S compared to that of NS after 6h of INO (67% decrease from baseline S vs. 39% for NS; p=0.003) (Figure I). At 6h of INO treatment, 1(4%) S and 8(35%) NS were non-responders (<10% reduction in OI from baseline) with an 89% positive predictive value for non-survival. Causes of death were refractory hypoxemia (8), multi-organ failure (7), treatment withdrawal (6) and others (2). During NICU stay, 23 S (96%) developed complications including: chronic lung disease (n=22, 92%), intraventricular hemorrhage (n=9, 38%), nosocomial infection (n=7, 29%), retinopathy of prematurity (n=6, 25%), and necrotizing enterocolitis (n=5, 21%). At 18-24 months, 2 (8%) were lost to follow up; 7 (29%) developed significant disabilities including: hearing impairment requiring amplification (4, 17%), cognitive delay (4, 17%), cerebral palsy (3, 12%), and blindness (1, 4%) with 4 (17%) multiply disabled. **Conclusion:** In

very preterm neonates with severe HRF rescued by HFOV and INO, many survived without neurodevelopmental disability at early childhood despite multiple short-term complications. Early response to rescue INO might predict non-survival. Further research is necessary to understand the clinical course and risk factors of adverse outcomes and to improve the management care of these critically ill neonates.

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A PILOT STUDY OF CONTINUOUS NEURALLY ADJUSTED NON-INVASIVE VENTILATION (NEUROPAP) IN PRETERM INFANTS

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Introduction: Neurally adjusted ventilatory assist (NAVA) delivers synchronized and proportional assist based on the electrical activity of the diaphragm (Edi), but on inspiration only, PEEP is fixed. NeuroPAP is a new non-invasive mode, in which the pressure is continuously (during both inspiration and expiration) proportional to Edi, providing the possibility of a neurally adjusted expiratory pressure. **Objective:** To evaluate the feasibility and tolerance of NeuroPAP in preterm infants. **Methods:** This is a prospective feasibility study in a single level 3 NICU approved by the local Research Ethics Board and Health Canada. Infants born at 26 and 34 weeks of gestational age (GA), aged 3 and 30 days old, ventilated in non-invasive positive pressure ventilation (NIPPV), and in stable condition were eligible. After parental consent, ventilation pressures, Edi, SpO2, and ECG were continuously monitored during four conditions: NIPPV with unmodified pre-study settings (NIPPV1- 30 min.), in NeuroPAP with minimal pressure (Pmin) set at the level of pre-study PEEP (NeuroPAP1, 60 min.), in NeuroPAP with Pmin reduced by 2 cmH20 (NeuroPAP2, 60 min.), and again in NIPPV (NIPPV2, 30 minutes). NeuroPAP level was 0.4 0.1 cmH2O/V and the maximal pressure was set at 18 cmH2O. **Results:** 18 patients with mean SD GA at birth 27+6 1 weeks (range 26-29+6/7) and 11 8 days old were studied. NeuroPAP was clinically well tolerated and could be used during the entire planned period (2 hours) in all patients. Backup ventilation was accurately activated on 28 occasions during NeuroPAP for apneas > 10s. The evolution of the respiratory variables is detailed in the table, with no significant change observed between the modes. During NeuroPAP, the end expiratory pressure transiently increased during increase in tonic Edi, but the mean value over the entire recordings was not different from the set minimal pressure. Prolonged positive support (> 15 cmH2O during 2 seconds) during tonic Edi bursts occurred in 6 patients, for a total of 12 occurrences, without adverse events. No abdominal distension was noted. **Conclusion:** NeuroPAP is feasible and well tolerated in stable preterm neonates. While the mean PEEP seemed to be controlled by the set minimal pressure, transient and safe increases in PEEP were possible in response to tonic Edi increases. The potential benefit of this neurally adjusted PEEP in terms of lung recruitment and bronchopulmonary dysplasia reduction should be assessed in future studies.

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DEVELOPMENT OF NEWBORN OVINE MODELS OF BACTERIAL AND VIRAL NEONATAL INFECTIONS.

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Introduction: Neonatal infections occurring several days or weeks after birth remain a major problem in pediatrics. Bacterial and viral infections often lead to severe apneas and/or bradycardias during late-onset sepsis of preterm newborns, and are involved in apparent life-threatening events and sudden infant death syndrome (Moscovis, 2015). However, the link between the neonatal infection-related inflammation and the altered cardiac and respiratory activity is still poorly understood. Activation of the prostaglandin E2 (PGE2) pathway has been shown to inhibit respiratory centers in newborn mice and has been linked to apneas in preterm newborns with late-onset bacterial sepsis (Hofstetter, 2007; Siljehav, 2015). To our knowledge, PGE2 has not been shown to explain the severe bradycardias observed with bacterial infections or the apneas-bradycardias during viral infections. **Objective:** To develop neonatal ovine models mimicking the systemic inflammation related to a bacterial or to a viral infection. **Methods:** Toll-like receptor agonists (TLR) were injected intravenously to 6 newborn lambs, 2-4 days of life, in order to mimic a systemic infection-related inflammation. Three lambs received 2.0 µg / kg of E. Coli lipopolysaccharides (LPS 0127: B8, Sigma-

Aldrich), a classical TLR-4 agonist, mostly involved in Gram-negative bacterial infections. Three other lambs received 200 or 300 µg / kg of polyinosinic-polycytidylic acid (Poly I:C, Vivogen), a TLR-3 agonist, which is involved in rhinovirus, influenza and respiratory syncytial virus infections. A six-hour polysomnographic recording was carried out in all animals. The criterion for reaching significant systemic inflammation was an increase in body temperature 40.5 °C. **Results:** In the LPS group, rectal temperature reached its target in 30 ± 10 min, then returned progressively to normal after 140 ± 45 min. In Poly I:C lambs, two peaks of temperature were observed, at 35 ± 15 min and 170 ± 6 min after injection, and the temperature returned back to normal after 320 ± 75 min. In both groups, generalized hypotonia and an increased sleepiness and REM sleep epochs were observed. Cardiorespiratory irregularities such as repeated bouts of tachypnea + tachycardia for several minutes and an increased number of sighs and short apneas were present in both groups. Overall, these clinical signs persisted for 3 to 5 hours post-injection. **Conclusion:** The present preliminary results show the possibility to develop ovine models of systemic inflammation related to a bacterial or a viral infection. These models should help us to gain a better understanding of the apneas and bradycardias related to neonatal infections.

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PRACTICE VARIABILITIES IN THE EXTREME PRETERM NEONATAL RESUSCITATION BY THE DEDICATED RESUSCITATION STABILIZATION TEAM

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Objective: To evaluate the current practice variabilities during resuscitation of preterm infants by the dedicated Resuscitation Stabilization Team (RST) using videos and respiratory function recordings of the delivery room management. **Methods:** At our center, neonatal stabilization rooms are equipped with video recording and respiratory function monitor. We analyzed the first 10 minutes of delivery room stabilization of preterm infants at birth. The RST performance was evaluated and compared against the Canadian and regional Neonatal Resuscitation Guidelines. **Results:** Thirty infants were video recorded over 8 months, with mean gestational age (GA) 26 (±2) weeks and birth weight 960 (±315)g. There was 100% compliance with using the plastic drape for infants less than 28 weeks GA. EKG leads and Pulse Oximetry were applied to all 30 patients. The median time[IQR] for application of the pulse oximetry was 47 seconds [35- 65] from the time of arrival at the table. Only 9/30 infants were suctioned prior to starting the respiratory support. There were inconsistencies in drying and stimulation within first minute for infants less than 28 weeks GA. There was a trend of initiating mask Continuous Positive Airway Pressure (CPAP) prior to completing initial assessment for adequacy of spontaneous breathing. 14 infants were apneic when placed on the table. The median [IQR] time to initiate positive pressure ventilation (PPV) in these apneic babies was 26 seconds [12-37.5]. 5/9 apneic babies didn't have clinical assessment of heart rate as a part of initial assessment or to establish effectiveness of the ventilation. There were 10 events in 7 patients where PPV was interrupted by the PPV provider for purposes other than ventilation corrective steps. Early initiation of nasal CPAP i.e., less than 10 minutes was noted in 8 babies. **Conclusion:** The results of the RST performance are comparable to available literature. The results represent efficient neonatal stabilizations by a well-trained stabilization team. The variability of sequence in accomplishing each step of resuscitation could indicate resuscitator's training and experience for individual skill set or judgment on rapidly changing clinical situation. There is a need of ongoing resuscitation training with special focus on situational awareness to prepare the NRP providers for timely strategized performance. Resuscitation videos can be a useful tool for educational and training of NRP providers.

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EXPLORING SHARED DECISION MAKING DURING ANTENATAL COUNSELLING FOR ANTICIPATED EXTREMELY PRETERM BIRTH.

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Introduction: Discussions between physicians and families facing the anticipated birth of an extremely premature infant (22-25 weeks) are complex. The use of shared decision making (SDM) can support reaching a preference sensitive decision. A guideline was created to enhance SDM to facilitate decision making and increase parental and healthcare

provider satisfaction with the process. Little is known about the applicability of SDM, how healthcare providers conceptualize it in their practice, or about facilitators and barriers to implementing this process during antenatal counselling for anticipated extremely preterm birth. **Objective:** The purpose of this project was to explore healthcare providers' perceptions of and perspectives about using SDM within this clinical area. **Methods:** We examined data from a larger implementability assessment study during a pilot test of the above guideline. The study consisted of qualitative interviews with 25 healthcare providers (neonatologists and neonatal fellows, maternal fetal medicine specialists and fellows, obstetricians, paediatric and obstetric residents, birthing unit nurses, and neonatal nurses) involved in 5 cases at a tertiary care centre (October-November 2015). Semi-structured interviews were conducted over the phone or in person, and transcribed verbatim. Qualitative content analysis was used to code, categorize, and thematically describe the data. **Results:** Many participants understood and correctly described established elements of the SDM approach. A number had positive perspectives about this model of decision making and its usefulness in this clinical context. These participants valued SDM as an effective strategy to engage parents during the decision making process. Several participants challenged the usefulness of SDM and expressed concern that this approach increased decision making difficulties. Misunderstandings of this approach were also demonstrated, concerning the premise of SDM and the physician's role in this process. Examples of perceived barriers to the use of SDM during antenatal counselling included: timing of consults (at night or under stress), increased time needed for proper SDM, fear of creating false parental hope and misunderstandings regarding infants' long term needs, uncertainty towards use at 22 weeks, and concerns about burdening parents with this decision. **Conclusion:** This study has identified healthcare providers' diverse perceptions and perspectives about SDM and various factors that influence whether members of the healthcare team value SDM or are reluctant to engage in it during antenatal counselling for anticipated preterm birth. Addressing these misperceptions and barriers will help to facilitate improved implementation of this decision making model in the current setting and other facilities in the future.

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RADIAL ARTERY OCCLUSION AFTER CANNULATION IN NEONATES: A PROSPECTIVE COHORT STUDY

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Introduction: Radial arterial cannulation is used for continuous haemodynamic monitoring and for blood sampling in newborns requiring neonatal intensive care. Radial artery occlusion (RAO) and ischemic injuries have been reported with the use of radial cannula. There is very limited data on newborn infants and the risk of RAO. Doppler ultrasonography is the gold standard to assess this complication. However, other non-invasive tests have been studied in adult populations. Plethysmography seems to be a promising tool and has demonstrated a high correlation with doppler ultrasonography. **Objective:** The primary objective of this study was to assess the frequency of radial artery occlusion associated with arterial cannulation in preterm and term newborns. The secondary objective was to evaluate plethysmography as a screening tool for RAO in newborns. **Methods:** A prospective observational study was conducted in a level three neonatal intensive care unit. Patients with a radial arterial cannula were recruited. The evaluation of the permeability was realized with plethysmography curve (Masimo Radical Set Monitor) during the reverse Barbeau test, and then confirmed by doppler ultrasonography. The radial artery patency was assessed between 24 and 72 hours after removing the cannula, and weekly until patency normalization if it was found to be compromised. **Results:** Twenty-five infants were included in the study. The median gestational age was 35 weeks(minimum-maximum (min-max) 24-41) and the median birth weight was 2270 grams (min-max 640-4050). The main diagnoses of those patients were prematurity (36%) and surgical disease (28%). Most patients (92%) required invasive ventilation at the time of radial cannula installation. The median duration of radial cannulation was 92 hours (min-max 1-191). Two RAO were confirmed by doppler ultrasonography. Those patients did not present any clinical signs of RAO. One occlusion has resolved spontaneously 3 weeks after the initial diagnosis. The other patient died before reassessment. Plethysmography has 100% sensitivity and 86% specificity to detect RAO. **Conclusion:** Radial artery occlusion following cannulation was a rare finding in this study. Accordingly, radial cannula appears to be a safe arterial access for neonates. Furthermore, plethysmographic findings correlated well with doppler ultrasonography and is a promising screening tool for the clinician at the bedside. Plethysmography could allow quick and inexpensive assessment of radial artery patency.

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MTOR-NOTCH3-PDGF-B-RECEPTOR SIGNALING AXIS MEDIATES PULMONARY VASCULAR REMODELING IN CHRONIC HYPOXIA-EXPOSED NEONATAL RATS.

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Introduction: Pulmonary vascular autophagy is increased in adult experimental chronic pulmonary hypertension (PHT), but there is contradictory data on the effects of autophagy modulators in prevention and treatment of pulmonary vascular disease. Mammalian target of rapamycin (mTOR) activity is known to stimulate pro-proliferative pathways in smooth muscle that may or may not be directly related to autophagy, including activation of Notch signaling. **Objective:** Our aim was to examine changes in mTOR- and autophagy-related pathways and the therapeutic effects of autophagy modulators in experimental chronic neonatal PHT. **Methods:** Rat pups were exposed to normoxia or hypoxia (13% O2) from postnatal days 1-21, while receiving preventive treatment with chloroquine (inhibitor of autophagic flux), temsirolimus (mTOR inhibitor) or DAPT (Notch inhibitor). **Results:** Exposure to hypoxia increased autophagy and Notch3 signaling markers in lung and pulmonary arteries. Chloroquine had no effect on chronic hypoxic PHT. In contrast, temsirolimus prevented chronic PHT and attenuated arterial Notch3 signaling and platelet-derived growth factor (PDGF)-β receptor up-regulation in hypoxia-exposed lung and in serum-stimulated smooth muscle cells. These effects were replicated by DAPT. siRNA-mediated knockdown of Beclin-1, a key regulator of autophagy, had no effect on Notch3 signaling in smooth muscle cells. **Conclusion:** We provide the first evidence of a sequential role for mTOR-Notch3-PDGF-β receptor signaling in chronic neonatal PHT. Inhibitory effects of mTOR inhibitor on smooth muscle proliferation appear to be independent of up-regulated autophagy.

P91

A CORE OUTCOME SET FOR NEONATAL ABSTINENCE SYNDROME: STUDY PROTOCOL FOR A SYSTEMATIC REVIEW, PARENT INTERVIEWS AND A DELPHI SURVEY

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Introduction: The prevalence of neonatal abstinence syndrome (NAS) is increasing globally resulting in an increased incidence of adverse neonatal outcomes and health systems costs. Evidence regarding the effectiveness of NAS prevention and management strategies is very weak and further research initiatives are critically needed to support meta-analysis and clinical practice guidelines. In NAS research, the choice of outcomes and the use of valid, responsive and feasible measurement instruments are crucial. There is currently no consensus and evidence-based core outcome set (COS) for NAS. **Objective:** To develop a minimal core outcome set to be measured in Neonatal Abstinence Syndrome **Methods:** The development of the NAS-COS will include five stages lead by an international multidisciplinary steering committee; (1) qualitative interviews with parents/families and a systematic review (SR) to identify items for inclusion in a COS. The SR will also identify participants for the Delphi; (2) a three-round Delphi survey to gain expert opinion on the importance of health outcomes influencing NAS management decisions; (3), a consensus meeting to finalize the items

and definitions with experts and COS users; (4) feasibility and pilot testing, development of the COS and explanatory document, and (5) implementation planning. **Conclusion:** Standardized outcome measurement and reporting will improve NAS clinical research consistency, efficacy and impact.

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SKIN-TO-SKIN CONTACT FOR PROCEDURAL PAIN IN NEONATES: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSES OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Skin-to-skin care (SSC) or Kangaroo care is a non-pharmacologic method used to reduce neonatal procedural pain. The Cochrane review of SSC for procedural pain was last updated in 2014, and there has been considerable publication activity since. **Objective:** To assess the effectiveness of skin-to-skin care (SSC) alone compared to control or other interventions for pain in neonates undergoing painful procedures. **Methods:** The Cochrane Central Register of Controlled Trials (CENTRAL), PUBMED, Embase, and CINAHL was searched to February 2016. Studies with randomization or quasi-randomisation, with neonates receiving SSC for painful procedures, were selected. Bias was assessed using Cochrane guidelines. Quality of evidence was completed using the GRADE. **Results:** Twenty-five studies (n=2001 infants) were included. Studies were generally strong, and had low or uncertain risk of bias. Seventeen studies compared SSC to a no-treatment control and eight to another intervention. The Premature Infant Pain Profile was a primary outcome in five, favouring SCC at 30 seconds (MD −3.21, 95% CI −3.94 to −2.47), at 60 seconds (MD −1.64, 95% CI −2.86 to −0.43), and at 90 seconds (MD −1.28, 95% CI −2.53 to −0.04). Meta-analysis of heart rate (HR) during painful procedures showed a mean difference (MD) of −10.78 bpm, and duration of crying (seconds) from two studies on heel lance (MD =−34.16, 95% CI −42.86 to −25.45), and two on IM injection (MD = −8.83, 95% CI −14.63 to −3.02), favoured SSC. No differences were reported in HR post-procedure, HR variability, or oxygen saturation. Sweet taste in combination with SSC was more effective than either alone, but SSC alone was more effective that sweet taste. SSC in combination with breastfeeding favoured over a no-treatment control, but no better than breastfeeding. Combination with both sucrose and breastfeeding were more effective than SSC alone. Expressed breast milk compared to SSC in one study were found equally effective. Crossover studies comparing mother versus other provider (father, another female) found no significant difference. There were no studies with similar outcomes and painful procedures to compare age groups or duration of SSC. No adverse events were reported. **Conclusion:** SSC appears to be safe and effective as measured by composite pain indicators (physiological and behavioural) and independently with heart rate and crying time in preterm and full term infants undergoing a single painful procedure. Studies examining optimal duration of SSC, gestational age groups, repeated use, and long-term effects of SSC are needed.

P95

EXPLORING NEONATAL RESUSCITATION COMPETENCIES IN GRADUATING PEDIATRIC RESIDENTS

Mary Woodward, Connie Williams

Introduction: The skill of neonatal resuscitation includes a thorough knowledge of neonatal physiology, technical skills and the ability to lead a multidisciplinary team that includes members with different levels of expertise. Current literature speaks to an ongoing chasm that exists between clinical practice and guideline adherence. Competency has emerged as one of the reasons for the same. There is, therefore an ongoing concern with ensuring competency acquisition for the practice of neonatal resuscitation that includes knowledge, technical and behavioral skills. **Objective:** This study proposes an innovative educational framework describing competency acquisition in neonatal resuscitation incorporating elements of deliberate practice, distributive practice as well as self-reflection as described by Bandura's social cognitive theory. In addition, the development of strategies to deal with the 'choke phenomenon' (performance under pressure) further adds to perception of self-efficacy and preparedness for practice. The project will aim to answer the following research questions using focus groups in a qualitative research design. 1) How are residents prepared for competency acquisition and independent practice in neonatal resuscitation? 2) What are the perceived gaps in training? 3) Why, in their view, do these gaps exist? **Methods:** This project will employ a qualitative methodology grounded in the educational theory described above using focus groups for data collection. Using an interpretive qualitative research

design, this study will employ semi-structured focus groups for data collection. In this study, separate focus groups of residents in training and recent graduates will explore the reasons for gaps in training from first-hand experience. The analysis will be grounded in a framework using a three-stage method of constant comparison: open, axial and selective coding. **Results:** Preliminary results from the focus groups speak to the inadequacy of current residency training models to ensure competency acquisition in neonatal resuscitation. Technical skills seem an area of particular concern. Limited exposure has emerged as an evolving concern inhibiting competency acquisition. The use of simulation as a training modality, while acknowledged for some degree of knowledge transfer, has several limitations, primarily the inability to deal with the "choke" phenomena. **Conclusion:** This study explores and seeks to generate theory for the first time that addresses the question: "Why do residents feel unprepared for independent community practice in neonatal resuscitation?" using qualitative research methods. The results of this study will lend itself towards curriculum development across all levels of trainees.

P97

PHARMACOKINETICS OF INTRAVENOUS PENTOXIFYLLINE IN PRETERM INFANTS

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Introduction: Preliminary data suggest that the methylxanthine Pentoxifylline may improve survival in newborn infants with sepsis. There is a paucity of data on the pharmacokinetics of Pentoxifylline in preterm infants. **Objective:** A preliminary investigation of the pharmacokinetic properties of Pentoxifylline in very preterm infants. **Methods:** In this open-label pilot trial, very preterm infants with suspected late-onset sepsis and/or necrotizing enterocolitis were given intravenous Pentoxifylline and serial small volume blood samples were collected. Concentrations of Pentoxifylline and its metabolites M1, M4 and M5, and Caffeine, were measured using in both low-volume plasma and dried blood spot samples by LC-MS/MS analysis, for the purpose of population pharmacokinetic modelling. **Results:** 24 very preterm infants (mean birth gestational age 25.4 weeks; mean birth weight 784g) received adjunct treatment with intravenous Pentoxifylline for suspected late-onset sepsis and/or necrotizing enterocolitis (average postnatal age of onset: 20 days). No side effects were observed. Determination of the concentrations of Pentoxifylline and its metabolites in low-volume plasma and dried blood spot samples were feasible and showed high degree correlation. Preliminary results suggest that Pentoxifylline concentrations were in a similar range compared to previous data from term neonates. Further, Caffeine concentrations apparently were not affected by concurrent treatment with Pentoxifylline. **Conclusion:** Adjunct treatment with intravenous Pentoxifylline in very preterm infants was well tolerated and achieved concentrations comparable to reported target ranges in term neonates. Pentoxifylline is being assessed as adjunct treatment for late-onset sepsis and or necrotizing enterocolitis in a large international clinical trial.

P99

IMPACT OF ANTENATAL GLUCOCORTICOIDS IN PRETERM NEONATES BASED ON MATERNAL BODY MASS INDEX

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Introduction: Antenatal glucocorticoids (AGCs) are administered to women at risk of preterm delivery to reduce neonatal mortality and morbidity, but is currently dosed regardless of the maternal body mass index (BMI). The impact of AGCs in the context of maternal BMI as it relates to neonatal outcomes remains unclear. **Objective:** To evaluate the interaction between ACG status (complete, partial or none) and maternal BMI on clinical outcomes of preterm infants. **Methods:** We performed a retrospective cohort study among neonates 23-33 completed weeks GA cared for at a tertiary level neonatal intensive care unit between 2011 and 2015. The cohort was stratified into 3 groups: a) partial ACG (N = 213), b) complete ACG 1-7 days prior to delivery (N = 360) and c) complete ACG > 7 days prior to delivery (N = 423).

Infants born to mothers with BMI > 25 (exposure) were compared to infants born to mothers with BMI < 25 (control) within each group. The primary outcome was a composite outcome of mortality or any one of the following morbidities: bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, nosocomial infection, severe brain injury. Logistic regression models were created adjusting for an allowable number of co-variates that were different in univariate analyses. Adjusted odds ratios and 95% confidence intervals for various neonatal outcomes were calculated, and p-value < 0.05 was considered significant. **Results:** Preterm neonates born to mothers with pre-pregnancy BMI > 25 and exposed to partial course of AGC (aOR 1.36 [0.52-3.60]), complete course of AGC 1-7 days prior to delivery (aOR 1.16 [0.59-2.26]), and complete AGC course > 7 days prior to delivery (aOR 1.45 [0.76-2.59]) were not at increased risk of the primary outcome compared to infants born to mothers with BMI < 25. Among preterm neonates exposed to partial course of AGC, maternal pre-pregnancy BMI > 25 led to increased the odds of mortality (aOR 3.40 [1.11-10.41]), but no difference was found in the complete AGC groups. There were no differences in individual neonatal morbidities in any of the 3 AGC groups based on maternal BMI status. **Conclusion:** Impact of AGCs on neonatal outcomes do not appear to be influenced by maternal BMI. Further research is required to elucidate the impact of BMI on ACGs with regards to neonatal outcomes.

P101

MILRINONE-INDUCED ANAPHYLAXIS IN A NEONATE: A CASE REPORT

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Introduction: Milrinone is increasingly used in neonates to improve cardiac function in cases of shock, pulmonary hypertension and post-cardiac surgery. Pharmacokinetic and safety data are limited, especially in preterm neonates. We describe an apparent anaphylactic reaction to milrinone infusion in a preterm neonate with pulmonary hypertension **Case Report:** A male preterm infant was born at 29 weeks' gestation to a hypertensive mother on labetalol. The baby was severely growth restricted (birth weight: 485 g) secondary to placental insufficiency. **Methods:** On the first day of age, he was transferred to the tertiary Neonatal Intensive Care Unit (NICU) at the IWK Health Centre with an intestinal perforation. Following resection of 8 cm of ileum and creation of mucous fistula, his course in the NICU was complicated by severe bronchopulmonary dysplasia requiring high setting of assisted mechanical ventilation. At 90 days of age (41 weeks corrected gestational age), he was started on inhaled nitric oxide for severe pulmonary hypertension diagnosed by echocardiography. Milrinone, at a dose of 0.5 microgram/kg/minute was later started because of markedly impaired right ventricular function. **Results:** The medication was stopped 12 hours later as the baby developed red raised rash on most of his trunk, cheeks and around the neck, hypotension (55/23, mean of 32 mmHg), and a temperature of 37.9oC. Blood pressure stabilized within half an hour of stopping milrinone infusion (57/35, mean of 44 mmHg). Temperature normalized within an hour and the rash gradually resolved the next day. The patient was being treated with Cloxacillin and gentamicin but complete blood count, C-reactive protein and blood culture showed no evidence of infection. The next day, he was started on Epoprostenol infusion for his pulmonary hypertension. Unfortunately, he died 7 days later due to worsening of his respiratory failure and pulmonary hypertension. **Conclusion:** To our knowledge, this is the first case report of an apparent anaphylactic reaction to milrinone in a neonate. Anaphylaxis is diagnosed when there is an acute onset of illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both AND at least one of the following: (a) Respiratory compromise (b) Reduced blood pressure or associated symptoms of end organ dysfunction. Although hypotension in our case could have been attributed to the milrinone vasodilator effect, the development of skin rash and fever, together with the rapid improvement on stoppage of the medication, support the diagnosis of an anaphylactic reaction. Clinicians prescribing milrinone for neonates should be aware of this uncommon occurrence.

P103

ESCALATED CARE EVENTS TO PREDICT NEONATAL OUTCOMES IN PRETERM INFANTS

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Introduction: Introduction-Infants admitted to neonatal intensive care unit (NICU) often experience escalated care

events (ECE), but their impact on outcomes is unknown. **Objective:** To determine the clinical outcomes of preterm infants < 33 weeks GA born to mothers with and without ECE. **Methods:** A prospective comparative study was conducted on all preterm infants <33 weeks' gestation admitted to a tertiary NICU between Nov 2015 & May 2016. ECEs made up the study group. ECEs included intubation/reintubation, initiation of inotropes, inhaled nitric oxide therapy, Plasma/Platelet transfusion, Cardiopulmonary resuscitation, and 2nd episode of positive pressure ventilation in a 12-hour period. Outcomes at discharge among infants with ECE were compared with infants without ECE. **Results:** Of 165 admitted infants, 51(30.9%) had ECE. The median gestational age was lower (30 weeks vs. 27 weeks), and SNAPPEII scores (7 vs 33) were higher in infants with ECE. Mortality [OR (95% CI) 12.2(1.39-108); P 0.02], BPD [OR (95% CI) 5 (2.2, 11.2); P 0.0001] and survival with morbidity [OR (95% CI) 7.34 (3.37-15.9); P <0.0001] were higher in infants with ECE. ECE was identified as an independent predictor of survival with morbidity [Adjusted OR (95% CI) 1.48 (1.48, 14.68)]. **Conclusion:** Infants experiencing ECE have higher mortality and morbidity. Whether precursors of ECEs are identifiable and timely intervention could avert ECEs should be explored.

P105

MIMICKING UPPER AIRWAY OBSTRUCTION INCREASES GASTROESOPHAGEAL REFLUXES IN NEWBORN LAMBS

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Introduction: Gastroesophageal refluxes (GER) are common in the healthy human newborn. In certain conditions, however, increased GER can cause deleterious complications, such as esophagitis and apnea-bradycardias. Studying the conditions that can raise the number of GER is essential to prevent those complications. Although it is a commonly accepted that upper airway obstruction (UAO) increases GER, direct evidence of this association is very scant. **Objective:** To test the hypothesis that mimicking a moderate/severe UAO increases the number of GER in newborn lambs. **Methods:** Ten newborn lambs were included in the study. They were instrumented with an esophageal impedance-pHmetry catheter as well as for recording states of alertness, EKG, tracheal pressure, respiratory movements, oximetry and arterial blood gases. In addition, a nasal mask with an adjustable inspiratory resistance was installed, in order to mimic a moderate to severe UAO, i.e., with a peak inspiratory tracheal pressure around - 15 cmH2O for several hours. Each lamb underwent 6-hour polysomnography recordings in control and UAO conditions, on two consecutive days and in a randomized order. Inspiratory O2 fraction was increased as needed to maintain PaO2 above 60 mmHg throughout the UAO recording. Statistical analyses of the tracings were done using IBM SPSS Statistics 22 and the R programming language. Results are expressed in medians and interquartile intervals. **Results:** The target tracheal pressure could be maintained in all lambs throughout the six-hour UAO recording [-13 cmH2O (-15, -12) in UAO vs. -1 cmH2O (-2, -1) in control condition, p = 0.005]. Increasing inspiratory O2 adequately limited the significant decrease in PaO2 during UAO [79 mmHg (75, 83) vs. 89 mmHg (87, 93) in control condition, p = 0.005]. Likewise, alterations of PaCO2 [42 mmHg (38, 47) in UAO vs. 41(37, 42) in control condition, p = 0.05] and pHa [7.43 (7.41, 7.73) vs. 7.45 (7.44, 7.46), p = 0.02] were significant but limited. Overall, the number of GER in six hours was significantly elevated in the UAO compared to the control condition [2(1, 4) vs. 0(0, 3), p = 0.02]. **Conclusion:** Our results bring direct evidence that GER are significantly, though modestly, increased in our unique newborn ovine model of UAO. Further studies will attempt to unravel the UAO-related alterations of the esophagogastric junction components responsible for ensuring the anti-reflux function, including the lower esophageal sphincter and the crural diaphragm.

THEME: Neonatology II – Neurosciences

P107

THE INFLUENCE OF PLACENTAL GROWTH FACTOR ON MOUSE RETINAL VASCULAR DEVELOPMENT

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Introduction: Preeclampsia, a human hypertensive disease of pregnancy, is associated with placental growth factor (PGF) deficiency. Children born to preeclamptic mothers display cognitive impairments and have structural and vascular alterations in the central nervous system including in the retina. Low angiogenic factor production in utero may be one mechanism by which offspring vascular changes occur. **Objective:** Since retinal vascular development in mice is well-described and easily visualized ex vivo, we investigated the role of PGF in vascularization of the retina using a Pgf gene-ablated mouse model. **Methods:** Retinal vessels were compared between normal C57BL/6 (B6) and congenic Pgf-/- mice at postnatal day (P)5, P8, P15 and in adult males, non-pregnant females and gestational day (GD)11.5 females. Vessels were imaged using whole mount immunofluorescence with isolectin B4, anti-α-actin and anti-collagen IV staining for endothelium and vessel wall components. The number of cells positive for the macrophage/microglia marker Iba1 as well as expression of VEGFA was examined with immunohistochemistry. Quantitative PCR was used to examine whole retina smooth muscle actin, collagen and chondroitin sulfate proteoglycan (NG2) expression. **Results:** Transient differences in neonatal angiogenesis that permanently altered adult vessel organization were identified in Pgf-/- retinas with greater impacts in males. In adult females studied at GD11.5, pregnancy had subtly altered B6 and Pgf-/- retinal vasculature. There were no differences in the number of Iba1+ cells or expression of VEGFA in neonatal retinas or in expression of smooth muscle actin, collagen IV or NG2 in adult whole retinas. Sexually dimorphic structure was present in the retinal plexus of both B6 and Pgf-/- mice. **Conclusion:** PGF has a role in vascularization of the developing retina suggesting that PGF deficiencies in preeclamptic pregnancies may contribute to the reported cerebrovascular alterations of offspring.

P109

CEREBRAL OXYGENATION MONITORING OF PREMATURE INFANTS DURING THE INFANT CAR SEAT CHALLENGE TEST

M. Farooqui, G. Srinivasan, Y. Ethawi, R. Alvaro, M. Narvey

Introduction: **I**nfant Car Seat Challenge (ICSC) prior to discharge is recommended by the American Academy of Pediatrics and Canadian Pediatric Society for all Preterm infants for to rule out systemic desaturation in a reclined Car Seat. Cerebral regional oxygenation through Near Infrared Spectroscopy (NIRS) determines whether or not regional oxygenation is affected during periods of systemic desaturation, bradycardia or both. **Objective:** To determine cerebral regional oxygenation during periods of systemic desaturation or bradycardia in infants ready for discharge while seated in a car seat. **Methods:** Prospective observational study in twenty infants {32 + 5 weeks (Mean + SEM) PMA 37+6weeks} performed by placing a NIRS transducer positioned on the head during ICSC. A failure of an ICSC was defined as two desaturations below 85% for more than 20 seconds or one event below 80% for ten seconds. **Results:** From June 2015 to February 2016 a total of 20 infants who met study criteria and were enrolled. For twenty patients, the lowest systemic saturation was 70% with a lowest NIRS recording of 68%. Heart rate but not systemic saturation appears to influence cerebral oxygen saturation. Three patients failed their ICSC, with none recording a cerebral saturation below 68%. **Conclusion:** We found no episodes of significant cerebral desaturation in any patients studied regardless of whether they passed or failed the ICSC. Heart rate but not systemic saturation appears to influence cerebral oxygen saturation. We postulate that former preterm infants are able to maintain adequate cerebral blood flow through cerebral autoregulation during periods of systemic desaturation or bradycardia when ready for discharge. Given the lack of effect on cerebral oxygenation, we question the need for such ICSC testing prior to discharge as part of routine planning.

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CEREBRAL OXYGENATION MONITORING OF PREMATURE INFANTS DURING THE INFANT CAR SEAT CHALLENGE TEST

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Introduction: The American Academy of Pediatrics and until recently the Canadian Pediatrics Society recommend preterm infants undergo an Infant Car Seat Challenge test (ICSC) prior to discharge to rule out systemic desaturation when placed at a 45-degree angle in a car seat. Near infrared Spectroscopy (NIRS) provides objective measurements of the impact of systemic oxygen desaturation, bradycardia or both on cerebral regional oxygen saturation (rSO2) **Objective:** To determine rSO2 during periods of systemic desaturation or bradycardia in infants ready for discharge while seated in a car seat. **Methods:** Prospective observational study in twenty infants {(32 ± 5 weeks (Mean) + SEM 5, SD22)} PMA 37 ± 6 weeks (Mean), SEM 5, SD 2. A failure of an ICSC was defined as two oxygen desaturation events below 85% for more than 20 seconds or one event below 80% for ten seconds. From previous research a normal rSO2 is generally accepted to be 55 – 85%. **Results:** The lowest SO2was 70% with a lowest NIRS recording of 68%. Three patients failed their ICSC, however none of these patients recorded a cerebral saturation below 68%. Heart rate but not SO2 appears to influence rSO2 over the range of cerebral oxygenation seen **Conclusion:** We observed no episodes of significant cerebral oxygen desaturation in any patients studied regardless of whether they passed or failed the ICSC. We postulate that the former preterm infant is capable through cerebral autoregulation, to maintain adequate cerebral blood flow in the presence of systemic oxygen desaturation or bradycardia when they have reached the point of being ready for discharge. Given the lack of effect on cerebral oxygenation we call into question the need for performing such ICSC testing prior to discharge as part of routine planning.

P113

LATE PRENATAL DEXAMETHASONE EXPOSURE AND INDUCED FETAL PROGRAMMING OF BEHAVIOURAL DEFICIENCIES

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Introduction: Prenatal exposure to stress during critical periods of fetal growth and development has serious behavioural and health implications for the offspring. The effects of prenatal exposure to stress are poorly understood; evidence is accumulating that these vulnerabilities span future generations. **Objective:** To investigate potential behavioural deficits on the F1 generation in response to prenatal stress exposure. **Methods:** Pregnant Wistar-Kyoto rats were exposed to one of two treatment regimes during the equivalency of the third trimester (beginning on gestational day 15): daily IP injections until birth of 1) a synthetic glucocorticoid, dexamethasone (DEX; 100µg/kg/day) or 2) vehicle (4% ethanol with 0.9% saline). A third group received only physical manipulation to serve as a naive control. The offspring from each litter (F1 generation) were allowed to mature and were tested during week 17 for indications of anxiety and depression through use of the Elevated Plus Maze (EPM) and the Porsolt Swim Test (PST) respectively. Neural tissue from each generation was collected and stored at -80°C for histological and immunohistochemical (IHC) processing to investigate deficits in neurogenesis and changes in glucocorticoid receptor expression. A 2.2 Multiple Analysis of Variance was conducted to analyze differences between gender and treatment conditions. **Results:** The F1 DEX condition spent significantly more time immobile during the Porsolt Swim Test than the Naive condition: $\lambda = 0.046$, $F(4, 12) = 61.977$, $p = 0.001$. Data from qPCR on hippocampal tissue will also be presented. **Conclusion:** Results indicate exposure to prenatal DEX predisposes adult offspring to exhibit depressive-like behaviours in adult offspring

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SEARCHING FOR THE "GOLD STANDARD" OF INFANT ACUTE PAIN ASSESSMENT: A SCOPING REVIEW OF NEUROCOGNITIVE METHODS

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Introduction: Untreated pain in infants is associated with immediate and long term adverse effects. Despite this, pain continues to be under assessed and treated. This may be associated with a lack of established "gold standard" to

measure pain in this non-verbal population. While infant pain assessment has historically relied on measuring behavioural pain responses, the study of neurocognitive imaging methods as a newborn pain indicator is an emerging trend. Such technology may enable novel research and clinical advancements in newborn pain assessment. However, to date, there is a lack of synthesis and evaluation of the neuroimaging technologies, data collection and analysis procedures, and study findings to allow recommendations for future work in the field. **Objective:** The aim of this work was to describe the neurocognitive methods that have been used to construct the scientific knowledge base in the field of infant acute pain assessment. **Methods:** A systematic search of key electronic databases (CINAHL, PubMed, PsycINFO, EMBASE) was conducted from database inception to October 2015. The search strategy included key terms for infant, acute pain, pain response, and neurocognitive imaging methods. Of the 2411 abstracts screened, 19 articles were retained and data on study methodology and results were extracted. **Results:** Of the included studies, nine utilized near infrared spectroscopy (NIRS), two utilized functional magnetic resonance imaging (fMRI), and eight utilized electroencephalography (EEG) as the primary outcome. There was variability in research designs and procedures in those studies utilizing NIRS, whereas studies utilizing EEG and fMRI reported consistent methods across studies. Of the eight EEG studies, six reported event-related potentials (ERPs) as the primary outcome. All of the ERP studies identified a distinct nociceptive-specific potential, which was found to be stimulus intensity dependent, independent of sleep state, and present in preterm and full term infants. **Conclusion:** Of the neurocognitive methods used to date, ERPs appear to be the most sensitive, specific, and reliable indicator of infant nociception. While additional research is needed, ERPs appear to be a valuable neurocognitive indicator to supplement behavioural pain tools for use in clinical research to advance our understanding of infant pain response.

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CEREBRAL SIALOGLYCOPROTEIN IMPRINTING FOLLOWING A PERINATAL INFLAMMATORY INJURY

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Introduction: White matter injury in the premature infants leads to substantial long-term neurodevelopmental disabilities and remains one of the most challenging clinical problems in neonatal neurology. A robust model of inflammatory white matter injury in the immature rat brain has been developed using ultrasound-guided injection of lipopolysaccharide (LPS) into the corpus callosum. Our preliminary data showed high resemblance between the pathological changes observed in LPS-treated neonatal brains with those observed during neurological lysosomal disorders suggesting that exposure to inflammation causes lysosomal accumulation and contributes to white matter injury and neuronal dysfunction. **Objective:** The aim of current study was to characterize short and long-term effects of inflammation in the neonatal brain on lysosomal catabolism and endo-lysosomal compartment in brain cells. **Methods:** Postnatal-day-3 (P3) rat pups were randomly distributed in two groups (n=8): (1) Escherichia coli LPS injection (62.5 mcg/kgBW) in the corpus callosum under ultrasound guidance; (2) Saline injection in the corpus callosum. Brains were collected at P4 (n=8) and P24 (n=8) and we measured specific activities of lysosomal enzymes - sialidase, β-galactosidase and β-hexosaminidase in the mid-region of brains homogenate were assayed using the corresponding fluorogenic substrates. **Results:** At both P4 and P24, sialidase activity level was significantly increased in the treated animals. After 24 hours of injection, the sialidase activity (nmoles/h/mg) reached to 6.13±1.00 compared with 2.87±0.57 in control animals ($p=0.0134$); at P24 the sialidase activity was increased in a similar manner, 4.08±0.26 for LPS-exposed as compared with 1.42±0.24 in control animals ($p<0.0001$). No apparent differences in β-galactosidase and β-hexosaminidase activities between treated animals and control group were observed. **Conclusion:** Altogether our data demonstrate that white matter injury results in changes of lysosomal catabolism at P4 that remained at P24. The increase of sialidase activity attributing to the elevated desialylation process may lead to desialylation of surface glycoproteins (and possibly glycolipids) on brain cells resulting in long-term alterations in CNS function.

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MATERNAL FACTORS INFLUENCING THE RISK OF ADVERSE OUTCOME IN ASPHYXIATED NEWBORNS TREATED WITH HYPOTHERMIA: PARITY AND LABOR DURATION MATTER

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Introduction: Birth asphyxia is a common cause of perinatal mortality and long-term neurodevelopmental sequelae. The only available treatment for this condition is hypothermia that may prevent the development of brain injury. However, the success of this therapy is limited and much remains to be understood why some asphyxiated newborns continue to develop brain injury despite hypothermia **Objective:** To determine the possible association between some maternal factors and the development of adverse outcome in asphyxiated newborns treated with hypothermia. **Methods:** We conducted a retrospective cohort study of asphyxiated newborns admitted in a single neonatal intensive care unit and treated with hypothermia between 2008 and 2015. Adverse outcome was defined as evidence of brain injury and/or death within the perinatal period; severity of brain injury was assessed on brain magnetic resonance imaging (MRI) using a previously described MRI score. Maternal characteristics were compared between the asphyxiated newborns treated with hypothermia who developed adverse outcome and those who did not. **Results:** Newborns born from mothers who did not have a previous child had significantly more risk to develop adverse outcome (61%), compared to newborns born from mothers who had already one (19%) or more children (20%) ($p = 0.002$). Longer duration of vaginal delivery was also associated with more risk of adverse outcome ($p = 0.03$). In addition, mothers whose pregnancy was complicated with diabetes had more risks to have a baby with adverse outcome ($p = 0.046$) **Conclusion:** Mothers who did not have a previous child, especially when they are experiencing prolonged duration of labour, are at higher risk to have an asphyxiated newborn developing adverse outcome despite therapeutic hypothermia. Labor duration beyond 10 hours in these women should be closely monitored.

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NEURODEVELOPMENTAL OUTCOMES OF PRETERM INFANTS <29 WEEKS GESTATION BASED ON LOCATION OF BIRTH IN CANADA

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Introduction: We have reported a higher risk of adverse neonatal outcomes in outborn infants compared to those born within a tertiary center; however data on neurodevelopmental outcomes are limited. Table 1: Comparison of outcomes adjusted for confounders * Any conductive or sensorineural loss #Unilateral or bilateral. **Objective:** To compare mortality and neurodevelopmental outcomes of preterm infants of <29 weeks gestation born in vs outside a tertiary care center **Methods:** Data were obtained from the Canadian Neonatal Network and Canadian Neonatal Follow-up Network databases for infants of <29 weeks gestation admitted to a tertiary NICU April 2009- September 2011. Death, significant neurodevelopmental impairment (sNDI) (severe cerebral palsy (CP), Bayley-III motor, language or cognitive score < 70 or severe sensory impairment) and NDI (any CP, any Bayley-III < 85 or any sensory impairment) at 18-21 months corrected age were compared between outborn and inborn infants after adjustment for confounders (GA, SGA, multiples, antenatal steroids, SNAP-II score and mode of delivery). **Results:** Of a total of 2951 infants, 2478 (84%) were inborn and 473 (16%) were outborn. Mean BW (897g vs 940g), receipt of antenatal steroids (94% vs 54%), SGA (9.4% vs 5.3%) and caregiver education were different between inborn and outborn respectively. Median SNAP-II score and 5 minutes Apgar were higher in inborn whereas admission TRIPS score was lower. **Conclusion:** Mortality or adverse neurodevelopmental outcomes are significantly higher in preterm infants <29 weeks GA born outside of a tertiary care center.

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MATERNAL NUTRIENT RESTRICTION (MNR) IN GUINEA PIGS LEADING TO FETAL GROWTH RESTRICTION (FGR): IMPACT ON BRAIN MYELINATION

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Introduction: FGR has been linked to later neurodevelopmental disability including cognitive impairment, ADHD and autism. Since these deficits often relate to memory and learning, aberrant neuronal connectivity in the hippocampus and its efferent tracts are likely to be involved. While studies in FGR guinea pigs after uterine artery ligation show myelination to be reduced, this has not been studied with MNR induced FGR which is likely to be insidious through pregnancy and more analogous to the human situation. **Objective:** To determine if moderate MNR in guinea pigs leading to asymmetric FGR results in reduced myelin basic protein (MBP) immunoreactivity (IR) as a critical protein in myelin formation and function. **Methods:** Guinea pig sows were fed ad libitum (Control) or 70% of the control diet pre-pregnancy increased to 90% at mid-pregnancy (MNR), with animals necropsied at 60/61 days gestation (term= 68 days). Control fetuses >80g (appropriate for gestational age or AGA, N=18) and MNR fetuses <80g (FGR, N=18) had brain tissues immersion fixed for immunohistochemical study of MBP IR using an Aperio Slide Scanner. Intensity of MBP was quantified using image analysis software for multiple white matter tracts including the fornix and alveus, as hippocampal efferent tracts. Results are presented as group means±SEM. **Results:** FGR-MNR fetal weights were decreased ~37% at 63±3g vs the AGA-Controls at 101±2g ($p<0.01$). FGR-MNR brain weights were also decreased, but less so, by ~12% at 2.40±0.05g vs the AGA-Controls at 2.74±0.05g ($p<0.01$) and indicating a degree of brain sparing. Examination of MBP IR revealed no significant differences in the alveus, fornix and optic tract. However, MBP intensity was increased in the FGR-MNR fetuses compared to the AGA-Controls in the corpus callosum at 84.18±2.96 vs 74.98±2.52 ($p<0.05$) and the parasagittal white matter at 111.73±3.60 vs 101.79±2.30 ($p<0.05$). **Conclusion:** Moderate MNR in guinea pigs results in asymmetric FGR and while brain weights are still reduced, there was no evidence for decreased myelination as assessed using MBP and seen with uterine artery ligation FGR. This may reflect the insidious nature of MNR FGR vs the abrupt nature of uterine artery ligation FGR and the extent to which protective mechanisms can be enacted to maintain myelination. However, the reduction in brain weights is likely to involve reduced neuropil, compacting axonal tracts which could be regional and accounting for the increased MBP intensity seen.

THEME: Nursing and Midwifery

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BREASTFEEDING IN THE CANADIAN HEALTHY INFANT LONGITUDINAL DEVELOPMENT (CHILD) STUDY: EARLY INTENSITY PREDICTS LONG-TERM DURATION

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Introduction: Breastfeeding is an important factor supporting infant growth and development. International breastfeeding guidelines recommend exclusive breastfeeding for 6 months and continued breastfeeding until 2 years. **Objective:** The aim of this study was to describe and explore associations between breastfeeding initiation, intensity and duration in a national cohort of Canadian children. **Methods:** We used data from 3412 children in the CHILD birth cohort across four Canadian communities. Newborn feeding was documented from hospital records and mothers reported infant diet at 3, 6 and 12 months. Breastfeeding status in hospital and at 3 and 6 months of age was classified as exclusive (human milk only), partial (supplemented with infant formula, other beverages or solid food), or none. Associations were determined by multiple logistic regression. **Results:** Initiation of breastfeeding was 97% with 76% exclusively breastfeeding in hospital. Breastfeeding rates were 83% (47% exclusive) at 3 months, 71% (13% exclusive) at 6 months, 40% at 1 year and 7% at 2 years. Exclusive breastfeeding in hospital predicted an increased likelihood of extended breastfeeding. Newborns who were exclusively breastfed in hospital were more likely to be breastfed at 3 months (OR=3.46 95% CI: 2.79-4.29), 6 months (OR=2.62, 2.17-3.15) and 1 year (OR=1.99, 1.64-2.40) compared to those who received supplements. These associations persisted after adjusting for maternal age and key predictors of supplemental feeding in hospital (caesarean delivery, low maternal education, ethnicity, and high maternal body mass index); adjusted odds ratios were 2.99 (CI: 2.28-3.94), 2.15 (CI: 1.72-2.69) and 1.69 (CI: 1.36-2.09), respectively. **Conclusion:** Breastfeeding exclusivity in the first days of life can be an important predictor of total breastfeeding duration. Baby-friendly initiatives that support exclusive breastfeeding of newborns could have a long-term impact on extended breastfeeding rates, with significant benefits for child health.

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USE OF A MATERNAL NEWBORN AUDIT AND FEEDBACK SYSTEM IN ONTARIO: A CASE STUDY COMPARISON

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Introduction: In November 2012, BORN Ontario implemented the Maternal Newborn Dashboard (MND), an audit and feedback system for all maternal-newborn hospitals in Ontario. As part of a larger study to evaluate use of A&F to improve care, we conducted a case study comparison of a diverse group of maternal-newborn hospitals in Ontario. **Objective:** To improve our understanding about the factors that explain variability in performance after implementation of the MND. **Methods:** A criterion-based approach was used to identify a purposeful sample of hospitals reflecting different levels of care, birth volumes, geographic locations, degree of engagement with the MND, and success related to improvement in rates on the MND key performance indicators (KPIs). The obstetrical director/manager from each hospital was contacted to invite the site to participate in a 1-2 day visit by the research team. The site visits comprised: (1) interviews and focus groups using a semi-structured interview guide with health care providers, leadership, and other key personnel involved in clinical change processes; and (2) observations and document review. Interviews and focus groups were audio-recorded and transcribed verbatim. Qualitative content analysis was used to code and categorize the data. **Results:** Between June and November 2016, we visited 13 maternal-newborn hospitals. Findings revealed diverse hospital experiences and numerous factors that contributed to the varying success of sites in facilitating practice change on the MND KPIs. Hospitals that were successful in making positive changes on the KPIs described facilitators including (i) useful features of the MND (e.g. visual cues and tangible metrics); (ii) trusting the evidence; and

(iii) team characteristics (e.g. interprofessional collaboration and communication). Hospitals with less change on the KPIs described barriers including (i) lack of alignment between KPIs and organizational priorities; (ii) lack of resources to implement changes; and (iii) challenges using and understanding the MND. **Conclusion:** This case study comparison has increased our understanding of factors that influenced use of the MND to improve practice related to six KPIs in a diverse group of hospitals in Ontario. The identified barriers and facilitators will inform strategies to improve the design and use of this audit and feedback system in the future.

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ORGANIZATIONAL READINESS FOR KNOWLEDGE TRANSLATION (OR4KT) IN ONTARIO MATERNAL NEWBORN HOSPITALS: OF A PROVINCIAL SURVEY

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Introduction: In November 2012, BORN Ontario implemented the Maternal Newborn Dashboard (MND), an audit and feedback (A&F) system for all maternal-newborn hospitals in Ontario. As part of a larger study to evaluate use of A&F to improve care, we conducted a survey, which included the OR4KT tool. **Objective:** To (1) validate the OR4KT tool in maternal-newborn hospital settings and (2) identify factors that influence MND use. **Methods:** The obstetrical director/manager at each Ontario maternal-newborn hospital was invited by email to complete the online survey including the OR4KT questions. The OR4KT is comprised of 6 dimensions each scored out of 50: organizational climate for change (respondents' appraisal of the internal organizational environment), organizational context (circumstances under which the change is occurring), change content (proposed or actual changes triggered by MND), leadership (collective involvement for change), organizational support (how organizations support and sustain change) and motivation (collective desire to make an effort toward goals). Responses were collected on a 5-point Likert scale. OR4KT responses were scored and descriptive statistics produced. **Results:** Between October 2015 and February 2016, the survey was sent to 88 contacts representing 94 Ontario maternal-newborn hospitals. The response rate was 51% (45/88). Sixty-seven percent (30/45) of respondents were managers/directors of maternal-newborn units. The mean total OR4KT score was 225.7 (range: 162-270) out of 300 (SD=22.0). The means for the 6 dimensions were: organizational climate for change, 38.6 (SD=4.7); organizational contextual factors, 36.5 (SD=4.2); change content, 39.2 (SD=4.0); leadership, 38.0 (SD=4.9); organizational support, 36.8 (SD=5.5); and motivation, 37.4 (SD=3.8). Collectively the sites surveyed demonstrated higher readiness for KT in the areas of climate for change, change content and leadership and less readiness in areas of organizational context, organizational support and motivation. **Conclusion:** The OR4KT has been validated in primary care settings, and the results of this survey will validate it for use in maternal-newborn care. Organizational barriers to change have been identified that will be used to develop tailored strategies to improve capacity for change and to facilitate uptake of best practices in maternal-newborn care.

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EVALUATING THE IMPLEMENTATION OF A RESIDENCY PROGRAM FOR NURSES IN A LEVEL 3 NEONATAL UNIT

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Introduction: The CHU Saint-Justine's neonatal unit includes a diverse and complex clientele where level 2 and 3 care is provided. Nurses working in this environment must possess a complete professional autonomy and a variety of skills and aptitudes to provide care to these families. However, over the past few years, the unit has been composed of a considerable amount of novice nurses with a high turnover rate. The existing training program was given over only a few weeks and had a success rate of 73% with an 85% retention. In this context, a new training program, in the form of a residency, was developed. The aim of this program is the fostering of skills development and the acquisition of professional autonomy for nurses joining the unit. Additionally, the implementation also aims to retain nurses and improve the quality of care provided. This program, which spans over a one-year period, is a significant change in the orientation process: it is made up of five different phases which includes the combination of theoretical and practical training, as well as autonomous practice. **Objective:** The objective of this research project is to assess appreciation, skill

development, as well as retention and success rates of novice nurses who joined the neonatal unit care team with the residency program. **Methods:** A survey was conducted with 42 nurses who joined the neonatal unit between June 2015 and October 2016. All nurses in the new training program filled an electronical survey, following the Likert model, after 3, 6 and 12 months of practice. The nurses' success and retention rate were also measured. **Results:** The results indicate that 92% of the nurses judged the training relevant to their practice, while 100% stated that the requirements of the program were adequate. 83% of the respondents confirm having acquired confidence in their organization and prioritization of care, while 75% consider to have developed their communication skills with families. The residency program increased the success rate to 98% with a retention rate of 85%. **Conclusion:** The results of the survey show that the residency program is an effective strategy for skills development and a successful orientation.

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EXPERIENCES OF MIDWIVES WHO ARE FACED WITH NEWBORNS AFFECTED BY BIRTH ASPHYXIA IN RURAL BIRTH SETTINGS, SOUTHERN GHANA

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Introduction: The increasing trend in global neonatal deaths over the past fifteen years has engaged global, regional, and national communities in seeking sustainable approaches to improve neonatal health outcomes. The major causes of these deaths are: preterm birth complications, intra-partum related complications (including birth asphyxia), and sepsis. Understanding the dynamic contextual factors underlying these neonatal deaths are important to inform priorities for improving newborn health outcomes in the new Sustainable Development Goal (SDG) 2015-2030 era. Birth asphyxia, a preventable respiratory emergency that leaves survivors with irreversible neuro-muscular deficits is associated with the quality of antenatal and intra-partum care. The worst affected are people who reside in rural communities within Sub-Saharan Africa where inequitable health coverage predominantly influences survival. In low-and-middle income countries, very little information exists on care experiences of midwives regarding birth asphyxia. However, midwives have developed rich experiences in maternal and newborn health as frontline health workers. Predominant factors related to the occurrence of birth asphyxia include lack of access to basic and comprehensive emergency obstetric and newborn care, poor referral systems, shortage of skilled staff, lack of basic life-saving devices, and care provider inadequacies. **Objective:** To understand, unveil the meanings and articulate the experiences of midwives who are faced with newborns affected by birth asphyxia in rural birth settings within southern Ghana. **Methods:** Interpretive phenomenology that incorporates Heideggerian philosophy was used to explore, unveil the meanings and articulate the experiences of midwives. Thirteen midwives were purposively sampled from rural birth settings in Southern Ghana. Data were generated through audio-recorded conversations with the midwives, field notes, and reflective journal. Emerging themes were synthesized from the verbal transcripts, field notes, reflective journal and commentaries from second readers to produce detailed understandings of the midwives' experiences. **Results:** Rural midwifery practice in Ghana is grounded in harmonious communal relationships within restricted health care spaces where silent suffering occur. Midwives experience moral distress and situation-helplessness within hegemonic power structures, and suffer emotional drowning when faced with asphyxiated newborns. The midwives subsequently adopt spirituality as a coping mechanism. Newly qualified midwives practice without mentorship in unsafe clinical spaces where ethical questions emerge as family members assist in resuscitative procedures **Conclusion:** New knowledge serves as basis for scaling up safe clinical practice, directing capacity building strategies and implementing research-informed policies to support midwifery practice, prevent birth asphyxia and improve newborn health outcomes in rural Ghana.

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FERTILITY PROBLEMS AND MENTAL HEALTH IN A POPULATION BASED COHORT

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Introduction: Infertility affects up to 15% of reproductive-aged couples worldwide and 16% of couples in Canada. The infertility rate for women ranges from 6-19% in the general population. Infertility is often considered only a medical condition but the experience of infertility has a considerable social, emotional, and psychological impact on women. **Objective:** To describe the characteristics of women who report a history of fertility problems during pregnancy, and

assessment of depression, anxiety, and stress during pregnancy and the postpartum period for women with fertility problems compared to women with no fertility problems. **Methods:** Population/Sample: The All Our Babies (AOB) is a prospective population based cohort study starting in May 2008 and designed to assess maternal and infant outcomes during pregnancy and the postpartum period in Calgary, Alberta. Methods/Measures: Women completed three questionnaires during pregnancy and at four and twelve months postpartum. Data was collected on maternal mental health through standardized tools including the Edinburg Postnatal Depression Scale (EPDS), the Spielberger State Anxiety Inventory (SSAI), and the Perceived Stress Index (PSI). **Results:** The proportion of women who reported a history of fertility problems was 7.2% of the entire AOB sample with longer times time to get pregnant for women who had a history of fertility problems, mean time to conceive of 22.3 months, compared to those women with no fertility problems, mean time of 4.3 months. Women who had a history of fertility problems were more likely to have had a previous first trimester miscarriage (51.8%) than women without fertility problems (34.4%). More women who required fertility treatment were over 35 years old compared to women without fertility problems. There were no significant differences in perceived stress and anxiety levels at any time point between the women with fertility problems and those without. At four months postpartum there was a difference between depression scores with 4.6% of women with no fertility problems having EPDS scores greater than 13 compared to women with fertility problems (2.5%). **Conclusion:** In the (AOB) population based cohort there were few significant differences between those women who required fertility treatments to conceive compared to those women who did not. Women who required fertility treatment took longer to conceive and had more first trimester miscarriages. More women with fertility problems were over the age of 35 years compared to those women who did not have fertility problems. Interestingly, women with fertility problems had a significantly lower likelihood of EPDS scores greater than 13 at the four-month postpartum time point. A possible explanation for women who conceive using fertility treatment is that having the experience of infertility positively alters women's perception of stress, disappointments, and worries.

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SYSTEMATIC REVIEW OF INTERVENTIONS FOR PARENTAL SENSITIVITY FOLLOWING PRETERM BIRTH.

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Introduction: Parental sensitivity predicting long term attachment is central to neurologic development in preterm infants. Although studies evaluating interventions promoting parental sensitivity in the neonatal intensive care unit (NICU) have been conducted, a systematic review of these studies is necessary for determining their overall effect and to make recommendations to guide clinical practice. **Objective:** To examine the effectiveness of interventions enhancing parental sensitivity of preterm infants' parents in NICU settings. **Methods:** The systematic review will be conducted following the roadmap for systematic review by Pai & al. (2004) and reported according to the PRISMA Statement. A systematic review of English and French articles will be done using CINAHL, PubMed and Medline, Embase, PsycInfo, Web of Science, Scopus and ProQuest with the key words sensitivity, premature infant and their related terms. References of identified papers will be searched to identify additional relevant studies. All experimental studies of interventions for enhancing parental sensitivity following preterm birth will be included. Study selection and quality assessment will be done by the two authors independently. **Results:** Preliminary results (including 9 articles) of the systematic review show that these interventions: are individualized and include parental participation in the preterm infant's care and teaching and learning of infant's communication cues. **Conclusion:** Preliminary results of this systematic review will guide clinical practice by formulating recommendations for implanting interventions in NICU clinical settings for enhancing parental sensitivity and hence, optimizing neurologic development of preterm infants. Furthermore, recommendations will also be made for research to further develop and evaluate interventions for enhancing parental sensitivity.

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BREAST MILK EXPRESSION AT THE NICU: EXPERIENCES OF MOTHERS EXPRESSING AT THEIR PRETERM INFANT'S BEDSIDE OR IN A BREAST MILK EXPRESSION ROOM

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Introduction: Breast milk expression at the preterm infant's bedside is recommended to promote breast milk production. However, there is limited evidence supporting this intervention and only a very few studies report on mothers' experiences of breast milk expression at their preterm infant's bedside. **Objective:** This pilot study with a mixed-method evaluation aimed to assess mothers' acceptability of breast milk expression at their preterm infant's bedside, explore their experiences, and compare these with those of mothers expressing in a room reserved for this purpose. **Methods:** Thirty-six mothers of preterm infants <30 weeks of gestation admitted to a level III neonatal intensive care unit (NICU) were recruited and randomly assigned to breast milk expression at their preterm infant's bedside in an open-bay unit (experimental group) or in a room (control group). After a three-week period, mothers' acceptability and experiences were evaluated through questionnaires and individual semi-structured interviews with open-ended questions. Interviews were recorded and transcribed for conventional content analysis. **Results:** Preliminary results show that both conditions were acceptable. Mothers who expressed at their preterm infant's bedside reported that it optimized their presence at the bedside, increased their physical and emotional closeness, and promoted involvement in care. The NICU stressful environment, as well as the lack of space and intimacy, were identified as the most difficult aspects of their experiences. Mothers in the control group appreciated the intimacy, comfort, convenience, and tranquillity of the room, but deplored its limited availability. They also reported being worried about missing medical rounds and important information. **Conclusion:** This pilot study has the potential to contribute to knowledge development on breast milk expression at the NICU, enlighten clinical practice, inform NICU design decisions, and guide future research on the promotion of breast milk production in mothers of preterm infants.

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FEASIBILITY OF REDUCING LIGHT AND NOISE LEVELS IN THE NICU DURING KMC: OF A PILOT STUDY.

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Introduction: Studies report that intense lighting and noise in the NICU influence outcomes of preterm infants and their mothers when they are experiencing KMC sessions. During KMC, intense lighting is reported as interfering with infants' quiet sleep, while mothers expressed that noise is a disturbing factor. As a dimmed and quiet environment during KMC may be beneficial for infants' and mothers' outcomes, the feasibility of reducing light and noise levels in the NICU during KMC was evaluated with a pilot RCT study. **Objective:** Evaluate the feasibility of reducing light and noise levels in the NICU during KMC. The intervention is intended to favor infants' physiological stability and sleep states as well as to reduce maternal anxiety and stress. **Methods:** Pilot RCT where 30 mothers-preterm infants were recruited from a level III NICU were randomly allocated to an experimental group [EG] (NICU light and noise reduction + KMC) (n=15) or to a control group [CG] (only KMC) (n=15). In both groups, the dyads were experiencing 3 KMC sessions lasting 1-hr over 7 days, so light and noise levels were recorded for a total of 90 KMC sessions (45 sessions/groups). In the EG, ambient lighting was reduced by turning off ceiling lights, procedural lamps, and closing windows blinds. Noise levels were lowered by reducing alarms equipment and telephone ringer along with closing the door's room and limiting entries of professionals/visitors in the room during KMC with a door sign. No attempts to modify light and noise levels were made in the CG during the KMC sessions. Light and noise levels were measured with a datalogging light meter and with a sound dBA-weighted scale meter that were placed near the dyads during the KMC sessions. **Results:** For mean light levels, a significant difference was obtained between the KMC sessions of the EG compared to the CG (EG:14.8 lux vs. CG:141.1 lux, p=0.01). The mean difference between light levels was still significant after controlling for the time of year and the time of the day. For ambient noise levels, no significant difference was obtained between the groups (EG: 47.3 dBA vs. GC: 49.4 dBA, p=0.08), but a significant difference was obtained for the proportion of time where the recommended maximum value of 65 dB was exceeded during the KMC sessions (EG: 0.52% vs. CG: 6.53%, p=0.0017). **Conclusion:** Findings of this pilot study confirm that it is feasible to reduce light and noise levels in the NICU during KMC and support a full-scale RCT evaluating the effects of this intervention on infants' and mothers' outcomes. Findings provide incentive toward the clinical guidelines relating to KMC as well as to the reduction of NICU light and noise levels.

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CONTINUITY OF MIDWIFERY CARE MODERATES THE EFFECTS OF PRENATAL MATERNAL STRESS ON POSTNATAL MATERNAL WELLBEING: THE QF2011 QUEENSLAND FLOOD STUDY

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Introduction: Poor postnatal mental health is a major public health issue, and risk factors include experiencing adverse life events during pregnancy. We assessed whether Midwifery Group Practice (MGP), compared to standard hospital care, would protect pregnant women from the negative impact of a sudden-onset flood on postnatal depression and anxiety. **Objective:** To determine the extent to which being followed in a Group Midwifery Practice buffers pregnant women from postnatal depression following exposure to the stress from a major natural disaster. **Methods:** Women received either MGP care in pregnancy, in which they were allocated a primary midwife who provided continuity of care; or they received standard hospital care provided by various on-call and rostered medical staff during labor and birth, and postnatally. All women in the study were pregnant when a sudden-onset flood severely affected Queensland, Australia, in January 2011. At recruitment into the QF2011 Queensland Flood Study within a few months of the disaster, women (n = 112) completed questionnaires on their flood-related hardship (objective stress), their emotional reactions (subjective stress), and cognitive appraisal of the impact of the flood (positive, neutral, or negative). Self-report assessments of the women's depression and anxiety were obtained during pregnancy and at 6 weeks and 6 months postnatally. **Results:** Controlling for all main effects, regression analyses showed there was a significant interaction between maternity care type and objective flood-related hardship and subjective stress, such that depression and anxiety scores at 6 weeks postpartum increased with increasing objective and subjective stress in the standard care group, but not in the MGP group, suggesting a buffering effect of continuity of midwifery care. There was no buffering effect, however, against postnatal distress at 6 months postpartum. **Conclusion:** The benefits of midwifery continuity of care in pregnancy clearly extend beyond a more positive birth experience and better birthing and infant outcomes, to mitigating the effects of high levels of objective hardship and subjective stress experienced by women in the context of a natural disaster on their mood up to 6 weeks postpartum.

P133a

EXPECTATIONS VERSUS REALITY: A SYSTEMATIC QUALITATIVE REVIEW OF IMMIGRANT WOMEN'S EXPERIENCE OF PREGNANCY IN A NEW COUNTRY

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Introduction: To date, most of the literature about immigrant women & pregnancy focuses on maternal & fetal outcomes, interactions with health care systems (HCS), & ethnographic studies exploring cultural beliefs in pregnancy. However, how immigrant women navigate these challenges is less well understood. **Objective:** The objective of this study was to understand the lived experiences of immigrant women in Canada & the United States, during pregnancy. Through synthesis of the current qualitative literature, we strove to develop a comprehensive framework to understand how different aspects of an immigrant women's life intersect to influence her overall experience of pregnancy. **Methods:** Five electronic databases were searched. To be included in our review, articles had to be of a qualitative study design, where data collection took place in North America, & focused on immigrant women's experiences of pregnancy. The Thomas & Harden (2008) thematic synthesis methodology was followed, which involved a 3-stage data analysis approach. **Results:** 19 of 3482 articles met the study inclusion criteria, were appraised, analysed & synthesized. "Expectations of pregnancy from home" & "reality of pregnancy in the host HCS" emerged as two of our meta-themes. These were connected by our third meta-theme, "social support", which acted as the broker between pregnancy expectations & reality. Women's expectations of pregnancy were influenced by their home traditions, which were supported by family & friends. However, having strong home expectations of pregnancy sometimes led to resistance with the host HCS. Specific host practices during pregnancy & labour, commonly differed from the way things were done in the country of origin. If women had limited support from their family, they turned to other immigrants & healthcare providers to be their primary sources of support. If positive relationships were developed with other immigrants &

providers, the immigrant mothers were more receptive to the host HCS. Finally, having a lack of any support resulted in the women having challenges navigating & interacting with the host HCS. **Conclusion:** As far as we know, this is the first study to provide a systematic review of immigrant women's experiences during pregnancy in both Canada & the United States. Immigration is a relevant issue in Canada, & pregnant women are among the most vulnerable. This study suggests that support from community sources can improve the chance that a new immigrant will affiliate with the HCS. HCS's may benefit from strategic investment in health care brokers for pregnant women, to improve the experiences of immigrant women & optimize pregnancy outcomes.

P133b

NEONATAL PAIN MANAGEMENT: BARRIERS TO AND FACILITATORS OF DATA ENTRY IN THE BETTER OUTCOMES REGISTRY & NETWORK (BORN) ONTARIO INFORMATION SYSTEM

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Introduction: All newborns undergo routine newborn screening, which causes pain and distress. In April 2014, a new data element was added to the Better Outcome Registry & Network (BORN) Information system (BIS) to capture information on use of three effective pain reduction strategies during newborn screening: breastfeeding, skin-to-skin care, and sucrose. **Objective:** The objective of this study was to identify the barriers and facilitators to (1) data entry of newborn pain treatment into the BIS and (2) implementation of pain treatment during newborn screening. **Methods:** Nurse managers from a representative sample of level I and II maternal-newborn sites in Ontario were invited by email to participate in a telephone interview. Using a semi-structured interview guide, participants were asked seven open-ended questions about pain management use at their hospital, barriers and facilitators to entering pain management information into the BIS, and suggestions for improvement. Interviews were transcribed verbatim and qualitative content analysis was completed to code and categorize data. **Results:** From May to August 2015, 16 nurse managers or their delegates from 15 sites were interviewed. Participants described barriers to entering pain management data into the BIS including lack of required documentation of pain treatment used in patient charts; lack of awareness of the data element; and perceived lack of importance of the data element due to it not being mandatory. Sites described variable use of pain management. Commonly identified challenges to using pain treatment included ergonomics and staff discomfort, and lack of education and policies. Facilitators to using pain management included consistency with the Baby-Friendly Initiative and best practice guidelines, and parent advocacy. Many participants identified the addition of the pain management data element in the BIS as a driver for improving clinical practice. **Conclusion:** Implementation of pain management strategies during newborn screening remains challenging. However, the introduction of the pain management element into the BIS has been driving practice change. The results of this study will be used to develop strategies to address the identified barriers to using pain management and entering the data in the BIS.

THEME: Perinatal Epidemiology

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COMPARISON OF OBSTETRICAL PRACTICES AND NEONATAL MORTALITY OF PRETERM INFANTS BORN IN FRANCE AND ONTARIO

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Introduction: The incidence of preterm birth has been steadily rising. There are notable practice variations between countries in the management of these births and consequently, differences in outcomes **Objective:** To compare obstetrical management and survival of preterm infants in France and Ontario using two large population based cohorts. **Methods:** EPIPAGE 2 is a population based prospective cohort study that collected information on maternal, pregnancy and obstetrical characteristics/interventions and neonatal outcomes from 25/26 regions in France on infants born between 22 to 34 weeks gestation over a period of 8 months in 2011. BORN (Better Outcomes Registry & Network) Ontario is a provincial pregnancy, birth and childhood registry that routinely collects maternal, obstetrical, and intrapartum information on all hospital births in Ontario. Data from the Canadian Institute for Health Information was used to supplement neonatal information collected within BORN. From BORN we extracted a cohort of babies with a similar sample size to EPIPAGE 2 at lower gestations. Variables with comparable definitions pertaining to maternal demographics, pregnancy characteristics, obstetrical management and neonatal death were extracted. Maternal, obstetric, intrapartum and infant characteristics were stratified by gestational age and compared in a univariate analysis. Death prior to discharge from NICU as a proportion of live births was evaluated using a multivariate regression analysis. **Results:** On preliminary analysis, France has a statistically significant greater proportion of women who attended a prenatal visit in the first trimester and delivered in a level 3 center for all gestational age groups. There were also statistically significant differences in maternal age, BMI and birth weight between the two cohorts. There were sporadic differences at certain gestational ages for gestational hypertension and rates of assisted reproductive therapy, labour induction, caesarean section and antenatal steroid use. We also observed higher adjusted odds of neonatal death in the French cohort which is more pronounced at lower gestational ages (Table 1). **Conclusion:** There are differences in maternal and neonatal characteristics, rates of pregnancy complications and obstetrical management and possible better access to obstetrical care and level 3 NICUs in France. Despite adjusting for these differences, the higher rate of neonatal death in France especially at lower gestational ages suggests a need for further exploration.

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ARE THERE GENDER ASSORTATIVE PATTERNS IN CHILDHOOD BODY MASS INDEX?

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Introduction: Genetic, intrauterine and environmental factors, including parental behaviours, are thought to be contributors to the obesity epidemic observed among children. One hypothesis suggests that parental influence on child body weight is gender assortative, such that mother-daughter associations in body mass index (BMI) are stronger than mother-son associations (and likewise for father-son versus father-daughter associations). Understanding the determinants of childhood obesity is important for identifying prevention strategies. **Objective:** To determine whether there are gender assortative patterns of BMI in girls and boys according to mothers' and fathers' BMI. **Methods:** This study utilized data from the Maternal Infant Research on Environmental Chemicals (MIREC) study, in which pregnant women were recruited from 10 Canadian sites between 2008 and 2011. The analysis was restricted to singletons who participated in the MIREC Early Childhood Biomonitoring and Neurodevelopmental follow-up study. The BMI of the children and parents was determined from measured weight and height. The BMI of the children was represented as z-scores based on the World Health Organization references by age and sex. The BMI of the mothers and fathers was categorized as <25 kg/m2 (underweight/normal), 25-<30 kg/m2 (overweight), or ≥30 kg/m2 (obese), and the mean BMI z-score of the children was compared across these categories using multiple linear regression. Mothers and fathers were analyzed separately adjusting for the BMI of the other parent and for birth weight-gestational age z-score. **Results:**

Mean age at follow-up was 3.6 years for the 338 daughters and 341 sons included in this study. The mean BMI z-score increased in both girls and boys according to mother's BMI category, indicating that the association between mother's BMI category and child BMI z-score did not differ according to sex of the child (interaction p-value=0.27). The association between BMI category in fathers and the child's BMI z-score differed by the child's sex (interaction p=0.01). In boys, the mean BMI z-score was 0.6, 0.5 and 0.5 respectively, for underweight/normal, overweight and obese fathers. In girls, however, the BMI z-score was 0.2, 0.4 and 0.6 respectively, for underweight/normal, overweight and obese fathers. **Conclusion:** Discussion: Our data do not support a gender-assortative hypothesis in early childhood BMI. These data suggest that maternal BMI, either through intrauterine factors or maternal-child interactions in early childhood, may impact early childhood BMI. It is difficult to determine why paternal BMI is associated with daughter's BMI, but not the son's BMI. Continued follow-up of the MIREC cohort will help in understanding the mechanisms underlying the association of parental BMI on obesity in childhood.

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CHARACTERIZING THE PREGNANCIES OF A SELECT GROUP OF WOMEN WITH PREVIOUS CAESAREAN SECTION: A POPULATION BASED STUDY.

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Introduction: The Modified Robson Criteria classifies deliveries in broad groups within which Caesarean section (CS) rates can be compared over time and between regions. Robson Group 5 (RG5) includes the subset of women with at least one previous CS who, at term, have a singleton infant in cephalic presentation. **Objective:** To determine the proportion of women in RG5 who were eligible for a trial of labour after Caesarean (TOLAC) and, among eligible candidates, identify determinants of having a TOLAC and subsequent vaginal delivery (VD). To estimate the minimum rate of CS that could be observed if all eligible women in RG5 had a TOLAC. **Methods:** This population-based cohort study used data derived from the Nova Scotia Atlee Perinatal Database. Deliveries from 1998-2014 to women in RG5 were included. Eligibility for a TOLAC, based on the SOGC's criteria, was no previous CS with a documented inverted T, J, or classical uterine incision, no history of uterine surgery or rupture, no placenta previa in the index pregnancy, and a cephalic fetus. A TOLAC was defined as undergoing either induction or spontaneous labour. Prelabour factors investigated in relation to the odds of TOLAC and VD included sociodemographic, obstetric history, and antenatal characteristics. Independent predictors were identified with multivariable logistic regression. The model developed for VD was used to estimate the theoretical probability of VD in the group who did not have a TOLAC. **Results:** Of the 15,111 included in RG5, 75.3% of deliveries were by CS. Of the 14,763 women who were eligible, 5,488 (37.2%) had a TOLAC, of which 3,739 (68.1%) resulted in a VD. Some predictors of VD among women having a TOLAC included high area-level income and either a CS without labour or a spontaneous VD in the last pregnancy. While mode and method of previous delivery were also predictors of TOLAC among those who were eligible, high area-level income was associated with a reduced odds of TOLAC. The probability of VD in the group that did not undergo TOLAC was estimated to be 48.3%, and combined with the proportions ineligible for TOLAC and achieving VD following TOLAC, the minimum CS rate estimated for RG5 is 45.6%. **Conclusion:** Clinical and nonclinical factors influence rates of TOLAC and subsequent VD in eligible women. The actual CS rate (75.3%) is higher than the minimum rate estimated herein (45.6%), suggesting that the CS rate in RG5 could be reduced. Further research into improving clinical prediction of a successful VD among women in RG5 is warranted.

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CHARACTERISTICS ASSOCIATED WITH BREASTFEEDING PATTERNS IN THE ALBERTA PREGNANCY OUTCOMES AND NUTRITION STUDY

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Introduction: Infant feeding practices are often categorized in simplified groups such as exclusive breast or formula feeding and mixed feeding (a combination of both). However, there is a lack of information as to whether these groups

accurately reflect the way in which women feed their infants. **Objective:** To examine 3-day prospective breastfeeding diaries to describe how women feed their babies and explore characteristics associated with feeding patterns. **Methods:** The APrON study is a prospective cohort of women during pregnancy and their children. Women recruited to the study reported demographics and pre-pregnancy weight. Height and weight was measured at each trimester and 3 months postpartum. Physical activity was assessed at 3 months postpartum using the Baecke questionnaire. Prospective breastfeeding diaries which collected information on number of feeds, and duration and method of every feed over 3 days were also completed at 3 months postpartum. Complete data for all assessments were available for 1075 women. **Results:** Women reported feeding their babies using combinations of up to 4 different methods (at breast, expressed breastmilk in a bottle, formula, mixed breastmilk and formula in the same bottle) in any one day. For the ongoing analyses women were categorized into 5 groups based on the number and type of feeds reported/day: 1) at breast only (n=609), 2) at breast and expressed breastmilk (n=223), 3) formula only (n=14), 4) mixed feeding using 2 methods (n=120) and, 5) mixed feeding using 3 or 4 methods (n=109). Those who fed using a combination of 2 mixed feeding methods were more likely to be educated below university level (p=0.002), have entered pregnancy overweight or obese (p=<0.001) and report sleeping for less time (p=0.03) compared to those who fed at breast only. Those who fed using 3 or more methods were more likely to be feeding their first child (p=<0.001), be older (p=0.005), and also have entered pregnancy overweight or obese (p=0.01) and report sleeping for less time (p=0.03) compared to those who fed at breast only. There were no differences in physical activity scores or postpartum weight retention between the different feeding method groups. **Conclusion:** Women who are older, new mothers, who enter pregnancy with a higher BMI and with lower levels of education, appear more likely to use a combination of mixed methods to feed their infants. The causality of the association between sleep duration and feeding method is unclear and warrants further investigation. The impact of these complex feeding patterns on maternal and child outcomes is an important area for future research.

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THE IMPACT OF PEDIATRIC IN-HOUSE CALL HOUR RESTRICTIONS ON RESIDENT EXPOSURE TO NEONATOLOGY AND HOURS WORKED IN THE NICU

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Introduction: Working more than 16 consecutive hours has been associated with chronic fatigue and lower work performance. In 2011, consecutive in-house hours worked by residents in Quebec were reduced from 24 to 16 hours but there were no restrictions on total hours worked. **Objective:** To assess the impact of reducing consecutive hours worked on-call by pediatric residents on exposure to Neonatology and total hours worked in the NICU. **Methods:** A 6-year retrospective cohort study in a Level-3 NICU. We compared Epoch 1 (2008-2011, 24-hour shifts) to Epoch 2 (2011-2014, 16-hour shifts). Total hours worked by residents for each level of training were obtained from resident scheduling. On-call hours were defined as hours worked from 5pm to 8 am from Monday to Friday and from Friday 5pm to Monday 8am. Wilcoxon Mann Whitney tests were used to compare variables between the 2 periods. **Results:** In Epoch 2, there was a significant decrease in the median number of on-call hours worked by all residents (250.5 h vs. 184.0 h, P <0.0001) and in total hours worked in the NICU (381.0 h vs. 276.0 h, P < 0.001). In the subgroup of 1st year residents, median total hours worked per year were also decreased in Epoch 2 (663.0 h vs. 544.0 h, P<0.0001). However, more residents were present during the day throughout their NICU rotation (4.0 vs. 3.0, P<0.0001) in Epoch 2 than Epoch 1, and the percentage of days' present during the NICU rotation did not change significantly between periods (75.0% vs. 72.5%, P=0.07). **Conclusion:** The reduction in consecutive residents on-call duty hours is associated with a reduction in the number of hours worked in the NICU. The most significant reduction was in hours worked on nights and weekends. This raises potential challenges for residency programs to adequately train residents with fewer hours of clinical exposure.

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IS 40 THE NEW 30? AGE-PERIOD-COHORT EFFECTS IN PRE-EXISTING AND PREGNANCY-ASSOCIATED DISEASE IN PRIMIPAROUS WOMEN IN THE UNITED STATES.

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Introduction: The rate of severe maternal morbidity and mortality has increased over time in the United States (US), and much of this increase has been attributed to delayed childbearing and advanced maternal age. While the average age at first birth has steadily increased in the US and other developed countries, relatively little attention has been paid to temporal changes in maternal health status and the role that maternal health status prior to and during pregnancy have on adverse pregnancy outcomes. **Objective:** To examine age, time period, and birth cohort effects in the prevalence of pre-existing and pregnancy-associated disease in primiparous women. **Methods:** Deidentified data on primiparous women delivering a singleton liveborn infant in the US in 1989, 1994, 1999, 2004, 2009, and 2014 were obtained from the US Natality Files (n=6,857,185). Maternal age was categorized into 5 year increments, and age-period-cohort effects in the prevalence of pre-existing medical conditions (i.e., chronic hypertension and pre-existing diabetes) and the incidence of pregnancy-associated diseases (i.e., gestational hypertension, eclampsia, and gestational diabetes) were examined. **Results:** The median age at first birth increased from 23 in 1989 to 26 in 2014 ($p<0.001$). While the prevalence of pre-existing conditions increased with maternal age, a higher rate of pre-existing disease was seen over time in all age groups. For example, from 1989 to 2014, the prevalence of chronic hypertension increased from 0.32% (0.30-0.35) to 0.56% (0.53-0.60) in 15-19 year olds and from 2.00% (1.84-2.16) to 2.66% (2.55-2.77) in 35-39 year olds. This resulted in 30-34 year olds delivering in 2014 (1.67%, 1.62-1.72) having the same prevalence of chronic hypertension that 35-39 years olds had in 1999 (1.68%, 1.57-1.80). Similar patterns were observed for gestational hypertension, gestational diabetes, and pre-existing diabetes; however, the opposite pattern was seen for eclampsia, which decreased in all groups over time. **Conclusion:** Across all age categories, women are increasingly entering pregnancy with poorer health and developing pregnancy-associated conditions at higher rates, suggesting factors other than advanced maternal age contribute to the increased rates of adverse pregnancy outcomes. Though maternal age is an important consideration, greater attention needs to be paid to the role of maternal health status across all age categories when investigating temporal changes in adverse obstetric events.

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A SYSTEMATIC REVIEW OF ADVERSE PREGNANCY OUTCOMES AMONG WOMEN WITH ENDOMETRIOSIS

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Introduction: Endometriosis is a benign chronic inflammatory disease characterized by ectopic endometrial tissue implants outside the endometrial cavity. Implications of endometriosis on the success of in-vitro fertilization have been explored, however the importance of endometriosis during pregnancy and at the time of delivery is unclear. Studies have shown endometriosis can be associated with both maternal and fetal risk during pregnancy including spontaneous hemoperitoneum, post-partum hemorrhage, placenta previa, preeclampsia, prematurity, intrauterine fetal growth restriction and miscarriage. **Objective:** The purpose of this review is to systematically assess the observational studies in the literature to determine the risk of adverse perinatal outcomes for women with endometriosis compared to healthy controls. **Methods:** Using a search protocol developed with a research librarian, Medline, Embase, and the grey literature were searched for studies published from January 1990 to March 2015. Inclusion criteria were observational studies, women greater than 20 weeks gestational age with diagnosed endometriosis prior to pregnancy, and a control group of individuals without endometriosis. Two independent reviewers completed data extraction from the included studies and determined risk of bias for each using the Newcastle-Ottawa Scale. **Results:** An electronic search identified 2,460 studies after removal of duplicates. We completed a title and abstract screen and identified 75 articles for full text review. Of those, 18 articles were eligible for inclusion in this study. Endometriosis was found to be associated with maternal outcomes of placenta previa (8 studies, OR 2.90 [1.40-6.00]), caesarean section (8 studies, OR 1.62[1.29-2.05]), and postpartum hemorrhage (1 study, OR 1.3[1.1-1.6]). Endometriosis was also found to be associated with the fetal/neonatal outcomes of preterm birth (11 studies, OR 1.43[1.23-1.65), and preterm premature ruptured of membranes (1 study, OR 2.0[1.4-3.2]). No association was found between endometriosis and gestational hypertension/preeclampsia, gestational diabetes, low birth weight, small for gestational age, NICU admission or placental abruption. **Conclusion:** Though further analysis is required to evaluate the effect of clinically important confounders, these preliminary results suggest associations between the presence of endometriosis and several

important adverse pregnancy outcomes. The outcomes of this review will provide insight into perinatal risk assessment and counseling for women with endometriosis in pregnancy.

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ASSESSMENT OF EARLY TERM ELECTIVE REPEATED CESAREAN DELIVERY AND ASSOCIATED NEONATAL MORBIDITY AND MORTALITY IN BREECH AND CEPHALIC BIRTHS.

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Introduction: Previous studies have shown lower neonatal morbidity associated with planned cesarean delivery (CD) versus planned vaginal delivery in women with breech presentation at term. It is uncertain whether early term fetuses in breech and cephalic presentation born by elective repeat CD (ERCD) have any impact on neonatal outcomes. **Objective:** To examine the effect of early term ERCD (37-38weeks) compared with full term (39-40weeks) on neonatal morbidity and mortality in breech and cephalic births. **Methods:** A retrospective cohort study was conducted using data from the National Center for Health Statistics in the United States from 2005 to 2010. The study population included 728,732 singleton births, delivered at 37-40 weeks' gestation by mothers with previous CD, who had no labor or medical problems (pre-existing or pregnancy-related diabetes or hypertension). Log binomial regression models were fitted to estimate risk ratios (RR) and 95% confidence interval (CI) of the effect of early term versus full term ERCD on neonatal morbidity and mortality in the overall study population and for breech and cephalic population. **Results:** In the overall study population, early term ERCD neonates compared with full term ERCD neonates had more than one-fold increased likelihood of requiring assisted ventilation, 5 minutes Apgar score at <4 and 4-6, neonatal intensive care unit (NICU) admission and neonatal mortality (p=<0.001) respectively. Analyses of cephalic presentation births showed babies born by early term ERCD compared with full term ERCD were more likely to receive ventilation (RR=1.21, 95%CI: 1.18-1.24), birth injury (RR=1.45, 95%CI: 1.06-1.99), 5 minutes Apgar score <4 (RR=1.26, 95%CI: 1.09-1.45), 5 minutes Apgar score 4-6 (RR=1.24, 95%CI: 1.15-1.33), NICU admission (RR=1.58, 95%CI: 1.54-1.63) and neonatal mortality (RR=1.69, 95%CI: 1.38-2.08). Among the breech presentation group, neonates born by early term ERCD compared with full term ERCD had increased likelihood of assisted ventilation (RR=1.25, 95%CI: 1.13-1.39) and NICU admission (RR=1.52, 95%CI: 1.35-1.70). However, the babies with breech presentation births born by early and full term ERCD had similar rates of birth injury (p=0.0816), 5 minutes Apgar score<4 (p= 0.4685) and neonatal mortality (p= 0.4312). **Conclusion:** While newborn birth injury, 5 minutes Apgar score<4 and mortality were comparable in early and full term ERCD babies in breech presentation, all other neonatal morbidity and mortality were associated with early term ERCD births than full term births, irrespective of whether the births were by cephalic or breech presentation.

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DOES SON-BIAS PERSIST AMONG SECOND GENERATION SOUTH ASIAN WOMEN IN ONTARIO?

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Introduction: Gender-bias which disadvantages girl's and women's health and well-being is pervasive in Canadian society but is expressed differently in different communities. Previous research in Ontario has found that first generation Indian women with two previous daughters gave birth to about half the expected number of daughters compared to sons at the third birth and that such biased sex ratios are likely facilitated by sex-selective abortion. **Objective:** Our objective was to examine whether son-biased sex ratios persist among second generation South Asian women in Ontario. **Methods:** We analyzed births to immigrant and Canadian-born South Asian women as well as the general population who gave birth in Ontario between 1991 and 2014. South Asian women were identified using a comprehensive list of exclusively South Asian surnames [positive predictive value = 89.3%; sensitivity (vs. self- report) = 50.4%]. South Asian immigrants were identified using a combination of this list and an official immigration database (1985-2012). Second generation South Asian women excluded immigrants and was further restricted to women who were eligible for provincial health care insurance before April 1, 1990 or were eligible within 1 year of their birth date as well as those who were born in Ontario. Male to female (M:F) ratios and 95% confidence intervals (95% CI) were

calculated according to the sex of previous live births for each group and further stratified by those who did and did not have an abortion since the previous live birth. **Results:** For births to South Asian immigrants (n = 41,664, 65% of whom were from India), the M:F ratio at the third birth among women with two previous daughters was 1.53 (95% CI 1.37-1.70), 1.32 (95% CI 1.17-1.49) for women with no previous abortion since the second birth and 2.45 (95% CI 1.94-3.08) for women with at least one previous abortion since the second birth (n=348). Biased sex ratios among births to second generation South Asian women (n=10,427) were evident only among those with two previous daughters and at least one previous abortion (n=47) [2.62 (95% CI 1.38-4.96)]. M:F ratios were in the expected range for the general population. **Conclusion:** Son-biased M:F ratios generally do not persist among second generation South Asian women with the exception of a minority of women with two previous daughters who had at least one abortion since their second birth.

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AN INTERVENTION STUDY TO IMPROVE PREGNANCY AND NEWBORN OUTCOMES FROM THE FORT MCMURRAY WILDFIRE (FMMW).

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Introduction: The FMMW of May 2016 forced the evacuation of 88,000 people of whom we estimated 1250 were pregnant women and 600 more would conceive in the six months following the fire. Canadian data studying other natural disasters (Quebec Ice Storm, floods) unequivocally documents that pregnant women are at risk for preterm birth and other adverse pregnancy outcomes and their children for cognitive delay. It was imperative we trial an intervention to mitigate adverse outcomes due to the disaster. **Objective:** To study the effectiveness of a simple expressive writing intervention (developed by Dr. J Pennebacker, U Texas) - short bursts of expressive writing (15-20 min) each day for four days - to allow for emotional disclosure to improve outcomes. We hypothesize that the intervention will reduce stress, increase resilience and improve pregnancy and children's outcomes. **Methods:** Women were recruited with the support of the Wood Buffalo Primary Care Network and local pregnant and postpartum women. Advertisements were placed in the Network clinics, The FMM Facebook 'Mommy Network,' and purchased in Facebook. Consented women were randomized into three groups: a control no writing group, a writing group addressing healthy lifestyle issues, and a writing group addressing their deepest, innermost feelings about the fire. The outcome measures are: 1a) To determine how well the expressive writing intervention supports maternal resilience by using qualitative methodology involving thematic content analysis of the writing data; will foster resilience; 1b) To test the effects of the intervention on objective prenatal maternal stress (PNMS), cognitive PNMS, peritraumatic and current distress on maternal and infant outcomes; 2) To develop a new allostatic load (AL) index of modifiable maternal stress 'omics markers for predicting risk and responsiveness to the intervention, and will be contrasted with resiliency; 3) To integrate knowledge engagement so that the processes and outcomes of research are beneficial to the community and stakeholders. The findings will inform decision-making and elucidate an effective mechanism for reducing the prenatal and post-traumatic stress of pregnant women during a disaster or emergency evacuation. **Results:** Monies were raised, recruitment is proceeding as predicted and innovative strategies are overcoming hurdles. **Conclusion:** Several valuable lessons have been learned about responding rapidly to a natural disaster in terms of raising funds for studies, working with community organizations, leaders and local victims, recruiting using social media and developing an effective intervention.

P155

ADVERSE BIRTH OUTCOMES AMONG FIRST NATIONS IN CANADA ACCORDING TO REGISTERED INDIAN STATUS AND ON-RESERVE RESIDENCE

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Introduction: Studies to date of perinatal health outcomes in First Nations populations of Canada have been limited to specific geographical regions and to on-reserve populations, therefore hindering analyses and comparisons of First Nations populations across regions, or between on-reserve and off-reserve populations. **Objective:** To examine adverse

birth outcomes for singleton pregnancies of First Nations mothers by residence and registered Indian status, based on a nationally representative sample. **Methods:** Data were from the 2006 Canadian Birth-Census Cohort, which includes births from May 2004 to May 2006. We compared rates of adverse birth outcomes between on- vs. off-reserve and status vs. non-status First Nations populations. Outcomes examined included preterm birth (PTB), small- and large-for-gestational-age (SGA, LGA) birth, stillbirth, infant mortality, and neonatal and postneonatal mortality. Risk ratios were estimated with adjustment for parental characteristics to examine disparities in non-fatal outcomes. **Results:** 13,506 singleton births were included in the analysis. Mothers living on-reserve and those with status tended to be younger, have lower education levels, and be of higher parity compared to those living off reserve and those without status. After adjusting for maternal age, parity and both parents' education levels, on-reserve mothers and those with status had a reduced risk of SGA and elevated risk of LGA compared to off-reserve and non-status mothers, respectively (on-reserve vs. off-reserve: adjusted RR = 0.84 (95% CI = 0.68-1.03) for SGA; 1.30 (1.17-1.43) for LGA; status vs. non-status: 0.60 (0.45-0.81) for SGA; 1.63 (1.28-2.08) for LGA). Rates of PTB did not vary substantially by residence or status. Crude rates of stillbirth were higher among off-reserve and non-status mothers (off-reserve: 11.4 per 1,000; on-reserve: 9.4; status: 14.4; non-status: 9.8). On-reserve mothers had elevated crude rates of infant mortality compared to those off-reserve (10.9 vs. 7.7 per 1,000 live births), particularly for neonatal mortality (6.1 vs. 2.9). However, caution should be used when interpreting apparent differences for fatal outcomes because of limited precision due to sparse events. **Conclusion:** This study presents the first examination to date of perinatal outcomes by registered Indian status and by residence on Indian reserves among First Nations populations in Canada. Differences in rates of SGA and LGA were not explained by differences in maternal characteristics. These results suggest future investigations should explore community factors such as access to health care, food security, and other risk factors that may explain disparities in these outcomes between different First Nations populations.

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PREECLAMPSIA AND THE RISK OF MATERNAL RETINAL DISORDERS LATER IN LIFE

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Introduction: Preeclampsia is associated with a greater risk of retinopathy and retinal detachment during pregnancy and the immediate postpartum period. The possibility of an association between preeclampsia and retinal disorders later in life, however, has yet to be explored. **Objective:** To evaluate the potential association between preeclampsia and maternal retinal disease in the decades after pregnancy. **Methods:** We performed a longitudinal cohort study of 1,108,541 women who delivered infants in hospitals of Quebec, Canada between 1989 and 2013. We identified women with preeclampsia at delivery, categorized by severity (mild or severe) and onset (before or at 34 weeks or more of gestation). We then tracked women over time for any subsequent hospitalizations for retinal disorders, with follow-up ending March 31, 2014. Main outcomes were hospitalizations and inpatient procedures for retinal detachment, retinopathy, or other retinal disorders. We used Cox regression models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for retinal disorders, comparing preeclampsia with no preeclampsia. Models were adjusted for diabetes and hypertension. **Results:** Compared with women who did not have preeclampsia, women with preeclampsia had a higher incidence of ophthalmological procedures for retinal detachment (52.9 vs. 23.9 per 10,000), retinopathy (60.5 vs. 8.0 per 10,000), and other retinal disorders (13.3 vs. 7.3 per 10,000). In regression models, preeclampsia was significantly associated with traction detachments (HR 2.39, 95% CI 1.52-3.74), retinal breaks (HR 2.48, 95% CI 1.40-4.41), and diabetic retinopathy (HR 4.13, 95% CI 3.39-5.04). Compared with mild or late onset preeclampsia, severe and early onset preeclampsia were associated with even higher risk of retinal disorders. **Conclusion:** Preeclampsia, especially severe or early onset preeclampsia, is associated with an increased long term risk of maternal retinal disease. Women with preeclampsia may merit ophthalmological screening to capture retinal disease at an early stage.

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VALIDATING DATA ACCURACY IN THE BORN ONTARIO REGISTRY FOR THE MATERNAL NEWBORN DASHBOARD

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Introduction: The Better Outcomes Registry & Network (BORN) Information System (BIS) was launched in January 2012, to enable the collection and access to data on every birth in Ontario. Sourced from hospitals, labs, midwifery practice groups and clinical programs, these data are collected through a variety of mechanisms including manual entry into a secure portal, batch upload and HL7 feed. These data have robust validation and entry rules, ensuring the highest possible quality. The Maternal Newborn Dashboard (MND) is an audit and feedback tool within the BIS that provides feedback on six key performance indicators (KPIs). **Objective:** We aimed to validate data entered in the BIS for a selection of data elements that are involved in the MND KPIs. **Methods:** The first step in our assessment of data accuracy was to determine which data elements should be included. We identified the data elements that were used in the KPI calculations and then assessed the distribution of the response options for each variable on a provincial level. We selected ten hospitals for inclusion based on level of care, birth volume and geography. One hundred mother-baby chart pairs were selected for each site and data from the charts were re-abstracted at each site. These data were then compared with the corresponding data entered in the BIS using percent agreement, kappa statistics and intraclass correlation coefficients (ICCs). **Results:** We found that the percent agreement for the majority of variables was greater than 90 percent. There were almost perfect (0.81-0.99) kappa statistics for a number of elements including: type of birth, indication for cesarean section, labour and birth complications and fetal surveillance. The lowest kappa statistics were observed for newborn discharge to/transfer to (kappa=0.46; 95%CI: 0.25–0.68) and maternal smoking at prenatal visit (kappa=0.56; 95%CI: 0.49–0.62). High intraclass correlation was found for the variable number of fetuses (ICC=0.90; 95%CI: 0.89–0.91), whereas maternal height and maternal weight at end of pregnancy were lower (ICC=0.54; 95%CI: 0.50–0.59 and ICC=0.49; 95%CI: 0.44–0.55). **Conclusion:** Overall, data elements used in the MND audit and feedback system were found to have good agreement with data from the patients' charts. Therefore the output from the MND should be considered as an accurate assessment of a hospital's success rate for the six KPIs.

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GAPS IN PRENATAL HEALTHCARE PROVIDER – PATIENT COMMUNICATION

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Introduction: Pregnancy is considered one of the most critical periods of growth and development across the lifespan. Gestational weight gain (GWG) is an independent and modifiable factor for a healthy pregnancy. Low or high GWG is known to impact both maternal and fetal health (e.g. gestational diabetes, risk for small or large for gestational age). Maternal nutrition and physical activity (PA), known contributors to GWG and healthy fetal development, are key health promotion messages during pregnancy. However, there appears to be discrepancies regarding prenatal health communication between healthcare provider (HCP) and patients. **Objective:** To examine prenatal health communication regarding GWG, nutrition and PA between HCPs and their prenatal patients. **Methods:** A reliable and recently validated Electronic Maternal Health Survey was administered to pregnant women, or women who had given birth in the last 5 years. The cross-sectional web-based questionnaire was self-administered and took about 10-25 minutes. **Results:** A total of 1677 women from mostly Canada (96.3%) and the United States participated in the survey. Just over half (55%) of patients reported talking about GWG limits, and 49.6% of HCPs gave a target GWG amount. Of the HCPs discussing GWG, only 3% discussed GWG at each visit. PA was a commonly discussed topic with the HCPs that initiated GWG discussions. Although a large number of women (80%) had intentions of exercising throughout pregnancy, only 30% of women actually followed through with their goals. Common barriers to physical activity included lack of time, feeling ill or feeling too tired. With regards to nutritional counselling, 44% of women reported their HCP discussed necessary dietary changes for pregnancy and only 54.8% of all women were familiar with their personal calorie requirements over the course of pregnancy. **Conclusion:** It is clear that there is a gap in prenatal health communication between HCPs and patients, especially concerning GWG, nutritional and PA counseling. These findings highlight areas for improvement in prenatal healthcare dialogue in order to better health outcomes for both mother and baby. Resources like the Canadian Obesity Network's 5A for Healthy Pregnancy weight gain tool kit are being developed to assist HCPs with engaging in this important dialogue with patients.

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BREASTFEEDING SUPPORT IN CANADIAN NEONATAL INTENSIVE CARE UNITS

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Introduction: The health benefits of breastfeeding for preterm infants and their mothers are well established. However, the prevalence of breastfeeding initiation, duration, and exclusivity among mothers of preterm infants is consistently lower than that of full-term infants, both globally and in Canada. Comprehensive breastfeeding support is needed in neonatal intensive care units (NICUs) to address the suboptimal breastfeeding outcomes in the preterm population, yet researchers have not examined this topic in a Canadian context. **Objective:** The purpose of this study was to determine, using an environmental scan, the types and frequencies of breastfeeding supports and resources available in NICUs across Canada. **Methods:** A qualitative research design was used in that semi-structured interviews were conducted with 33 key informants (e.g., lactation consultants [LCs], nurse educators, etc.) from 29 tertiary care NICUs across Canada. Interview questions related to general NICU characteristics and the types of breastfeeding resources available within the unit. Data were member-checked by key informants and analyzed using both deductive and inductive content analysis procedures. **Results:** Six categories of breastfeeding resources were identified: breastfeeding-friendly layout, breastfeeding support personnel, breastfeeding education, breast pump-related support, coordination of post-discharge breastfeeding support, and breastfeeding/skin-to-skin-related policies. The most commonly cited resources included the availability of printed breastfeeding education materials (100% of NICUs), pumps for in-unit use (100%), mandatory breastfeeding training for nurses (93%), opportunities for rooming in (93%), privacy measures (93%), provision of free pumping kits (86%), implementation of a skin-to-skin policy (82%), and referral to public health upon discharge (79%). Although LCs were reportedly available in 86% of NICUs, key informants stated that only one third of NICUs (34%) had LCs providing early support to all mothers, regardless of feeding situation. Formal peer breastfeeding support was reported in 17% of NICUs. Informants described breastfeeding education approaches to include electronic materials (55%) such as websites, videos, or smartphone apps, and group education (38%). Lastly, whereas 61% of NICUs were reported to have implemented a breastfeeding policy, only one quarter (25%) of all NICUs were reported to have a breastfeeding policy specific to preterm infants. **Conclusion:** This study provides a national summary of the breastfeeding support available for mothers of preterm infants in Canadian tertiary care NICUs. A wide range of breastfeeding resources will be discussed, along with potential strengths and weaknesses related to the current provision of breastfeeding support in NICU settings. NICU staff will be encouraged to connect with other NICUs to facilitate the exchange of breastfeeding resources and best practices.

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POSTPARTUM UTALIZATION OF THE EMERGENCY DEPARTMENT FOR WOMEN WITH A HYPERTENSIVE DISORDER OF PREGNANCY.

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Introduction: Hypertensive disorders of pregnancy (HDP) occur in 10% of all pregnancies and are a leading cause of maternal and perinatal morbidity and mortality. HDP are characterized by hypertension, often with vague symptoms (e.g headache, nausea) and lab abnormalities (e.g proteinurea). As many as 30% of HDP cases arise postnatally, and are one of the most common reasons for mothers to visit the Emergency Department (ED) within 42 days of delivery. Despite this, postnatal HDP is highly understudied in comparison to antenatal HDP. Furthermore, symptoms are varied and there are no specific screening or treatment guidelines in Canada. These factors make it difficult to recognize and manage postpartum HDP in the ED thereby leading to potentially preventable severe maternal complications such as stroke and heart failure. Knowledge of the accuracy of ED diagnosis of postpartum HDP would help inform the care of patients and future research. **Objective:** Our study aimed to investigate the accuracy of the diagnosis of postpartum HDP in Calgary EDs by ED physicians as well as administrative classification. **Methods:** Participants (n=113) were women who had delivered a live or stillborn infant, and presented to an ED in Calgary within 42 days postpartum from 2011-2012. A random sample of charts for women with a diagnostic code for HDP (gestational hypertension, preeclampsia, eclampsia, or HELLP) were examined (n=41), as well as control cases who presented with alternate yet related diagnoses such as headache or nausea (n=72). Information on patient diagnoses and management was collected via chart review using a

standardized data collection form, and was reviewed independently by two obstetric medicine (OB Med) specialists to determine if the patient had postpartum HDP. Accuracy of administrative claims data and ED physician diagnoses to identify postpartum HDP compared to expert Ob Med review was assessed using positive predictive values and kappa statistics. **Results:** Our data showed a 64.49% agreement between ED physician and OB Med diagnoses (kappa=0.3581), and 68.14% between administrative data and OB Med review (kappa=0.3937). Positive predictive values were 87.8% between administrative data and OB Med review, and 100% between ED physician and OB Med diagnoses. **Conclusion:** Postpartum HDP is under-recognized in EDs, as evidenced by low agreement between ED records and OB Med review. However, those cases that are diagnosed in the ED are generally true cases of postpartum HDP, as evidenced by high positive predictive values. Ultimately the administrative case definition to identify postpartum HDP developed for this study could be applied in future studies examining ED treatment of postpartum HDP, but will underestimate the incidence of the condition due to under diagnosis.

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EVALUATION OF A NON-RANDOMIZED OBSTETRICAL PATIENT SAFETY PROGRAM: AND CONSIDERATIONS

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Introduction: Evaluation of large, phased-implementation quality improvement programs requires rigorous methodological and analytic approaches, as uncontrolled before-and-after comparisons are vulnerable to temporal confounding. Approaches can include the stepped wedge (SW) cluster randomized design, and the interrupted time series (ITS) design. In 2002, a patient safety program was implemented across Ontario, with the goal of improving maternal and neonatal outcomes. Challenges encountered include heterogeneity in outcomes and numbers of patients, and variability in program implementation and duration across hospital sites. **Objective:** To describe three different approaches to the evaluation of an obstetrical patient safety program and discuss their methodological implications and challenges. **Methods:** We obtained 12 fiscal years of data (2002/03-2014/15) from the CIHI Discharge Abstract Database (DAD). The primary outcome was a previously developed composite obstetric safety indicator, the Adverse Outcome Index (AOI). We compared the results from three methodological approaches: 1) a random effects logistic regression model based on the SW design; 2) a random effects logistic regression model using segmented regression (combination of ITS and SW approaches); and 3) separate segmented regression analyses to obtain hospital-specific estimates of program effects with estimates pooled across sites using meta-analysis (ITS and meta-analysis) **Results:** The final study dataset included 1,324,330 deliveries from 44 hospitals. Overall across the 12 years, the AOI rate was 5.8% (n=76,355). All three analytic approaches found no significant effect of program implementation on the AOI. The SW approach yielded an odds ratio (OR) of 1.02 (95% CI 0.93 to 1.11), p=0.70). The combination of ITS and SW approaches yielded an estimated change in intercept of 1% (OR=1.01 (95% CI 0.51 to 2.02) and no change in slope (OR=1.00 (95% CI 0.99 to 1.01)). The ITS and meta-analysis approach yielded a non-significant increase in AOI rate of 0.99% at 3 months after the end of program implementation (95% CI: -0.76, 3.23). Each approach had advantages and disadvantages. **Conclusion:** We found the site-specific ITS approach with estimates pooled via meta-analysis to be the most useful approach for assessing the effect of program implementation across multiple sites with varying date and duration of implementation. Our study demonstrates that the impact of such a program can be assessed using a robust design.

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INVESTIGATING THE INCREASED INCIDENCE OF SHOULDER DYSTOCIA IN NOVA SCOTIA: A RETROSPECTIVE DATABASE AND CHART REVIEW.

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Introduction: Shoulder dystocia is defined as a vaginal cephalic delivery requiring additional obstetric maneuvers to deliver the fetal shoulders when routine traction has failed. The prevalence of shoulder dystocia recorded in the Nova Scotia Atlee Perinatal Database (NSAPD) dramatically increased from 1.8% of vaginal singleton deliveries in 1995-1999 to

4.9% in 2010-2014. Further, the most recent rates of shoulder dystocia derived from this database are substantially higher than those reported in other reviews. It is possible that these increased rates are due to ambiguous documentation or coding errors. **Objective:** To estimate the proportion of deliveries recorded in the NSAPD as being complicated by shoulder dystocia that contain documentation in the medical chart supporting the diagnosis, and to describe the nature of this documentation. **Methods:** A retrospective database and chart review was performed for 400 randomly selected deliveries between 2006 and 2015 at the IWK Health Centre in Halifax which were coded in the NSAPD as complicated by shoulder dystocia. Information examined in the medical charts included whether there was explicit documentation of shoulder dystocia, as well as clinical signs or obstetric maneuvers indicative of the condition. Data were analyzed using descriptive statistics and logistic regression. **Results:** Shoulder dystocia was explicitly documented in the majority of medical charts (95%), with little variation in this proportion during the ten-year study period. Few charts (16%) contained documentation of any clinical sign associated with shoulder dystocia. A majority of medical charts (90%) contained documentation of an obstetric maneuver executed in the management of shoulder dystocia. The obstetric maneuvers most often performed were McRobert's maneuver (84%) and suprapubic pressure (66%). Most charts (81%) included a note regarding the severity of the shoulder dystocia. Of these cases, 69% were described as mild and the remainder (31%) were considered moderate or severe. Shoulder dystocia was more frequently described as mild in more recent years ($p<0.05$). **Conclusion:** The increased rates of shoulder dystocia with time derived from the NSAPD do not appear to be a result of over-coding, as the vast majority of cases was supported by documentation in the medical chart. Further research will be needed to determine the contribution of improved diagnosis, documentation, or over-diagnosis to the apparent increases in the incidence of shoulder dystocia in Nova Scotia.

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FACEBOOK AS AN EFFECTIVE RE-ENGAGEMENT TOOL FOR A LONGITUDINAL PREGNANCY COHORT IN ALBERTA, CANADA

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Introduction: Retaining and engaging participants is an essential component of longitudinal research. Due to restrictions on accessing personal information from database resources in Canada, few alternatives exist for researchers to re-identify and engage with participants when traditional communication tools fail. Facebook represents a novel platform that may enable the identification and re-engagement of participants previously considered lost to follow-up. **Objective:** To investigate the efficacy of Facebook as a re-engagement tool among participants previously considered lost to follow-up in a longitudinal pregnancy cohort. **Methods:** This study used data from the All Our Babies (AOB) study, a prospective community-based pregnancy cohort situated in Calgary, Alberta, Canada (n=3388). Women were recruited during pregnancy and were followed-up at seven time points during the perinatal and early childhood period. Participants considered lost to follow-up were identified on Facebook if their online profile displayed at least two socio-demographic characteristics that matched information previously collected by the study. Once identified on Facebook, participants were sent a friend request and a personal message asking them to verify their enrolment in the AOB study. For the purpose of this analysis, participants were considered contacted if security settings allowed a friend request and a personal message to be sent. If a participant accepted our friend request and/or replied to our message, they were considered re-connected with the study. Finally, if a participant responded to our messages and provided their up-to-date contact information, they were considered re-engaged with the study. **Results:** Of the 237 AOB participants considered lost-to-follow-up, 113 (47.7%) participant profiles were identified using Facebook. Among the 113 identified profiles, 87 (77.0%) were contacted, 37 (32.7%) were re-connected with the study and 20 (17.7%) were re-engaged with the study. Participants considered lost-to-follow-up differed from continuing participants in maternal age, household income and education. No significant differences were observed between those whose Facebook profiles could or could not be identified. **Conclusion:** Together, our results and the literature suggest that Facebook is an effective tool for re-engaging with participants. Its broad use and publicly available information make Facebook an alternative mean of re-identifying participants lost to follow-up, especially in Canada.

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UNEXPLAINED ABNORMAL 1ST AND 2ND TRIMESTER MATERNAL SERUM ANALYTE RESULTS AND ADVERSE MATERNAL AND PERINATAL OUTCOMES.

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Introduction: The publication of a Canadian clinical practice guideline in 2008 summarizing the risks for adverse pregnancy outcomes associated with unexplained abnormal maternal serum analytes has led to recommendations for obstetrical consultation and increased fetal surveillance. An analysis of analyte cutoffs in relation to maternal and perinatal outcomes using Nova Scotia data was undertaken to optimize both patient and health care resource utilization **Objective:** To determine the performance of maternal serum analyte levels, using traditional and alternate cutpoints, for the prediction of adverse maternal and perinatal outcomes. **Methods:** The study population included residents of Nova Scotia who underwent 1st or 2nd trimester maternal serum screening (MSS) and delivered a singleton nonanomalous infant >500g or >20 weeks' gestation between 2005 and 2014. Women with previous or current complications for which they would have increased surveillance irrespective of MSS results were excluded. Data were obtained from the Atlee Perinatal Database with linkage to the provincial MSS database from which multiples of the median of MSAFP, 1st or 2nd trimester hCG, uE3, and PAPP-A were derived. Outcome measures included composites of stillbirth, preterm birth, pre-eclampsia, and small for gestational age (SGA, < 10th percentile). **Results:** 39,689 women met eligibility criteria. Uptake of both 1st and 2nd MSS increased from 2005 to 2014 (p<.05, respectively). The prevalence of the first composite outcome (stillbirth, preterm birth <32 weeks or pre-eclampsia) was 2.6% and the prevalence of the second composite outcome (pre-eclampia with SGA or preterm birth <34 weeks) was 0.5%. No single analyte predicted these composite outcomes well (AUC 50-60%). Low sensitivity (<1% for all analytes except 1% for hCG) and high specificity (target="1">99% for all analytes) were observed for commonly used cutpoints in the prediction of the composite outcomes. **Conclusion:** Adverse maternal and perinatal outcomes for which obstetrical consultation and increased fetal surveillance would be intensified were uncommon in the population. There was a low detection rate for composite outcomes using maternal serum analytes.

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PATTERNS OF CHANGE IN ANXIETY AND DEPRESSION DURING PREGNANCY PREDICT PRETERM BIRTH

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Introduction: In Canada, approximately 8% of all live births are preterm. Anxiety and depression may influence the risk of preterm birth (PTB), although the literature is inconsistent. Measuring changes in anxiety and depression at two distinct time points during pregnancy, as well as assessing chronic stress as a potential modifier, may help clarify the relationship with PTB. **Objective:** The aim of this research was to determine whether changes in anxiety and depression during pregnancy influence the risk of having a PTB, and whether chronic stress modifies this relationship. **Methods:** The data source for the current study is the All Our Babies prospective cohort (AOB), conducted in Calgary Alberta, between 2008 and 2011. Anxiety and depression were measured at 17-24 weeks and again at 32-36 weeks gestation using the Spielberg State Anxiety Scale and the Edinburgh Postnatal Depression Scale, respectively. Chronic stress was assessed at 17-24 weeks gestation as a potential covariate, and was measured using the Perceived Stress Scale. Multivariable logistic regression modeling was used to assess each relationship. **Results:** Women who experienced an increase in anxiety scores, (time point 32-36 weeks, compared to the earlier time point 17-24 weeks), had 2.70 times higher odds of preterm delivery, compared to those with a reduction in anxiety scores (95% CI 1.28, 5.69). Increasing and consistently high depression scores did not significantly influence the odds of PTB compared to a decrease in depression scores. A co-occurring increase in anxiety and depression scores was not found to increase the odds of PTB, and chronic stress did not modify any of these relationships. **Conclusion:** The current study identified that changes in the anxiety of the participant during pregnancy increased the risk of a preterm delivery. However, this study was limited by a relatively

small sample of women who delivered preterm, and therefore it was not possible to conduct additional analyses. Further, the analyses were limited to mostly late preterm infants. These findings should be validated with additional cohorts and a larger sample size. Ultimately, primary prevention should be considered, to reduce anxiety during pregnancy.

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COMPARISON OF MORPHINE TREATMENT WITH CONCOMITANT CLONIDINE AND MORPHINE ADMINISTRATION FOR NEONATAL ABSTINENCE SYNDROME: A POPULATION COHORT STUDY

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Introduction: Clinically significant neonatal abstinence syndrome (NAS) most often occurs in infants who are exposed to opioids in utero. NAS can involve a variety of signs resulting from increased neurological excitability and autonomic dysregulation. There are a number of pharmacologic treatment options available to clinicians when treating NAS. In 2010, the tertiary-care center involved in this study adjusted the treatment guidelines for NAS to include concomitant clonidine and morphine administration. To date there has been no evaluation of this practice change or confirmation of the perceived benefit on neonatal outcomes. **Objective:** To compare length of treatment and need for breakthrough doses between the clonidine + morphine regimen and morphine alone for the treatment of NAS in a neonatal intensive care unit from 2006-2015. **Methods:** This project is a retrospective population-based cohort study using a linkage of database information with chart review data. A cohort of infants treated pharmacologically for NAS resulting from opioid exposure in utero delivered between 2006-2015 were identified using the Nova Scotia Atlee Perinatal Database (NSAPD). Maternal, obstetrical, and perinatal characteristics of eligible infants was obtained from the NSAPD. Chart reviews were completed for each infant to gather treatment information. **Results:** 146 infants coded as being treated for NAS were identified. The number of coded NAS diagnoses steadily increased from 2006-2015; 28 infants were treated with morphine alone and 97 were treated with clonidine and morphine. The remaining 21 infants either received a different pharmacologic agent such as phenobarbital, or did not receive medication before discharge. In the morphine + clonidine group the mean duration of morphine treatment was 18.5 days (SD=12.4) and in the morphine alone group, the average length of treatment was 11.9 days (SD=7.3). At least one breakthrough dose of morphine due to high Finnegan scores was administered to 49.5% of infants in the morphine + clonidine group and 21% of infants in the morphine alone group (p=0.009). **Conclusion:** The morphine + clonidine combination for the treatment of NAS was associated with longer duration of treatment and a higher need for breakthrough dosing compared to morphine alone in the current study.

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PRETERM INFANT GROWTH VELOCITY CALCULATIONS: A SYSTEMATIC REVIEW

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Introduction: Preterm infant growth rates are faster than other age groups. Preterm infants can double or triple their weight during their first few months compared to 4-5 months for term infants to double their weight. Clinicians assess the healthy growth of preterm infants in part by comparing to published values of growth velocity. However, researchers use a variety of methods to summarize growth velocity of preterm infants. **Objective:** To determine the frequency of use of numerical methods used to quantify weight, length, and head circumference growth velocity in preterm infants (< 37 weeks at birth) including g/kg/day, g/day, cm/week, and change in z-scores/standard deviation scores in a systematic review using PRISMA methods. **Methods:** A search was conducted of the MEDLINE Database using PubMed up to April 2015 for studies that measured growth as a main outcome in preterm neonates between birth and hospital discharge or 40 weeks postmenstrual age. English, French, German and Spanish papers were included. Two reviewers extracted the data, with any disagreements being resolved in discussion with a third reviewer. The methods

reported in the included studies were described using frequencies and percentages, with frequencies of the method used over time illustrated graphically. The statistical comparison of the frequencies of velocity calculations before and after 2005 were made using Fisher's Exact test. **Results:** Results revealed a wide range of methods used: g/kg/day: 40%, g/day: 35%, change in z-scores/standard deviation scores: 24%. For g/kg/day, the time for the calculations varied: 63% began at birth/admission, 39% began at the weight nadir or after birth weight was regained; 16% used a unit-less exponential formula. For the denominators used in g/kg/day calculations, 61% did not define the denominator. Temporal trends in head circumference growth and length gain changed from predominantly centimeters/week to predominantly z-scores. **Conclusion:** The lack of consistency of methods used to quantify preterm infant growth presents an obstacle for the use of research results to guide clinical practice, illustrating a need to develop clinical practice recommendations to standardize preterm infant growth calculations to allow for comparisons between studies.

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BISPHENOL A EXPOSURE AND CHILDHOOD OBESITY: A SYSTEMATIC REVIEW

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Introduction: Bisphenol A (BPA) is an endocrine disrupting chemical. Previous research suggests that it can alter growth and metabolism, and is associated with obesity in children. **Objective:** To conduct a systematic review of the research literature that has investigated the associations between prenatal and childhood exposure to BPA and obesity in children up to 19 years of age. **Methods:** We searched electronic bibliographic databases (MEDLINE, PubMed, EMBASE, PsycINFO, CINAHL, and ERIC); reference lists of included articles, and conference abstracts (American Psychiatric Association, American Academy of Neurology, Pediatric Academic Societies and International Society of Environmental Epidemiology). **Results:** From 3506 citations, 15 articles met our inclusion criteria. Descriptive analyses revealed that prenatal exposure to maternal BPA was associated with alterations (increases or decreases) in body mass index and waist circumference ratio in four studies. In four studies no associations were found. Childhood BPA concentrations were found to be associated with body mass index and waist circumference ratio in seven studies; no association was reported in three studies. **Conclusion:** Limited observational evidence suggests potential associations between prenatal or childhood exposure to BPA and childhood obesity. Prospective longitudinal cohort studies are needed assess whether level of BPA exposure prenatally or in childhood contributes to the risk of childhood obesity.

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TRAJECTORIES OF MATERNAL ANXIETY AND CHILD DEVELOPMENT AT THREE YEARS

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Introduction: Approximately 17% of children experience developmental problems at school entry. Risk factors for these delays include biological risk factors(e.g. preterm birth),socio demographic risk factors (e.g. poverty),and psychosocial risk factors(e.g. maternal depression, anxiety). 12 to 24% of women experience depression during pregnancy and approximately 19% suffer from anxiety and depression in the first year postpartum. Maternal anxiety during the early childhood period can have serious consequences and can compromise child development. Existing literature on maternal anxiety has focused on anxiety during the pregnancy or postnatal period and its association with child development. However, few studies have investigated the relationship between maternal anxiety symptoms over time and child developmental delays. **Objective:** The aim of this study is to examine the consequences of antenatal and postnatal exposure of maternal anxiety on child global development. **Methods:** The All Our Babies (AOB) study is an ongoing prospective pregnancy cohort of mothers and children from Canada. A total of 1983 participants were included in the current study. Study participants completed three questionnaires spanning pregnancy to four months postpartum and participated in the follow up study. Maternal anxiety was assessed using Spielberg State Anxiety Inventory (SSAI). Child development was measured using The Ages and Stages Questionnaires (ASQ) across five domains: Communication; Gross Motor; Fine Motor; Problem Solving and Personal-social. Latent class analysis was conducted to identify trajectories of women's anxiety across six time points (pregnancy to three years postpartum). Logistic regression was used to explore the relationship between the anxiety trajectories and child developmental delays while adjusting for covariates. **Results:** The majority of participants were between 25-34 years (73%), were partnered (96%), had some

post-secondary education (92%), had family incomes ≥ 80,000 (73%), and were born in Canada (82%). 10% of children were delayed on two or more ASQ domains at age 3 years. Three distinct trajectories of maternal anxiety symptoms were identified over time: minimal anxiety symptoms (n =1100, 55%); sub-clinical anxiety symptoms (n =727, 37%);and persistent high anxiety symptoms (n = 156, 8%. Multivariate analysis showed mothers assigned to the subclinical or high anxiety symptoms classes were associated with an increased risk of developmental delays in children at 3 years. **Conclusion:** With more than 25% of women experiencing poor mental health from conception to one year postpartum,identifying those with subclinical or persistent high symptoms for early intervention may mitigate the risk of child developmental delays.

P185

RECENT TRENDS IN BIRTH PREVALENCE OF CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT) IN CANADA AND POTENTIAL REASONS FOR CHANGE.

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Introduction: CAKUT are common malformations with varied genetic and environmental causes. They are the primary cause of childhood end-stage kidney disease, and may lead to renal failure later in life. **Objective:** This study aimed to examine recent changes in the birth prevalence and epidemiology of CAKUT in Canada. **Methods:** Data on livebirths, stillbirths and identified terminations of pregnancy in Canada (excluding Quebec) between 2002 and 2013 were obtained from the Canadian Institute for Health Information. CAKUT cases were coded using ICD-10 CA and classified into various subtypes including renal agenesis, renal dysplasia, hydronephrosis or obstructive nephropathy and autosomal recessive polycystic kidney disease (ARPKD). **Results:** A total of 16 200 cases was identified, yielding an overall birth prevalence rate of 48.4 per 10,000 total births, with a male to female ratio of 2.2. Rates of renal agenesis, renal dysplasia and hydronephrosis respectively increased from 3.4, 1.7, 16.7 per 10,000 to 4.2, 3.5 and 22.6 per 10,000 (p value for trends all <0.001) between 2002 and 2013, while ARPKD declined from 1.88 to 0.41 per 10,000 (p<0.001). Obstructive nephropathy (36.6%), unilateral renal agenesis (6.0%) and multicystic dysplasia (5.1%) were the commonest malformations. Seventeen percent had associated anomalies, including chromosomal abnormalities (1.4%), nonchromosomal recognizable disorders (2.8%) and other patterns of multiple malformations (13.0%). **Conclusion:** Changes in utilization of prenatal screening, frequency of abnormal developmental processes (intrauterine reprogramming of renal physiology), and coding practices are likely contributors to the changes observed in the birth prevalence of CAKUT. Further investigation is warranted, including the possible role of maternal factors in accounting for increases in renal agenesis and obstructive nephropathy.

THEME: Reproductive (Epi)genetics/Fertility

P194

SPECIFIC ALTERATIONS IN THE HISTONE MODIFICATION LANDSCAPE AS A CONSEQUENCE OF TRANSIENT DNMT1 DEFICIENCY IN MOUSE ES CELLS

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Introduction: Genome-wide demethylation and remethylation of DNA during early embryogenesis are essential for mammalian development and genome integrity. Through mostly unknown mechanisms, imprinted germline differentially methylated domains (gDMDs) are able to retain their methylation profiles during the reprogramming period. Using an embryonic stem (ES) cell line, in which Dnmt1 is regulated by a tet-off system (Dnmt1tet/tet ES cells), we recently showed that a temporary lack of Dnmt1 activity triggers the inherited loss of gDMDs and gDMD-like DNA methylation profiles, whereas most regions of the genome are able to recover original DNA methylation levels. **Objective:** Here, we investigate how the transient lack of Dnmt1 activity influences global gene expression and epigenetic landscape. **Methods:** Our RNA-seq experiment highlighted two noteworthy gene clusters; one set of genes that become strongly activated and one that become strongly inactivated. We then explored by ChIP-Seq if the transient lack of Dnmt1 protein prompts rearrangements in the histone mark landscape (H3K4me3, H3K27me3, H3K27ac) associated to these two gene clusters. **Results:** For some genes, we believe that alterations in the histone landscape impede the recruitment of DNMTs as for others, the perturbations occur with the absence of neighbouring inherited loss of DNA methylation. **Conclusion:** The present study highlights new perspectives on how alterations in Dnmt1-dependent methylation maintenance can alter DNA methylation profiles, histone modification cross-talk and gene expression as well as explain inherited epigenetic dysregulation events that could occur in abnormal cells and during early embryo development.

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DETERMINING THE LINKS BETWEEN BODY MASS INDEX, FOLATE, HOMOCYSTEINE AND FERTILITY PARAMETERS IN MEN

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Introduction: Infertility occurs in 15% of couples with male factors implicated in 30-40% of identifiable causes. Numerous factors contribute to infertility such as obesity, smoking and other lifestyle factors. The role of paternal diet and obesity in reproductive health, specifically folate is unclear. In a mouse model lifetime paternal folate deficiency was associated with increased birth defects and an altered sperm epigenome (Lambrot et al. Nat Commun 2013). **Objective:** The objective of this study is to explore folate status in men and its relationship to sperm quality, and the heritable sperm epigenome. We hypothesized that levels of folate, homocysteine (HCY) and BMI in the overweight and obese (O) group will be associated with altered fertility parameters. **Methods:** In a pilot study, men (n=60) were recruited at the CReATe fertility centre, (IRB approval McGill and U Toronto) for BMI assessment, semen and blood collection. Semen samples were analysed for fertility parameters (DFI, count, motility, volume) and blood samples for RBC folate and plasma HCY. RBC folate values were assessed using RBC hemolysate method, folate deficiency (FD) was defined as <320 nmol/L RBC. Plasma HCY levels were measured by ADvia Centaur immunoassay, elevated HCY was defined as >11 umol/L. Participants were measured for weight and height to calculate BMI. The O group was defined as BMI ≥25 kg/m2. **Results:** The mean age of study participants was 38.5 years ± 6 years. The majority of participants were classified as overweight and obese (68%, n=41/60, mean 30 kg/m2, range 25 to 41 kg/m2). FD was detected in 45% of men (n=24/53,

mean 275 nmol/L, range 210 to 319 nmol/L). FD, overweight and obese men had an increased mean sperm DNA fragmentation (DFI) (t test, p=0.04), and reduced mean motility (t test, p=0.04). HCY was elevated in 48.7% of men (n=27/58, mean 12.4 umol/L, range 11.1 to 15.81 umol/L). Elevated HCY was associated with reduced mean semen volume (t test, p=0.04). **Conclusion:** This preliminary analysis suggests that folate status, overweight status and fertility parameters are interrelated. The suggestions of new links between obesity, FD and increased DFI are intriguing as high DFI is associated with increased pregnancy loss (Robinson et al. Hum Reprod 2012). In our ongoing studies, data on 200 men will confirm these relationships and the link to the sperm epigenome.

P196

THE INFLUENCE OF THE SEROTONIN TRANSPORTER GENE (5-HTT) ON THE RELATIONSHIP BETWEEN PRENATAL MATERNAL STRESS AND DELAYED GRATIFICATION.

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Introduction: Delayed gratification (DG) is the ability to resist temptation of an immediate reward in order to obtain a higher one afterwards and has been shown to predict better SAT scores, educational attainment, and body mass index. Inability to demonstrate DG in childhood has been associated with drug addiction, and obesity, and adolescent behaviour problems, particularly aggression in boys. Animal studies suggest that the serotonin transporter gene (5-HTT) has various consequences regarding emotional and behavioral conduct, through its effect on the executive attention network involved in self-regulation. The SS 5-HTTLPR polymorphism is linked to the risk of aggression in childhood. Specifically, PNMS has been shown to be associated with externalizing problems during childhood. **Objective:** The objective of this study was to determine whether 5-HTTLPR polymorphism moderates the relationship between disaster-related PNMS and DG. **Methods:** DG (time to failure), was assessed in 95, 4 year-old children (43 girls) using the Stanford marshmallow experiment. PNMS (i.e., objective hardship, subjective distress and cognitive appraisal) were assessed by questionnaires following the 2011 Queensland Flood. The SS 5-HTT was used as a moderator and was available for a subset of 80 children (38 girls). DNA was extracted from the saliva sample using PrepIT-L2P kit (DNA Genotek Inc.) according to the manufacturer's instructions. Polymerase chain reaction (PCR) was performed to span the central portion of the repeats in the 5-HTTLPR and genotyping was conducted using agarose gel analysis of PCR product. The three genotypes s/s, s/l, l/l were analyzed. Survival analysis and Cox regression model were used for data analysis. **Results:** Negative maternal cognitive appraisal of the flood was associated with increased risk of failing the DG task in children with the SS 5-HTT polymorphism only (p=.003). **Conclusion:** PNMS may hinder the development of DG in children already genetically susceptible for problems in self-regulation. Further research is required to determine if problems in DG predict outcomes in the present cohort.

P197

MATERNAL VITAMIN D RECEPTOR GENES, VITAMIN D STATUS AND RISK OF PRETERM BIRTH

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Introduction: Vitamin D is a known immune system modulator and has been shown associated with inflammatory response. Vitamin D's effects are exerted via the vitamin D receptor (VDR) and there is VDR genetic variation in the population. However, there is lack of evidence on how the maternal vitamin D status interact with the VDR gene single nucleotide polymorphisms (SNPs) and risk of spontaneous preterm birth. **Objective:** To determine the relationships among maternal vitamin D receptor polymorphisms, vitamin D status in pregnancy and risk of preterm birth. **Methods:** This is a prospective cohort study of 697 pregnant women. Maternal plasma 25(OH)D at 12-18 weeks gestation were measured using chemiluminescence immunoassay. Polymerase chain reaction/restriction fragment length polymorphism was applied to test the genotype frequency of vitamin D receptor gene polymorphisms [ApaI (rs7975232), BsmI (rs1544410), Cdx2 (rs11568820), FokI (rs2228570), TaqI (rs731236) and Tru91 (rs757343)]. **Results:** Maternal vitamin D receptor gene BsmI and TaqI polymorphisms were associated with low vitamin D status [25(OH)D

less than 50 nmol/L] (both p <.005). The frequency of BsmI GG+AG genotype, TaqI TT+CT genotype were significantly higher in women who developed preterm birth compared with those who did not (24.0% vs. 14.1%, P = 0.01; 22.7% vs. 14.5%, P = 0.04; respectively). The vitamin D receptor gene ApaI , Cdx2, FokI , and Tru91 polymorphisms did not show any difference in patients who developed preterm birth compared with those who did not (P >0.05). After adjusting for potential confounding factors, logistic regression analysis showed that both BsmI GG+AG and TaqI TT+CT genotype were associated with an increased risk or preterm birth (aOR 3.09, 95% CI 1.14 - 8.43; aOR 3.06, 95%CI 1.08-8.67) in only women with low vitamin D status [25(OH)D < 50 nmol/L]. **Conclusion:** Our findings suggest that maternal vitamin D receptor gene BsmI and TaqI polymorphisms may be associated with risk of preterm birth in pregnant women with low vitamin D status.

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HEDGEHOG SIGNALING DYNAMICS DURING EXTRAEMBRYONIC ENDODERM DIFFERENTIATION

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Introduction: Hedgehog (Hh) proteins play a role in patterning of the vertebrate embryo. In mouse, Indian Hedgehog (IHH) is linked to eXtraembryonic ENdoderm (XEN) formation, later forming the yolk sac. By the late blastocyst stage, the ICM gives rise to the epiblast and the primitive endoderm (PrE), the latter contributing to parietal (PE) and visceral endoderm (VE). Collectively, PrE, PE, and VE comprise the XEN. **Objective:** Currently, details regarding the role and mechanisms of the Hh signaling pathway during XEN differentiation is unknown. **Methods:** F9 teratocarcinoma cells treated with retinoic acid (RA) mimic the differentiation to PrE, while subsequent treatment with db-cAMP commits the cells to PE. Differentiation in vitro involves several signaling pathways including canonical Wnt/B-catenin, which is activated by GATA6. **Results:** This master regulator of endoderm and XEN formation also up-regulates Ihh, which when translated serves as a ligand activating the Hh pathway that is required, but not sufficient, to differentiate F9 cells to PrE. No change in GLI1-3 mRNA expression with differentiation indicates a change in proteolytic processing of these proteins, altering the stoichiometry of transcriptional repressor to activator forms. Results show a change in endogenous full-length GLI3 with differentiation to PrE. Interestingly, the overexpression of GLI3A, the transcriptionally active form, is sufficient to differentiate F9 cells into a XEN lineage. **Conclusion:** Based on these results and the fact that B-catenin can interact with the GLI3 repressor (Ulloa et al., 2007), we propose that there is an interaction between Hh and Wnt signaling that contribute to the differentiation of XEN.

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THE ROLE OF EPIGENETIC REGULATORS IN THE FETAL PROGRAMMING OF HYPERTENSION

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Introduction: The causes of hypertension are complex and involve both genetic and environmental factors. A sub-optimal environment during fetal development has been linked to the development of adult diseases including hypertension; a concept known as fetal programming. Animal studies show that timed in-utero exposure to high levels of glucocorticoids results in the postnatal development of hypertension in adulthood. Evidence suggests that in utero stress can alter patterns of gene expression, possibly a result of alterations in the topology of the genome by epigenetic markers such as DNA methyltransferases (DNMTs) and histone deacetylases (HDACs). **Objective:** The objective of this study was to determine the role of epigenetic regulators in mediating the fetal programming of hypertension. Specifically, this study examined the effects of the HDAC inhibitor valproic acid (VPA) or the DNMT inhibitor 5-aza-2'-deoxycytidine (5aza2DC) on blood pressure (BP) and phenylethanolamine N-methyltransferase (PNMT) gene expression in programmed adult rats. PNMT, the terminal enzyme in the catecholamine biosynthesis pathway, is responsible for the biosynthesis of epinephrine, and is a candidate gene for hypertension. **Methods:** Pregnant Wistar Kyoto (WKY) dams received daily (GD.14-21) dexamethasone injections (Dex; a synthetic GC) (100ug/kg) S.C. or saline. Following birth,

subsets of programmed offspring were given either VPA (250mg/kg/day) or 5aza2DC (1mg/kg/day) or saline via I.P. injection starting at the onset of hypertension (week 12). BP of the offspring was measured into adulthood (weeks 5-14) and adrenal tissue was assessed for gene expression levels of catecholamine biosynthetic enzymes using qRT-PCR. **Results:** Data from blood pressure measurements show that prenatal Dex exposure increases BP, and that these epigenetic inhibitors attenuate the Dex-mediated development of hypertension. This observation is supported with concurrent decreases in PNMT and TH in both male and female in the Dex +VPA/5aza2DC offspring when compared to the Dex group. Interestingly, preliminary data from a qRT-PCR array shows that Dex programmed animals display altered HDAC I levels. **Conclusion:** This evidence suggests that fetal programming of the catecholamine biosynthetic pathway is mediated through epigenetic mechanisms. Investigations into causes of altered epigenetic machinery may reveal a link between the in utero environment and the fetal programming of cardiovascular disease.

P200

DNA METHYLATION PROFILES IN AN ANIMAL MODEL OF NEONATAL INFLAMMATORY WHITE MATTER INJURY

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Introduction: Preterm infants are vulnerable to inflammation-induced white matter injury (WMI) which is associated with neurocognitive impairment and increased risk of neuro-psychiatric diseases in adulthood. Epigenetic mechanisms play a role in normal development and also in pathological adaptation in response to environmental challenges. Furthermore, changes in DNA methylation, which is considered the most stable and well-characterized epigenetic modification, were associated with preterm birth (Cruickshank et al., Genome Med, 2013). We hypothesize that perturbations in normal methylation profiles following inflammation-induced WMI in the neonatal period could be implicated in the processes leading to known neuropsychiatric diseases in adulthood. **Objective:** The aim of this study was to assess DNA methylation profile in the brain of neonatal rats subjected to WMI compared to controls at 24h (P4) and 21 days (P24) post-injury. **Methods:** We injected LPS (1mg/kg) or sterile saline in the left side of the corpus callosum of P3 rat pups. Brains were collected at P4 (n=8) and P24 (n=8). We extracted genomic DNA from ipsilateral brain hemisphere and produced multiplex libraries of reduced representation bisulfite sequencing to establish genome-wide quantitative DNA methylation profiles. Genomic regions (100bp, 2 CpG min, 15x sequencing) with a ±≥10% average CpG methylation differences between groups of replicates (Ctrl vs LPS) were designated as differentially methylated tiles (DMTs). Functional enrichment analyses of genic associated DMTs were generated using Metascape (http://metascape.org). **Results:** A total of 1590 and 1838 DMTs were observed at P4 and P24 respectively. At P4 and P24, inflammation induced hypermethylation in genes related to nervous system development and hypomethylation of genes associated with inflammatory pathways (see table). **Conclusion:** Neonatal WMI resulted in perturbed brain DNA methylation profiles of genes promoting inflammatory pathway at P4 that remained at P24. It also caused a persistent alteration of brain DNA methylation profiles in genes related to normal development of nervous system (P4 and P24). Further analysis of target genes through qPCR will be performed to determine if alterations in DNA methylation are associated with aberrant gene expression regulation.

THEME: Developmental Origins of Health and Disease

P2

INTENSIVE GESTATIONAL GLYCEMIC MANAGEMENT AND CHILDHOOD OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Hyperglycemia in pregnancy is associated with increased risk of offspring childhood obesity. Treatment reduces macrosomia, however it is unclear if this effect translates into a reduced risk of childhood obesity. **Objective:** We performed a systematic review and meta-analysis of randomized controlled trials to evaluate the efficacy and safety of intensive glycemic management in pregnancy in preventing childhood obesity. **Methods:** We searched MEDLINE, EMBASE, CENTRAL, and ClinicalTrials.gov up to February 2016 and conference abstracts from 2010 to 2015. Two reviewers independently identified randomized controlled trials evaluating intensive glycemic management interventions for hyperglycemia in pregnancy and included four of the 383 citations initially identified. Two reviewers independently extracted trial-level data with piloted forms and evaluated internal validity of included studies using the Cochrane Collaboration's Risk of Bias tool. Data was pooled using random effects models. Statistical heterogeneity was quantified using the I2 test. The primary outcome was age- and sex-adjusted offspring obesity measured in childhood. Secondary outcomes included offspring waist circumference and weight in childhood and maternal hypoglycemia during the trial (safety outcome). All outcomes were specified before the start of the review. **Results:** The four eligible trials (n=767 children) similarly used lifestyle and insulin to manage gestational hyperglycemia. We found no association between intensive gestational glucose management and childhood obesity at 7-10 years of age (relative risk 0.89, 95% CI 0.65 to 1.22; 2 trials; n=568 children). Waist circumference also did not differ between treatment and control arms (mean difference −2.68 cm; 95% CI −8.17 to 2.81 cm; 2 trials; n=568 children). **Conclusion:** Intensive gestational glycemic management is not associated with reduced childhood obesity in offspring, but randomized data is scarce. Long-term follow up of trials should be prioritized and comprehensive measures of childhood metabolic risk could be considered as outcomes in future trials.

P4

EXERCISE IN PREGNANCY AND CHILDREN'S CARDIOMETABOLIC RISK FACTORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Two in three Canadian children have at least one risk factor for cardiovascular disease before they reach 18 years old. Although exercise interventions during pregnancy were thought to decrease this risk, individual studies provide conflicting results. **Objective:** We wanted to determine, from the current literature, if prenatal exercise could positively impact offspring cardiometabolic health. **Methods:** We searched Pubmed, MEDLINE, EMBASE, and CENTRAL up to May 2016. Two reviewers independently identified observational studies and randomized controlled trials (RCTs) evaluating prenatal exercise and offspring cardiometabolic outcomes and extracted trial-level data with piloted forms. The primary outcome was birthweight; secondary outcomes included large-for-gestational age status, fat and lean mass, dyslipidemia, and blood pressure. All outcomes were specified before the start of the review. We included 47 of the 10 574 citations initially identified and evaluated their internal validity. Data was pooled using random effects models.

Statistical heterogeneity was explored and quantified using the I2 test. Analyses were done between July and September 2016 **Results:** We included 12 observational studies (n=165 230 children) and 24 RCTs (n=4930 children). Observational studies were highly heterogenous and had discrepant conclusions. Meta-analyzed RCTs indicated that prenatal exercise did not significantly impact birthweight (mean difference [MD] −45.8g, 95% confidence interval [CI] −156.1 to 64.5g) or large-for-gestational age status (risk ratio 1.45, 95%CI 0.97 to 2.17) compared to no exercise. Sensitivity analyses of RCTs showed that prenatal exercise reduced birthweight only in women with a body mass index <25 kg/m2 (MD −238.5g, 95% CI: −475.1, −1.8g). Other outcomes were too scarcely reported to be meta-analyzed. **Conclusion:** Prenatal exercise does not significantly impact birthweight or large-for-gestational-age status and is not sufficient to reduce birthweight in women with overweight. Longer follow up of offspring exposed to prenatal exercise is needed along with measures of relevant metabolic variables (eg. fat mass).

P6

EARLY POSTNATAL STRESS ACCELERATES FUNCTIONAL DEVELOPMENT OF THE VISUAL SYSTEM

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Introduction: Early life stress (ELS) has been associated with long-term adverse health outcomes. Previous studies have suggested that adverse perinatal programming by stress may increase the risk of depression, schizophrenia and behavioural disturbances in children. However, little is known about the mechanisms underlying how ELS alters brain developmental trajectories to result in behavioural and neurological disturbances later in life. We hypothesize that partial loss of function is due to regional precociousness, which desynchronizes the topographically coordinated patterns of brain development. Here, we propose that ELS may desynchronize brain development by accelerating maturation of areas relevant to survival in a stressful environment, as reflected by a premature shift in critical developmental periods. **Objective:** To determine whether ELS alters the developmental timing of the visual system, the premier model of developmental brain plasticity. **Methods:** Mice either served as controls or were stressed from postnatal days (P) 12-13. Animals were then assessed for eye-opening twice daily from P13-15. Depth perception was assessed on P20 using a visual cliff task, and anxiety-like behaviour was assessed on P20, P28 and P35 using the elevated plus maze. **Results:** Stressed animals opened their eyes significantly earlier than controls ($p < 0.01$). In the visual cliff task, stressed pups also spent significantly less time in the “open” side ($p < 0.01$), had a significantly higher latency to enter the “open” side ($p < 0.01$) and made significantly fewer “open” side entries ($p < 0.01$). Thus, stressed animals showed a side preference and exhibited cliff avoidance, indicating greater depth perception than controls. In addition, stressed animals performed significantly fewer open arm entries on the elevated plus maze than did controls at all time points, indicating that ELS experience promoted anxiety-like behaviours. **Conclusion:** We found that ELS induced accelerated development of the visual system in association with heightened affective state later in life. Accelerated brain development may present an evolutionary advantage to support survival in a stressful environment, but it may also lead to topographical desynchronization and impair certain functions and behaviours.

P8

A SINGLE COURSE OF PRENATAL GLUCOCORTICOID TREATMENT MODIFIES THE STRESS RESPONSE AND PITUITARY GENE EXPRESSION ACROSS TWO GENERATIONS

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Introduction: Pregnant women at risk for preterm delivery (approx. 10% of pregnancies) are treated with synthetic glucocorticoids (sGC) to mature the fetal lungs and reduce infant mortality. Single course treatment with sGC has been linked with increased hypothalamic-pituitary-adrenal (HPA) axis response to stress in children and altered HPA stress response in young second generation sheep offspring (F2). **Objective:** To investigate the effects of prenatal sGC on the cortisol response to stress and expression of HPA regulatory genes in the anterior pituitary of F1 and F2 adult male and female guinea pigs. **Methods:** Pregnant guinea pigs (F0) were treated with a single course of the sGC betamethasone (Beta; 1mg/kg) or saline (Veh; 1ml/kg) on gestational days 50 and 51. F1 female offspring were mated with control males to produce F2 offspring. Salivary cortisol response to open field stress was measured in adult F1 and F2 males (~day 80).

Data were analyzed for net (AUCN) and total area under the curve (AUCT). Avpr1b, Crhr1, Pomc, Nr3c1 (Gr), and Nr3c2 (Mr) mRNA were analyzed in the anterior pituitary by qRT-PCR in F1 and F2 animals. **Results:** sGC exposure did not modify the cortisol stress response in F1 or F2 females but led to a reduced cortisol stress response in F1 males (decreased AUCN¬; P<0.05) and an increased cortisol stress response in F2 males (AUCT; P<0.05). F1 generation Beta males exhibited a decreased expression of Mr, whereas Beta females were unaffected. F2 Beta males displayed a reduced expression of Avpr1b, and F2 Beta females demonstrated an increase in Gr expression and a decrease in Pomc expression. **Conclusion:** This is the first study to demonstrate that single course prenatal treatment with sGC programs HPA function in adult F2 offspring. Reduced HPA response to stress in F1 males was associated with decreased expression of Mr, which mediates HPA negative feedback. The increased cortisol stress response in F2 males was associated with a reduction in pituitary sensitivity to vasopressin, though how this relates to the HPA stress response requires further investigation. In F2 females, the HPA stress response was unaffected with treatment, despite increased Gr and decreased Pomc, both of which would be expected to decrease cortisol release. These data also reveal that a single course of sGC results in long-term programming of the HPA axis across 2 generations. This is clinically important since alterations in HPA function can result in adverse cardiometabolic and neurobehavioural health outcomes. Supported by CIHR

P10

THE NEXT GENERATION STUDY: AN UPDATE ON THE BIOLOGICAL RISK FACTORS FOR TYPE 2 DIABETES IN INDIGENOUS CHILDREN IN MANITOBA

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Introduction: Children born to a parent with type 2 diabetes (T2D) are at an increased risk of developing T2D at a young age. Since the first diagnosis in Manitoba in 1984, the rate of T2D in children has been reported as 10-15 times higher than any other Canadian province, with the majority affected having Indigenous heritage. Although some risk factors for T2D have been identified (such as obesity and family history), much of the biological risk factors for childhood-onset T2D remain unknown. **Objective:** This study aims to (1) determine the natural history and risk factors of T2D in children and (2) to prevent, delay, and treat T2D in at-risk children. **Methods:** The study is a cohort of children born to a parent with pre-gestational T2D. Annual data collection included height, weight, and urine albumin to creatinine ratios from ages 1-6. From the age of 7, additional study variables included waist circumference, blood pressure, 75g oral glucose tolerance test, glycated hemoglobin (A1c), measures of inflammation, and liver and kidney function. Testing for the genetic polymorphism HNF1α G319S genotype was done at age 7. **Results:** Currently, 206 children (108 females, 97 males) born to 97 parents (88 mothers, 9 fathers) are followed in this study. Twenty-nine of these children (20 females; 9 males) have been diagnosed with T2D at a median age of 12 years, with 28 (97%) born to a mother with pre-gestational diabetes. Of the children diagnosed with T2D, HNF1α status was GS (n=19, 66%), SS (n=7, 24%), and GG (n=3, 10%). This differs from the status prevalence in the Manitoba clinic population (GS=32%, SS=12%, GG=56%). An additional 11 children (5 females, 6 males) were diagnosed with impaired glucose tolerance (a form of pre-diabetes), with 9 (82%) born to mothers with pre-gestational T2D. **Conclusion:** We observed that children born to mothers with childhood-onset T2D are at a very high risk of developing T2D in childhood. The rate of childhood-onset T2D in our birth cohort is much higher than provincial rates. Offspring who developed T2D in childhood were also more likely to harbour one or two of the risk alleles of HNF1α suggesting genetics and in-utero exposure to pre-gestational diabetes play an important role in childhood T2D. Recently, this study expanded to follow Indigenous women through their pregnancies and to collect cord blood samples at birth. The future collection and analyses of cord blood may provide us with an opportunity to explore the possible fetal origins of T2D and further understand the effect of intrauterine exposure to maternal T2D.

P11

RESEARCH ADVANCEMENT THROUGH COHORT CATALOGUING AND HARMONIZATION (REACH): A MAELSTROM RESEARCH INITIATIVE FACILITATING COLLABORATIVE DOHAD RESEARCH

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Introduction: Numerous population-based cohorts have been established worldwide to support innovative research. Millions of citizens contributed time, information and biological specimens to these cohorts, which in turn led to major scientific progress and to a better understanding of the relation between various risk factors and health outcomes. However, detailed information about these studies and the data collected is often unavailable or difficult to obtain. This represents a major barrier for investigators interested in using the data and hinders the establishment of cross-cohort collaborations. The research community is therefore stressing the importance of data discovery tools that facilitate access, retrieval, and reuse of existing cohort data. **Objective:** In 2016, Maelstrom Research launched the Research Advancement through Cohort Cataloguing and Harmonization (ReACH) initiative, a CIHR funded Developmental Origins of Health and Disease (DOHaD) research network. ReACH aims to enhance the potential for collaborative and cross-disciplinary research (outputs generated faster and at a lower cost), expand research perspectives (leverage national and international collaborations), improve quality of research practices, and foster the development of innovative evidence-based research on the DOHaD. **Methods:** In partnership with European and North American research networks, Maelstrom Research developed methods and software to leverage collaborative epidemiological research. Maelstrom Research resources include a study and variable catalogue offering web-based access to comprehensive descriptions of study characteristics as well as the complete list of variables collected by a selection of these studies. A search interface allows investigators to easily identify studies of interest and data items available to answer specific research questions. **Results:** Over the next 5 years, ReACH initiative will implement a comprehensive web-based catalogue and a data harmonization platform to facilitate the use and co-analysis of data and biological samples collected by Canadian pregnancy and birth cohorts. ReACH catalogue will include 26 cohorts (53,300 mother-child dyads and 17,800 fathers, totaling 125,000 participants) that directly address the DOHaD theme. **Conclusion:** We encourage new networks and studies to join Maelstrom Research efforts and invite investigators to make use of the ReACH initiative resources for their research projects.

P12

MOTHERS TO BABIES STUDY: AN EXPLORATION INTO PREGNANT WOMEN'S UNDERSTANDING OF DOHAD

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Introduction: The Developmental Origins of Health and Disease (DOHaD) paradigm explains how the early life environment modulates development to influence long term health outcomes. As epidemiological and experimental evidence in DOHaD grows, interest in the application and knowledge translation of DOHaD-based concepts is increasing. In this context, the Mothers to Babies Study (M2B) aims to 1) explore the relevance of DOHaD in women's perceptions of a healthy pregnancy and 2) use DOHaD evidence to develop a community-based intervention to support healthy pregnancies and healthy families. **Objective:** In this pilot survey, we aimed to explore gaps between DOHaD-based evidence of disease risk and the knowledge held by pregnant women. **Methods:** This pilot study used survey data from the M2B study. Data was collected from pregnant women, using a 169 item questionnaire. We surveyed pregnant women living in the Hamilton area on topics of pregnancy nutrition, health practices, and beliefs. Participants were recruited from prenatal classes, midwifery clinics, Ontario Early Years Centres, and social media platforms. **Results:** In total, 78 pregnant women from Hamilton, Ontario completed the M2B Study pilot questionnaire. The sample had a mean age of 29.97+ 5.3 years, with 41% of women being from low income households (defined as earning <39 999). Only 31% of respondents agreed that their diet prior to pregnancy affected their child's chance of becoming obese, 9% agreed their pregnancy diet affected their grandchildren's risk of obesity, and 36% agreed their diet during breastfeeding would impact their child's risk of obesity. In contrast, while respondents' understanding of DOHaD-based concepts was low, the majority of respondents agreed that what they ate influenced their risk of becoming obese, and that smoking during pregnancy would harm their baby (83% and 89%, respectively). **Conclusion:** Conclusion Few women in the surveyed population had a general understanding of DOHAD-based concepts; however, most women were aware of mainstream healthy pregnancy practices, such as the effects of smoking during pregnancy. The data shows a gap

between the evidence for DOHaD-based concepts, and public knowledge of these concepts. It is clear that alongside other health education strategies, specific efforts to educate pregnant women on DOHaD-based concepts are needed.

P14

EARLY POSTNATAL SHIPMENT STRESS REDUCES EXPLORATORY BEHAVIOUR THROUGHOUT LIFESPAN

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Introduction: Prenatal and early life stress has been associated with both short-term and long-term adverse health outcomes. Previous studies have shown that gestational stress influences programming of HPA axis activity and fetal brain development to permanently change stress response and vulnerability to psychiatric disorders later in life. **Objective:** To determine in a mouse model if early postnatal stress alters stress sensitivity, behaviour and long-term mental health outcomes. **Methods:** Stress was induced by shipment of pregnant mouse dams from an external breeder from Quebec to Lethbridge, Alberta. Shipment stress occurred on postnatal day 12 within a 12-hour time window. Mice bred in-house at the local vivarium served as non-stress controls. Multiple behavioural assessments were performed at different time points throughout the lifespan of both treatment groups. Tests included open field testing on postnatal day (P) 25 and exploratory activity in automated assessments on P30 and P45. **Results:** Mice exposed to early life stress displayed significantly reduced exploratory behaviour on P25 compared to non-stress control animals. At P30 and P45, non-stress control animals covered a larger total distance in the activity box compared to stress animals. Stereotypy behaviours and rearing activity was increased at P45 compared to P30 for both treatment groups and at both time points. Stress animals, however, displayed these behaviours more frequently than controls. **Conclusion:** Early life stress reduces exploratory behaviour and activity throughout adolescent and adult life. The exploratory behaviour and activity profiles indicate increased anxiety-like behaviours in stressed animals. These findings have important implications for standard research procedures involving laboratory animals but also support the finding that early life stress can induce long-term adverse health outcomes.

P16

EARLY-LIFE EXPOSURE TO GESTATIONAL DIABETES IMPAIRS MITOCHONDRIAL BIOENERGETICS AND CARDIAC FUNCTION IN THE RAT OFFSPRING

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Introduction: Gestational diabetes mellitus (GDM) is the most common complication of pregnancy. Children of mothers that had GDM are at increased risk for developing cardiometabolic diseases later in life. Though the mechanisms responsible are unknown, mitochondrial dysfunction is associated with cardiovascular disease. The heart depends on mitochondrial energy production and the energy-requiring process of calcium transport to maintain adequate contractility. We hypothesize that GDM induces fetal cardiomyocyte mitochondrial dysfunction and impaired calcium handling that conditions the offspring for heart disease later in life. **Methods:** To induce GDM, female rats were fed a high fat (45% kcal) and sucrose (HFS) diet prior to mating, throughout pregnancy and lactation. Lean control females received a low fat (LF; 10% kcal) diet. Fetal rat ventricular cardiomyocytes (FRVCs) were isolated from the hearts of e20 offspring. Mitochondrial respiration was analyzed using a Seahorse Extracellular Flux Analyzer. Calcium transport was analyzed using the molecular dye Fura-2. To assess cardiac function over the entire life course of the offspring, serial echocardiography was performed at e18 and at 3, 6, 9 and 12-months of age using a Vevo 2100 ultrasound. **Results:** Basal and maximal mitochondrial oxygen consumption was reduced for glucose (35%, 68% respectively) and fatty acid (49%, 52% respectively) substrates in FRVCs isolated from GDM offspring (all $p<0.05$). FRVCs isolated from GDM offspring exhibit impaired calcium transport and re-uptake. The integrated [Ca2+] response area under the curve was 1.5-fold greater and the rate of decay (effectiveness of calcium re-uptake) was 1.6-fold longer (both $p<0.05$). Fetal and 3-month old offspring exposed to GDM in utero exhibit compensatory cardiac hypertrophy as determined by increased left ventricle posterior wall thickness (both $p<0.05$). From 6 to 12-months of age, offspring exposed to GDM exhibit diastolic

dysfunction as assessed by increased isovolumetric relaxation time ($p<0.05$). **Conclusion:** GDM reduced mitochondrial substrate oxidation and ATP production. Calcium transport was also impaired. These early-life impairments in mitochondrial bioenergetics and calcium transport were associated with early-life cardiac hypertrophy, followed by later in life diastolic dysfunction. Combined, these mechanisms put offspring of GDM mothers at greater risk of developing heart disease.

P18

THE EFFECTS OF PRENATAL MATERNAL STRESS ON TODDLER BODY MASS INDEX AS MEDIATED BY BIRTHWEIGHT AND MODERATED BY SOCIAL SUPPORT: THE IOWA FLOOD STUDY

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Introduction: The intrauterine environment plays an important developmental role in obesity risk, both directly through effects on central regulators of metabolism, as well as through effects on early growth patterns that alter the child's long-term developmental trajectory. One prenatal factor linked to increased obesity risk is exposure to prenatal maternal stress (PNMS). In addition, a lack of social support in perinatal women has been linked to increased depression levels, pregnancy complications, as well as offspring birth weight which may prime the newborn for greater adiposity later in childhood. **Objective:** Our goal was to determine the moderating role of social support in the association between prenatal maternal stress (PNMS) and early childhood body mass index (BMI) in the context of the Iowa floods of 2008. In addition, the mediating role of offspring birth weight in the association between PNMS and childhood BMI was examined. **Methods:** The Iowa Flood Study was appended onto an existing study of pregnant women in Eastern Iowa. We re-recruited women from that study who were pregnant in June 2008 when disastrous floods occurred and who had completed a measure of social support before the flood. Within weeks of the flood, women completed self-report measures of PNMS: their objective degree of hardship, their subjective distress, and their cognitive appraisal of the consequences of the flood (negative, neutral, positive). Offspring anthropometric measures were collected at birth, and at 30 months their body mass index (BMI) was calculated. **Results:** Moderated mediation results indicated that greater PNMS predicted greater BMI at age 30 months, through effects on higher birthweight as a mediator, but only for participants with low social support. High social support (satisfaction or number) buffered the effect of PNMS on birthweight. The combination of high PNMS and low social support resulted in higher offspring birth weight, which predicted greater BMI at 30 months. **Conclusion:** Efforts to provide strong social support to pregnant women following a stressor might buffer the effects of PNMS on offspring birthweight and later obesity

P20

FETAL GLUCOCORTICOID EXPOSURE MODIFIES THE BLOOD-BRAIN BARRIER AFTER BIRTH

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Introduction: The blood-brain barrier (BBB) is formed by specialized endothelial cells connected by tight-junctions (TJ) to form a non-fenestrated vessel. The TJs together with luminal membrane transporters P-glycoprotein (P-gp; encoded by Abcb1) and breast cancer resistance protein (BCRP; encoded by Abcg2), separate the brain from the systemic circulation. The BBB responds to changes in microenvironment, such as inflammation, toxin exposure, or hormones. Extensive work in fetal sheep has shown that glucocorticoid exposure in utero increases expression and function of several TJ proteins, depending on time of exposure. Synthetic glucocorticoids (sGC) are administered to women at risk of preterm birth, to help drive final fetal organ maturation. Infants in the neonatal intensive care unit have increased exposure to drugs, many with neurological sites of action, and already represent a vulnerable population with respect to therapeutic efficacy of drugs. Changes in BBB function that persist after sGC exposure, could have ramifications for drug disposition in neonates. Currently, no studies have investigated whether fetal exposure to sGC leads to post-natal alterations in BBB integrity and function. **Objective:** Determine the effect of antenatal sGC treatment on tight junction and drug transporter expression in microvessels of the juvenile BBB. **Methods:** Guinea pigs were chosen for this study as they exhibit a similar pattern of neurodevelopment to humans, as well as similar developmental expression patterns

for P-gp in the placenta and BBB. Guinea pigs were bred and treated with three courses of either vehicle or betamethasone (1 mg/kg) at gestation day (GD) 40, 41, GD 50, 51 and GD 60, 61. Brain microvessels were collected from offspring at postnatal day (PND) 14 to analyze Abcb1, Abcg2, Cldn-5, Ocln, and Zo-1 mRNA in isolated brain microvessels by qRT-PCR. **Results:** With respect to TJ gene expression, sGC treatment resulted in increased Cldn5 expression ($p<0.05$) but not Ocln or Zo-1. sGC treatment did not affect expression of drug transporters Abcb1, or Abcg2. Expression of Cldn-5, the main TJ protein, was increased up to 24 days after sGC exposure. **Conclusion:** Future studies will be conducted to assess TJ and drug transporter protein expression, and function in vitro. Altered expression of TJs and drug transporters can lead to changes in BBB permeability. These changes could have profound implications in neonatal drug exposure, as this is a vulnerable population exposed to high numbers of drugs. Supported by CIHR

P22

SEX DIFFERENCES IN ADULT RENAL GENE EXPRESSION IN A FETAL PROGRAMMING MODEL OF HYPERTENSION

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Introduction: The kidney is an important regulator of blood pressure (BP) and can be involved in the pathogenesis of hypertension. The renin-angiotensin system (RAS) plays a role in regulating BP and all RAS genes are expressed in the kidney. The expression of several RAS genes has been shown to be altered in fetal and perinatal rats in glucocorticoid-induced fetal programming (FP) of hypertension. However, the expression of RAS genes in adult FP rats has not been fully characterized. Further, sex-specific alterations in the expression of these genes have not been examined. Additionally, there are BP-related genes, that are not connected to the RAS, that have not been analyzed in the adult FP kidney. Two notable genes in this group include the Na+-Cl- cotransporter (NCC) and renalase (Rnls), a novel enzyme that may regulate catecholamines. **Objective:** The purpose of this study was to identify any alterations in adult renal mRNA expression for genes associated with hypertension following prenatal exposure to elevated glucocorticoids. Potential sex-differences were also examined. **Methods:** Pregnant Wistar-Kyoto rats (WKY) were administered dexamethasone (Dex; 100 µg/kg/day) during the third trimester of pregnancy and tissues were collected for analysis postnatally at 19 weeks of age. Kidneys (n=6) were collected from both male and female rats and from three experimental groups: 1) naïve, 2) saline-exposed, and 3) Dex-exposed. Total RNA from kidney tissue was extracted from coronal sections through the hilus and homogenized with TRI reagent. Extracted RNA was DNAse-treated and reverse transcribed using M-MLV RT. qRT-PCR was performed for the following genes: Ace, Ace2, Agt, Agtr1a, Agtr1b, Agtr2, Atp6ap2 (PRR), Mas1, Ren, Rnls, and Slc12a3 (NCC). Fold-changes were calculated using the 2^ΔΔCt method. **Results:** Preliminary data show a significant decrease in angiotensinogen (AGT) mRNA for naïve, saline, and Dex-exposed females. Angiotensin type-1 receptor b (AT1Rb) was significantly reduced in the Dex-exposed female group. Lastly, angiotensin-converting enzyme 2 (ACE2) was significantly reduced in female naïve and saline groups, but not in the Dex-exposed group. All changes are compared to male naïve rats. **Conclusion:** This preliminary study provides new insight for these renal genes and their potential role in the FP-based and sex-based sensitivities to hypertension. By understanding which genes are altered in the adult kidney (e.g. ACE2), new physiological mechanisms of hypertension may be revealed.

P24

MATERNAL ANTIOXIDANT SUPPLEMENATION PREVENTS FETAL PROGRAMMING OF HYPERTENSION IN OFFSPRING

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Introduction: The in utero environment is an important determinant of postnatal cardiovascular health. Evidence suggests that elevated levels of glucocorticoid (GC) in utero can lead to diabetes and other cardiovascular diseases in adulthood, a phenomenon known as fetal programming. An increase in reactive oxygen species (ROS) has been suggested to be a mechanism of GC mediated programming effects. Studies are now examining if attenuating elevations in fetal ROS exposure by employing antioxidants can prevent fetal programming of adult diseases. A more thorough investigation into the role of ROS in this type of in-utero programming may provide significant insight leading to the

prevention and treatment of hypertension. **Objective:** Determine the effect of maternal antioxidant supplementation on GC-mediated fetal programming of hypertension. Specifically, we assessed the impact of maternal antioxidant supplementation on attenuation of elevated blood pressure and phenylethanolamine N-methyltransferase (PNMT) gene expression in the offspring. PNMT, the terminal enzyme in the catecholamine biosynthesis pathway, is responsible for the biosynthesis of epinephrine, and is a candidate gene for hypertension. **Methods:** WKY dams were supplemented with EGCG (0.1%) or TEMPOL (1mmol/L) in drinking water for the duration of the pregnancy. Pregnant dams received daily (GD.14-21) dexamethasone injections (Dex; a synthetic GC) (100ug/kg) S.C. or saline. BP of the offspring was measured into adulthood (weeks 5-14) and adrenal tissue was assessed for gene expression levels of catecholamine biosynthetic enzymes using qRT-PCR. **Results:** Antioxidant supplementation with both EGCG and TEMPOL resulted in a significant decrease in BP throughout adulthood. PNMT expression in both males and females and TH in males were decreased with either maternal antioxidant treatment. Further, preliminary data from a qPCR array showed that reduction in GPx with Dex treatment was restored by both TEMPOL and EGCG; and both the antioxidants attenuated the elevation in NoxA. **Conclusion:** Significant decreases in BP were observed and supported by decreases in catecholamine biosynthetic enzyme expression levels. Maternal antioxidant therapy with EGCG or TEMPOL are effective in the prevention of GC fetal programming of hypertension, possibly by attenuating ROS.

THEME: Maternal and Fetal Medicine I – Maternal Medicine

P26

FIRST TRIMESTER MEAN ARTERIAL BLOOD PRESSURE TO PREDICT RISK OF PREECLAMPSIA

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Introduction: There is a growing interest for the early prediction of hypertensive disorders of pregnancies (HDP) and preeclampsia (PE) using a combination of markers including maternal blood pressure. Mean arterial pressure (MAP) is one of the first-trimester biomarkers that has en highly associated with the subsequent PE, but there are controversial results regarding this predictive values. We hypothesize that the technique of measurement influences the predictive values. **Objective:** We aimed to compare the performance of MAP using blood pressure taken by an automated device and blood pressure collected in clinical setting using a manual device. **Methods:** A case-cohort study niched from a prospective cohort of 2,400 pregnant woman recruited at 11-13 weeks in a single-center was performed. MAP was calculated from blood pressure measured using automated device on both arms simultaneously and taking a series of recordings (min. 2)until stability was reached. A second MAP, calculated from blood pressure measured at the closest medical visit (11-15 weeks) using a manual device was also recorded. Cases of woman who developed PE and a cohort of 245 women randomly selected among the original cohort were used to perform ROC curves analysis. The screening performance [area under curve (AUC)] of MAP using each blood pressure technique was calculated. Optimal cut-off values of MAP to predict PE were identified along with their sensitivities and specificities. **Results:** The current study included 60 women who developed HDP, including 44 cases of PE and 185 did not developed HDP. We observed that MAP measured from manual device could not predict PE (AUC 0,56; 95%IC: 0,46-0,66), while automated device was significantly associated with the risk of PE (AUC:0,72; 95%IC:0,64-0,80). Using an automated device, MAP above 90mmHg at 11-13 weeks could predict 53% of all HDP, 51% of all PE and 62% of preterm PE, with a 19% false-positive rate (p<0.001). MAP above 95mmHg could predict 33% of all HDP, 34% of all PE and 39% of preterm PE, with 6% of false-positive rate (p<0,001). **Conclusion:** MAP measured using an automated device at 11-13 weeks could be useful to identify women at high-risk of preeclampsia in combination with other markers. Blood pressure measured using a manual device is not useful for such screening. However, the detection rate of HDP by MAP alone remains low and should be combined with other markers to be useful in clinical practice.

P28

MOTHERS OF THE LOWEST AND HIGHEST SOCIOE-CONOMIC DECILES ARE AT INCREASED RISK OF HOSPITALIZATIONS ASSOCIATED WITH DEPRESSION DURING THE PERINATAL PERIOD: A POPULATION-BASED STUDY

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Introduction: Research has consistently associated socio-economic status (SES) with depression, both generally and during the perinatal period. However, the relationship of SES with hospitalizations associated with maternal depression, before and during the perinatal period, remains unclear. **Objective:** We aimed to explore the relationship between SES and maternal hospitalizations associated with depression (hereafter referred to as hospitalizations) before the pregnancy and during the perinatal period. **Methods:** Using population-based datasets, we accessed population-based data for women who delivered live infants in British Columbia (1999-2009). We examined the relationship between SES and hospitalizations during the periods twelve months before, during and twelve months after the pregnancy. Birth records and Census data were linked to records of hospitalizations and SES deciles (1= lowest, 10= highest) where deciles were determined from area-based tax-file data of gross household income. We used binary logistic regression,

with mothers from decile 6 as the comparator group whilst allowing for maternal age and parity. **Results:** In our study were 348,273 pregnancies. From twelve months before conception to twelve months after the birth, disadvantaged mothers from Deciles 1 and 2 had significantly increased odds of a hospitalization [AOR=1.64(CI=1.33, 2.01) P-value <0.0005; AOR= 1.36(CI: 1.10, 1.69) P-value =0.004]. The odds were higher prior to pregnancy with the most disadvantaged mothers having nearly twice the odds of a hospitalization [AOR=1.93(CI: 1.23, 3.05) P-value =0.004]. During pregnancy, from Deciles 1 to 10, there was a significant negative trend for the odds of a hospitalization (P-value=0.001). Over all other periods, there were significant linear and quadratic associations with mothers from Decile 1 having highest odds (p-value<0.005), mothers from a middle income decile (5, 6 or 7) having lowest odds and mothers from Decile 10 having increased, though not statistically significant odds of hospitalization. **Conclusion:** The most disadvantaged mothers were at highest risk of a hospitalization associated with depression and the most advantaged mothers were at higher risk than mothers in middle SES groups in all but the prenatal period. During all other periods, the relationship between SES and risk for hospitalization had both linear and quadratic components, indicating that risk may be associated with factors beyond SES alone. Future research should explore why the most financially able mothers are at increased risk compared to middle income mothers and why they are protected during the pregnancy.

P30

AN ONLINE TO OFFLINE MODEL IN THE MANAGEMENT OF CRITICALLY ILL PLACENTA PREVIA ACCRETE PATIENTS IN GUANGZHOU, CHINA

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Introduction: Online-to-offline (O2O) commerce has become a popular business model in China in recent years. However, the O2O model for medical service has rarely been reported. Because of the ability to connect care providers with patients on instant basis, the O2O model seems an attractive model for emergent medical services. **Objective:** Here we describe an O2O model using the social media app of "Wechat", a popular app in China which has reached 800 millions of people worldwide according to the latest statistics, to manage for critically ill placenta previa accrete patients. **Methods:** Started from January 1, 2015, all patients who were diagnosed with placenta previa accrete in our center were registered in a "Wechat" group created by us. These patients were followed by a team of specialists during pregnancy, and were instructed for self-monitor for bleeding. If the amount bleeding exceeded 100 ml, the patients were instructed to seek emergent medical care and contact our specialist team through "Wechat" immediately. The patients could be admitted to our hospital within 5 minutes through a "green channel" that is also connected to the "WeChat" group and the operation could be started within 30 minutes. **Results:** Up to date, 133 placenta previa accrete patients have been registered into this system and 28 critically ill placenta previa accrete patients have been treated through this O2O model. No case of critically ill placenta previa accrete patient has died or seriously complicated in our center since started using this model. **Conclusion:** This O2O through "WeChat" is not only useful for consultation, but for emergent care of critically ill placenta previa accrete patients as well

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MATERNAL CEREBELLAR HEMORRHAGE DURING PREGNANCY: A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: Intracranial haemorrhage (ICH) is a rare detrimental event in pregnancy. The incidence varies from 0.01 to 0.05% of all pregnancies. Intracerebral hemorrhage, a subtype of ICH2, is located within the brain parenchyma. The hematoma locations can be deep within the basal ganglia and internal capsule, lobar, cerebellar, and in the brain stem3. The major established causes of pregnancy – related cerebral hemorrhages are preeclampsia/eclampsia, followed by

arteriovenous malformations (AVM) and aneurysms. Data devoted to the incidence and causes of intracerebellar bleed during pregnancy are scanty. Spontaneous cerebellar hematomas represent approximately 10%–15% of all intracranial hemorrhage. Few cases of cerebellar hemorrhage due to AVM in pregnancy were reported in the literature. **Objective:** In the current paper, we describe a case of 29 year nulliparous who presented with a thunderclap headache following a cerebellar bleed secondary to ruptured AVM malformations along with a review of the literature regarding this challenging complication of pregnancy. **Methods:** A case of maternal cerebellar hemorrhage secondary to ruptured AVM malformations is presented. A review of the literature was performed using the PubMed database, with the search terms ‘‘maternal cerebellar bleeding,’’ “ cerebellar hemorrhage in pregnancy”, Intracranial hemorrage and pregnancy”, ‘‘cerebellar hemorrhage in pregnancy and AVM malformations”, “AVM malformations and pregnancy”. The latest search was done in November 2016. Data regarding maternal age, gestational age at diagnosis, location, management, gestational age at delivery, mode of delivery, and outcomes were recorded. **Results:** Literature review showed 12 reports with a total of 14 cases of maternal cerebellar hemorrhage. The mean maternal age at diagnosis was 27 years, and the mean gestational age at diagnosis was 35 weeks. 8/14 (57 %) of cases were located in the left cerebellum and 3/14 (21%) were on the right cerebellum. Fetal outcome was not reported in 3 cases. There was one twin pregnancy. Fetal outcome was favourable for 11/12 (91%), Stillbirth occurred in 1/12 (8.3%). Maternal death occurred in 2/14 (14%). **Conclusion:** Maternal cerebellar hemorrhage is associated with high maternal morbidity and mortality. A close monitoring in a clinical care setting is recommended

P34

FACTORS ASSOCIATED WITH PRETERM DELIVERY AMONGST PATIENTS ADMITTED TO HOSPITAL WITH SHORT CERVIX

Sharma S & Morais M

Introduction: Preterm birth is a leading cause of neonatal morbidity and mortality, and identification of women who will deliver prematurely is difficult. Cervical length is one prediction tool. Management can include admission to hospital, although this has not been consistently shown to decrease the rate of preterm delivery. **Objective:** Our objective was to determine which factors were associated with either preterm delivery prior to 34 weeks' gestation, or delivery within two weeks of admission, amongst women admitted to hospital with a short cervix from 16-28 weeks' gestation in order to identify those who may benefit from inpatient observation. **Methods:** This was a retrospective chart review of patients who were admitted to hospital from January 1, 2007 to December 31, 2014 from 16-28 weeks' gestation with cervix length less than 25mm on transvaginal ultrasound. Pearson correlation was used to identify predictive variables. **Results:** Of the 608 patients identified, 158 met inclusion criteria. Inpatient antibiotic treatment, rupture of membranes, presence of contractions, earlier gestation at diagnosis of short cervix, and earlier gestation at admission were associated with delivery prior to 34 weeks. Delivery within 2 weeks of admission was significantly associated with a shorter cervical length at admission 5.3mm (SD=5.2mm) vs 8.6mm (SD=5.7mm, p=.002). **Conclusion:** This study supports that shortened cervical length, in combination with other factors, can be used as a predictor to identify women who are more likely to deliver prematurely. In turn, this may also distinguish those who may benefit most from inpatient observation.

P36

WOMEN'S PERCEPTIONS OF DISCUSSIONS ABOUT GESTATIONAL WEIGHT GAIN WITH HEALTH CARE PROVIDERS DURING PREGNANCY AND POSTPARTUM: A QUALITATIVE STUDY

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Introduction: Maternal body weight is an indicator of the health of a mother and her developing fetus. Risks of poor maternal and fetal health increase when women gain too little or too much weight during pregnancy. A study of 600 women from Alberta, Canada, reported that 30%, 46%, 80%, and 80% of underweight, healthy weight, overweight, and obese women, respectively, gained in excess of Health Canada gestational weight gain guidelines. Behavioural interventions during pregnancy may be effective in helping women to achieve gestational weight gain (GWG) recommendations and return to their pre-pregnancy weight, yet few health care providers (HCP) routinely discuss these topics with women. **Objective:** ENRICH uses an inter-disciplinary, multi-sectoral, integrated knowledge translation approach across multiple settings to: 1) advance knowledge of the size, scope and determinants of healthy weights and

nutrition in pregnancy and postpartum; 2) understand perceptions and experiences of diverse groups of women and care providers; and 3) identify opportunities in healthcare and community-based care delivery systems where these strategies can be promoted. As one of the ENRICH projects, this study explored women's experiences with GWG and their perceptions of discussions about GWG with HCPs during pregnancy and postpartum. It complements information from surveys with women from across Alberta and surveys and interviews with HCP about these same topics. **Methods:** Five focus groups (n=26) were conducted with women up to one year postpartum across the five Alberta health zones. Focus groups were transcribed verbatim and analyzed using qualitative content analysis. **Results:** GWG is important to women, for their health and for the health of their baby. They reported that in-depth conversations with HCPs about GWG or weight loss did not occur; however, women wanted the opportunity to discuss weight gain/loss with HCPs. Women would like discussions about gestational weight gain/loss to become part of standard care and offered to all women. **Conclusion:** Women suggested that discussions about GWG should occur with all women, and that HCPs could initiate these by asking women how they feel about discussing weight. Conversations should begin early on in pregnancy and continue through the postpartum period. This study helped to identify gaps in service delivery and highlight ways that may support women to achieve GWG recommendations. Interventions assessing discussions about GWG are being implemented and evaluated. Approaches that are successful will be considered for scaling up to support better health outcomes for women and children.

P38

MATERNAL OUTCOMES FOR PATIENTS WITH ADHERENT PLACENTA AFTER CHANGING MANAGEMENT POLICY IN A TERTIARY CENTER IN GUANGZHOU, CHINA

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Introduction: Adherent placenta (includes placenta accrete, increta, and percreta) has gradually increased with the caesarean section rising and the incidence is 1 in 533. Nowadays, China start universal two-child policy, big increasing pregnant women who have previous caesarean section undergo adherent placenta. So far, planned hysterectomy after Caesarean delivery is the standard recommended treatment option. Considering the interests or social factors of preserving fertility, conservative management has been proposed for decades. Conservative management describes any approach that does not include hysterectomy. However, this treatment is controversial because of the risk of subsequent complications, and there are few Chinese data reported. Therefore, the purposes of this study were to evaluate the effects on maternal outcomes of conservative management based on population selection in abnormal placentation in our center. **Objective:** To evaluate maternal outcomes after a change of management policy for patients with adherent placenta. **Methods:** Prior to 2014, patients affected by adherent placenta and admitted to our center, Guangzhou Medical Centre for Critical Obstetrical Care, were mainly treated by hysterectomy. On January 1, 2014, our center changed the management policy for these patients, with conservative treatment (leaving the placenta in situ or placental-myometrial excision and repair) introduced for eligible patients (women who have stable condition and want to preserve uterus). This study compared maternal outcomes in patients affected by adherent placenta treated in our center in 2014 and those treated in 2013. **Results:** There were 114 adherent placenta cases treated in our center in 2013 and 136 such cases treated in 2014. There were no differences in demographic and clinical characteristics between the two groups. All cases in 2013 were treated by hysterectomy, while in 2014, 53 (39.0%) were treated by hysterectomy. The use of blood products (-400 ml/per person), the need to transfer to intensive care unit (-14.4%), and ureteric injure (-15.3%) were all decreased in 2014 ($P<0.05$). Conservative treatment was successful in 53 patients. Two patients had delayed hysterectomies because of bleeding and infection. No death or serious complications were observed in patients with conservative treatment. **Conclusion:** Patients affected by adherent placenta with low risk can be treated conservatively safely, with preserve fertility and reduced morbidity and health care costs.

P40

RECURRENT PREECLAMPSIA AND LONG-TERM CARDIOVASCULAR RISK

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Introduction: Preeclampsia increases the risk of cardiovascular disease later in life, but the contribution of recurrent preeclampsia is unclear. Around 14% of women with preeclampsia have recurrent preeclampsia. **Objective:** We determined the relationship between recurrent preeclampsia and poor cardiovascular outcomes up to 25 years after pregnancy using a longitudinal population cohort. **Methods:** We extracted 606,820 women who were pregnant more than once between 1989-2013 from hospital discharge abstracts for the province of Quebec, Canada. We identified women with recurrent (n=6,066), nonrecurrent (n=33,493), or no preeclampsia (n=567,261). We extracted all future hospitalizations for cardiovascular outcomes or procedures, including heart failure, ischemic heart disease, stroke, any heart procedure, coronary artery bypass graft, coronary angioplasty, or aorta repair. Using time-to-event analysis, we estimated hazard ratios (HR) and 95% confidence intervals (CI) for each cardiovascular outcome, comparing recurrent and nonrecurrent preeclampsia with no preeclampsia. We adjusted for baseline age, diabetes, preexisting cardiovascular disease, socioeconomic deprivation, and year, and censored women who died or had no event by March 31, 2014, the last day of follow-up. **Results:** Incidence of any cardiovascular disease was higher for recurrent (281 per 1,000) and nonrecurrent (168 per 1,000) than no preeclampsia (73 per 1,000). Recurrent preeclampsia was more strongly associated with poor cardiovascular outcomes than nonrecurrent preeclampsia. Compared with no preeclampsia, women with recurrent preeclampsia had greater risk of any cardiovascular disease (HR 3.9; 95% CI 3.6-4.2), heart failure (HR 4.2; 95% CI 2.9-6.1), ischemic heart disease (HR 3.3; CI 95% 2.6-4.2), stroke (HR 2.8; 95% CI 1.9-4.0), any heart procedure (HR 1.7; 95% CI 1.3-2.3), coronary artery bypass graft (HR 3.5; 95% CI 1.4-8.6), coronary angioplasty (HR 3.6; 95% CI 2.4-5.4), and aorta repair (HR 5.3; 95% CI 2.6-10.9). Nonrecurrent preeclampsia was associated with any cardiovascular disease, but more weakly (HR 2.3; 95% CI 2.2-2.4). **Conclusion:** Recurrent preeclampsia presents greater risk for future cardiovascular disease than nonrecurrent preeclampsia. Previously reported long term cardiovascular risks may be disproportionately greater for women with recurrent preeclampsia. Cardiovascular screening should be performed earlier for women with recurrent preeclampsia.

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RELATIONSHIP BETWEEN BODY MASS INDEX (BMI) AND LIPOPHILIC PERSISTENT ORGANIC POLLUTANTS (L- POPS) LEVELS IN WOMEN OF THE MATERNAL-INFANT RESEARCH ON ENVIRONMENTAL CHEMICALS (MIREC) STUDY

Mariame Ouedraogo[1,4], Marianne Levesque[1,3], Elizabeth Bratton[1,5], Tye Arbuckle[4,6], Linda Dodds[7], Mark Walker[1-4], Laura Gaudet[1-4]
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Introduction: Mechanisms through which obesity may cause congenital anomalies remain unclear. Lipophilic persistent organic pollutants (L-POPs) are chemical compounds that are ingested mainly through diet and are stored in the adipose tissues. Evidence has suggested that L-POPs are able to reach the fetus across the placenta and are associated with an increased risk of adverse health outcomes. Knowledge concerning the relationship between body mass index (BMI) variations during pregnancy and L-POPs serum levels is limited. **Objective:** This study aimed to determine whether first trimester maternal BMI and L-POPs serum levels were associated. **Methods:** A cross-sectional study was performed using data from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, a prospective cohort that enrolled pregnant women from 10 different sites across Canada between 2008 and 2011. We used first trimester maternal BMI and serum levels of 41 L-POPs to create unadjusted and age-adjusted linear regression models. Pairwise comparisons of L-POPs levels between BMI categories were conducted when linear regression tests were determined significant. **Results:** The most abundant L-POPs were found to be Arochlor1260 (0.494 µg/L) and p,p'dichlorophenyldichloroethylene (0.589 µg/L), whereas the lowest Toxaphene Parlar 26 (0.005 µg/L) and Toxaphene

Parlar 50 (0.005 µg/L). 19 L-POPs {Polybrominated diphenyl ethers (PBDE) 100, 153, 47, and 99; Polychlorinated biphenyls (PCB) 138, 146, 153, 156, 163, 167, 170, 180, 183, 187, 194, 201, and 203; Arochlor1260, and Toxaphene Parlar 26} had concentration levels that significantly varied across BMI classes, and were used for pairwise comparisons between BMI classes. **Conclusion:** Our findings show that several L-POPs concentrations in first trimester maternal serum are significantly associated with first trimester maternal BMI. Most associations seem to be negative. Subsequent research is needed to evaluate L-POPs levels variations during pregnancy given gestational weight changes and potential teratogenic effects.

P44

MOMMY MONITOR: THE DEVELOPMENT OF A MOBILE APP TO REDUCE THE ADVERSE MATERNAL HEALTH EXPERIENCES OF RACIALIZED WOMEN IN CANADA.

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Introduction: Research continues to show that racialized women continue to experience poorer birth outcomes, compared to non-racialized women living in Canada (Urquia et al 2009), and need a shared model of decision-making with their provider to improve their maternal health care. **Objective:** The main objectives of this study were to 1) explore the experiences of immigrant women with prenatal care, 2) determine the perceived relevance of the topics taught in generic prenatal classes to immigrant women and 3) discuss the interplay between culture, perceived relevance, and use of prenatal care by these immigrant women. **Methods:** Ethics was received through McMaster University. A qualitative ethnographic study with eight in-depth one on one interviews with immigrant women. Convenience sample from a church and a prenatal program from Unison Community Health Centre in Toronto, Ontario. The women had more than one child, but no more than four children, and were between the ages of 30-50 years old, and lived in Canada between 2 to 37 years. Thematic analysis was conducted to draw upon four themes (the relationship with the health care providers, the perceived relevance of care, prenatal care and cultural competence and important topics in prenatal care. **Results:** The participants acknowledged the presence of prenatal care and services being provided by the healthcare system, though the majority did not attend prenatal classes. The immigrant women discussed a need for larger social support networks during and after pregnancy, and healthcare professionals that took the initiative to understand their cultural values and needs on an individualistic level. The participants highly preferred midwifery as a form of prenatal care, and were not concerned with receiving competent care from providers, but rather relied on their personal cultural networks for that cultural sensitivity. **Conclusion:** Based on these findings, four final recommendations were made to provide a platform for the enhancement of prenatal care and services to reflect the needs of the immigrant women population. A mobile health application is being developed as a method of translating the knowledge produced through this study. Phase two of the study includes the development of the "Mommy Monitor" app, in a Mixed methods study which will be used by pregnant racialized women living in Canada, to enhance surveillance, increase monitoring, provide access to social networking between these women, peer counsellor support, in addition to delivering a guideline for healthcare professionals to help them implement culturally sensitive healthcare.

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Mariame Ouedraogo[1,4], Marianne Levesque[1,3], Elizabeth Bratton[1,5], Tye Arbuckle[4,6], Linda Dodds[7], Mark Walker[1-4], Laura Gaudet[1-4]

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Introduction: Mechanisms through which obesity may cause congenital anomalies remain unclear. Lipophilic persistent organic pollutants (L-POPs) are chemical compounds that are ingested mainly through diet and are stored in the adipose

tissues. Evidence has suggested that L-POPs are able to reach the fetus across the placenta and may increase the risk of adverse health outcomes. Knowledge concerning the relationship between body mass index (BMI) variations during pregnancy and L-POPs serum levels is limited. **Objective:** This study aimed to determine whether first trimester maternal BMI and L-POPs serum levels are associated. **Methods:** A cross-sectional study was performed using data from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, a prospective cohort that enrolled pregnant women from 10 different sites across Canada between 2008 and 2011. We used first trimester maternal BMI and serum levels of 41 L-POPs to create unadjusted and age-adjusted linear regression models. Pairwise comparisons of L-POPs levels between BMI categories were conducted when linear regression tests were determined significant. **Results:** The most abundant L-POPs were found to be Arochlor1260 (0.494 µg/L) and p,p'dichlorophenyldichloroethylene (0.589 µg/L), whereas the lowest Toxaphene Parlar 26 (0.005 µg/L) and Toxaphene Parlar 50 (0.005 µg/L). 19 L-POPs {Polybrominated diphenyl ethers (PBDE) 100, 153, 47, and 99; Polychlorinated biphenyls (PCB) 138, 146, 153, 156, 163, 167, 170, 180, 183, 187, 194, 201, and 203; Arochlor1260, and Toxaphene Parlar 26} had concentration levels that significantly varied across BMI classes, and were used for pairwise comparisons between BMI classes. **Conclusion:** Our findings show that several L-POPs concentrations in first trimester maternal serum are significantly associated with first trimester maternal BMI. Most associations seem to be negative. Subsequent research is needed to evaluate L-POPs levels variations during pregnancy given gestational weight changes and potential teratogenic effects.

P48

HOW OFTEN ARE PROGESTERONE, PESSARY AND CERCLAGE BEING USED FOR PREVENTION OF PRETERM BIRTH IN PRIMARY, SECONDARY AND TERTIARY CANADIAN CENTRES?

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Introduction: Preterm birth (PTB) is the leading cause of infant mortality and morbidity. A 2013 Cochrane review reported a 45% reduction in PTB <37 weeks with progesterone, while the 2014 Cochrane cerclage review noted a 20% reduction. The present 2008 SOGC guideline advocated further study of progesterone. **Objective:** Our objective was to determine the proportion of women at risk for PTB according to a previous PTB or short cervix, who were offered PTB prevention with progesterone, cerclage, or pessary. **Methods:** A multicentre retrospective cohort study was conducted of women who delivered a singleton infant at a primary, secondary, or tertiary level centre from January to March. Descriptive statistics and Chi-squared tests were calculated. **Results:** Of the 1030 consecutively reviewed charts, 89 women had a previous PTB or short cervix, 17% of them were offered progesterone, 3% were offered elective cerclage and 2% were offered either progesterone or cerclage. Few women declined an intervention, with 15% of women at risk receiving progesterone and 4% receiving cerclage. At the primary, secondary and tertiary centres, prevention for PTB was offered to 0/8, 0/13 and 14/68 women with a previous PTB or short cervix, respectively ($\chi 2 = 3.84$, df=2, $p = 0.1461$ i.e. not significantly different between centres, modest numbers). **Conclusion:** Approximately 1 in 4 women at risk of PTB from a previous PTB or short cervix were offered prevention, while 1 in 6 was offered progesterone. There is an urgent need to promote prevention of PTB with progesterone, the most effective method.

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EXAMINING PRE-LABOR AND AFTER LABOR REPEAT CESAREAN DELIVERY INDICATIONS ASSOCIATED WITH ADVANCED MATERNAL AGE

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Introduction: Increasing cesarean delivery (CD) rates have generated concern in public health and obstetric care. Older mothers are more likely to have repeat CD than younger mothers. Understanding the contribution of CD indications associated with advanced maternal age at delivery will help identify possible areas for reduction of unnecessary CD. **Objective:** examine pre-labor and after labor indications for repeat CD in women aged ≥35 years versus women aged <35 years old. **Methods:** A retrospective study was conducted using data from 2006-2013 obtained from the Better Outcomes Registry & Network Ontario's (BORN). The study population included singleton births with gestational age at 37-41 weeks. The rates of pre-labor and after labor repeat CD indications were independently compared between women aged ≥35 years versus <35 years old using chi squared tests, with a p-value of <0.05 considered significant.

Results: Out of 80,643 women who met our inclusion criteria, 68,266 (84.7%) had pre-labor repeat CD whereas 12,377 (15.4%) had CD after labor. The four most common indications for prelabor repeat CD were having a history of previous CD (96.5%), breech (1.2%), fetal distress (0.4%) and placenta previa (0.4%). The four leading indications for repeat CD performed after labor were previous CD (74.3%), dystocia (13.0%), fetal distress (7.2%) and breech (2.9%). The majority of repeat CD after labor were by spontaneous onset of labor (94.0%) than induced (6.0%). Among women who had prelabor repeat CD, those who were ≥35years compared with <35years old had statistically significant likelihood of CD due to placenta previa (0.48% vs 0.33, p=0.0018) and preeclampsia (0.40 vs 0.28, p=0.0105) but had lower likelihood of an intrauterine growth restriction baby (0.15 vs 0.23, p=0.0203) respectively. Among women who had after labor repeat CD, those who were ≥35years compared with <35years old were more likely to have placenta previa (0.61% vs 0.24%, p=0.012) but were less likely to have dystocia (11.2% vs 13.9%, p=<.0001) respectively. The rate of all other indications for CD were similar between the ≥35 and the <35 years' old groups, irrespective of whether the women had prelabor or after labor repeat CD (p=>0.05). **Conclusion:** Having a history of previous CD was the most significant indication for prelabor repeat CD and contributed immensely to the overall rate of repeat CD. Placenta previa and preeclampsia were the common indications associated with maternal age ≥35 years. This information will be helpful in the management of CD performed, particularly among women with no clear specific maternal, fetal or obstetric indications for the procedure.

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MENADIONE AS AN ALTERNATIVE METHOD OF ENDOGENOUS CARBON MONOXIDE PRODUCTION IN MICE

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Introduction: Pre-eclampsia (PE) is a multifactorial disease affecting 5-8% of pregnancies worldwide. Previous work has shown that women who smoke have a significantly decreased risk of PE, which has been attributed to an increase in carbon monoxide (CO) concentration in the body, up to 14% carboxyhemoglobin (%COHb). Despite its vasodilatory and anti-inflammatory properties, therapeutic CO administration is not widely accepted. Menadione, a synthetic form of vitamin K, has been shown to increase endogenous CO production in perfused human term placental tissue. Thus, the use of menadione as an alternative method of inducing endogenous CO production in female mice was investigated. **Objective:** To determine the safety and dosing of menadione required to raise blood CO levels to 5-10%COHb in normotensive non-pregnant mice. **Methods:** A preliminary safety study was conducted in female CD-1 mice (Charles River, USA) to monitor for adverse effects as a consequence of administering 0.15 g/L menadione sodium bisulfite (MSB) (Sigma-Aldrich, Oakville) in drinking water for a duration of seven days. Water was provided ad libitum to all mice and measured as average daily water intake per gram of body weight (mL/24 hr:g). Baseline water intake was measured for four days prior to MSB treatment to monitor for signs of taste aversion to the drug. %COHb levels for the treated and control groups were compared and calculated from CO peak area values using gas chromatography (GC) to quantify the change in %COHb after daily MSB administration. 20% w/w sonicates of perfused liver, kidney and spleen tissue were also analyzed using GC to quantify tissue CO levels in the control and treatment groups. **Results:** The daily administration of 0.15 g/L MSB over a span of seven days did not result in notable adverse effects in treated mice. Daily water intake for mice given MSB appeared to be higher compared to control mice, though this difference is not yet significant. At this dose, there was no significant increase in %COHb or tissue CO levels compared to the control. **Conclusion:** The administration of 0.15 g/L MSB is a safe dose for use in non-pregnant female mice. Going forward, the dose of MSB administered will be increased within a tolerable range to attain the desired 5-10 %COHb level. In the future, MSB may hold promise as a method of CO delivery in pregnant mice.

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URINARY BISPHENOL A IS ASSOCIATED WITH DYSREGULATION OF HPA-AXIS FUNCTION IN PREGNANT WOMEN: FINDINGS FROM THE APRON COHORT STUDY.

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Introduction: Previous rodent studies suggest that exposure to bisphenol A (BPA) may disrupt the hypothalamic-pituitary-adrenal (HPA) axis. However, no human studies have investigated the possible dysregulation of HPA-axis due to BPA exposure. **Objective:** Our primary objective was to examine the association between urinary BPA concentrations and diurnal salivary cortisol in pregnant women. Our secondary aim was to assess whether this association is modified by fetal sex. **Methods:** Diurnal salivary cortisol and urinary BPA were collected from women (n = 174) who were part of a longitudinal birth cohort, Alberta Pregnancy Outcomes and Nutrition (APrON). Associations between BPA and daytime cortisol and the cortisol awakening response (CAR) were estimated using mixed models after adjusting for covariates. **Results:** Higher concentrations of total BPA were associated with reduced CAR, β=-.055, 95% CI (-.100, -.010), a flatter daytime pattern in linear slopes β=.014, 95 % CI (.006,.022) and a flatter daytime pattern in quadratic slopes β=-.0007, 95% CI (-.001, -.0002). The magnitude of the association attenuated when corrected for urinary creatinine. This association is not modified by fetal sex. **Conclusion:** Our findings suggest that BPA exposure is associated with dysregulation of HPA axis during pregnancy. Since the dysregulation of maternal HPA axis may effect fetal development, future prospective studies are needed to examine possible implications of these findings for children's development, and specifically for HPA function.

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COMPARISON OF DAILY STEP COUNTS IN PREGNANT WOMEN MEASURED BY PEDOMETERS AND ACCELEROMETERS

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Introduction: Studies assessing physical activity in pregnancy largely use self-report measures such as questionnaires. Objective measures of physical activity by pedometers and accelerometers are more accurate measures than self-report but compliance in wearing such equipment can be a challenge. We wished to determine whether pedometers and accelerometers produced similar data in pregnant women. **Objective:** To determine whether step counts measured and reported from a pedometer are similar to step counts measured by an accelerometer. **Methods:** The study was part of the ongoing two-site Be Healthy in Pregnancy (BHIP) randomized controlled trial. Women in the experimental group are provided with individualized counselling in a high protein low-fat dairy food plan, and a walking plan with a targeted step count of 10,000 steps per day. Daily step counts from a pedometer are recorded on a daily step count log by subjects for 7 days and collected at bi-weekly visits throughout pregnancy. The accelerometer SensewearTM Armband (BodyMedia, Pittsburg) is worn for 3 days in the 2nd and 3rd trimester from which step counts are downloaded. Comparison of step counts between the pedometer and SensewearTM Armband was conducted by T-tests. **Results:** Data was analyzed for 42 individual subjects (age = 31 ± 3.7 yr; BMI = 25.8 ± 5.1kg/m2, mean±SD). At the end of the 2nd trimester, step counts by accelerometry were lower than pedometer step counts whether the pedometer counts were collected two weeks prior (n = 36, median 6718 vs. 8831 steps/day, p = 0.002) or two weeks after (n = 33, median 6658 vs. 8858 steps/day, p = 0.002). The correlation between measures was r = 0.16, and r = 0.53, respectively. At the 3rd trimester time point, accelerometer step counts were also significantly lower than pedometer step counts collected two weeks prior (n = 21, median 4662 and 7664 steps/day, p = 0.03). **Conclusion:** Step counts measured by the pedometer and the SensewearTM Armband differed by about 2500-3000 steps and were not strongly correlated. The results differ from previous studies in pregnant women that have demonstrated strong correlations between pedometer and accelerometer data. Fewer women had pedometer step count data nearing the end of pregnancy likely due to lack of compliance as it became uncomfortable to wear. These findings will be useful in determining which measure to use to assess adherence to the exercise intervention. (Funded by CIHR).

THEME: Placental and Fetal Physiology

P65

FETOMATERNAL HEMORRHAGE AT TERM ASSOCIATED WITH INTRAPLACENTAL CHORIOCARCINOMA: CASE REPORT AND REVIEW OF THE LITERATURE,WITH RECOMMENDATIONS FOR CHEMOTHERAPY

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Objective: To describe a case of fetomaternal hemorrhage at term associated with intraplacental choriocarcinoma, with a discussion of the need of chemotherapy for this case. **Methods:** Clinical manifestations and results of pathological examination and laboratory investigation of the case were described and relevant literature was reviewed. **Results:** A male infant was born with severe anemia on March 3, 2016 in the obstetrics and gynecology department of the Six Affiliated Hospital, Guangzhou Medical University, Guangzhou, China. And the mother and infant were followed up for 3 months following delivery. Examination of the mother during follow-up revealed evidence of metastasis.Microscopic examination revealed a well-circumscribed lesion composed of atypical syncytiotrophoblasts and cytotrophoblasts with geographic tumor necrosis and hemorrhage. Investigations at higher magnification revealed nuclear pleomorphism and severe atypia. Immunohistochemical staining was positive for cytokeratin (CK), human chorionic gonadotropin (HCG), protein 63 (P63), nuclear-associated antigen Ki-67 (Ki-67), and cluster of differentiation 34 (CD34). Follow-up examinations revealed increased beta-human chorionic gonadotropin (β-HCG) serum levels from 31,280 IU/L (6 days post-delivery) to 192,070 IU/L (49 days post-delivery), which then steadily fell to 42,468 IU/L (3 months post-delivery) without any therapeutic intervention; this was highly unusual and the responsible mechanisms remain unclear. The patient subsequently died as a result of metastasis and cerebral hemorrhage. The infant's β-HCG level fell to within the normal range without chemotherapy. **Conclusion:** Fetomaternal hemorrhage at term associated with intraplacental choriocarcinoma is a rare and severedisease and chemotherapy should be considered in accordance with the conditionsof individual patients, particularly serum β-HCG.

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MATERNAL NUTRIENT RESTRICTION (MNR) IN GUINEA PIGS LEADS TO FETAL GROWTH RESTRICTION (FGR) WITH SEX-RELATED INCREASES IN TISSUE HYPOXIA

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Introduction: Maternal undernourishment can be causative for FGR with altered placental development and reduced nutrient transport for glucose, amino acids and lipids. However, whether oxygenation is also decreased as seen with placental insufficiency-related FGR, remains unknown. **Objective:** We have determined the extent to which MNR in guinea pigs as a causative factor for FGR impacts immunoreactivity (IR) for Hypoxyprobe-1 (HP-1), a widely used marker of tissue hypoxia. **Methods:** Guinea pigs were fed ad libitum (Control) or 70% of the control diet pre-pregnancy switching to 90% at mid-pregnancy (MNR). Near term, HP-1 was injected into pregnant sows with fetuses then necropsied for body/organ weights, and brain, liver, kidney and placental tissues were assessed for HP-1 IR. Statistical significance was assumed for $p<.05$. **Results:** FGR-MNR fetuses (8males/8females) were 36% smaller, while their brains and livers were 12% and 40% smaller, respectively, in comparison to the appropriate for gestational age (AGA)-Control fetuses (8males/8females). HP-1 IR in the male and female AGA-Controls was similar across the brain regions studied and throughout the liver, but increased in the renal proximal convoluted tubules vs the glomeruli, and in the placenta labyrinth lobules peripherally vs centrally, indicating regional differences in basal oxygenation. HP-1 IR was increased in the FGR-MNR fetuses by 2-4X in the brain and more so in males than females, by ~4X in the liver and proximal convoluted tubules and ~15X in the glomeruli but with no sex differences evident, and with no changes in the placenta. **Conclusion:** MNR in guinea pigs results in asymmetric FGR with increased HP-1 IR as an index of local tissue hypoxia in the brain which was more so in males than females, and in the liver and kidneys which was similar for males and females, but with no changes in the placenta. As such, chronic hypoxia is likely to be an important signaling mechanism for the decreased fetal growth seen with maternal undernourishment and programming of related adverse outcomes,

and appears to be largely post placental in nature. Moreover, there are sex-related differences in the brain, which may contribute to the sex-specific expression of adverse neurodevelopment in FGR offspring.

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PLACENTA-DERIVED SEROTONIN IN HIGHLY SEASONAL PREGNANT WOMEN

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Introduction: Preclinical studies have demonstrated that serotonin synthesized from maternal tryptophan at the placenta is an important trophic signal for establishing fetal brain circuitry (Bonnin et al., 2011). Furthermore, perturbations to the placental serotonin system have been shown to induce permanent brain deficits in adult mouse offspring (Goeden et al., 2016). Serotonin (5-HT), among all monoamine neurotransmitters, has a pronounced seasonal pattern in its availability and/or metabolism with decreases during the winter months. Moreover, people who exhibit strong seasonal changes in mental health have greater decreases in brain extracellular 5-HT compared to healthy controls in the fall/winter period (McMahon et al., 2016). It is possible that this seasonal rhythm of 5-HT parallels the peripheral placental serotonin system important for fetal neurodevelopment during pregnancy in highly seasonal women. **Objective:** To study placental 5-HT synthesis/metabolism in highly seasonal and healthy women enrolled in the Ontario Birth Study (located at Mount Sinai Hospital, Toronto, Ontario) during the fall and winter. We hypothesize that placentas from highly seasonal pregnant women delivering during the fall/winter period have reduced 5-HT content and that this is associated with reduced expression of 5-HT-synthesizing/metabolizing enzymes. **Methods:** Women with a score >11 on the Seasonal Pattern Assessment Questionnaire, administered at 12-16 weeks gestational age, were categorized as highly seasonal. Frozen placental tissues were collected from highly seasonal women (N=7) and healthy controls (N=15) who delivered between November 2015 and April 2016. The placental mRNA and protein expression of LAT1, IDO1, TPH1, MAOA and SERT were measured by qPCR and western blotting. Metabolites along this pathway were measured in placenta by mass spectrometry (LC-MS/MS). **Results:** qPCR, western blot and mass spectrometry revealed no significant differences in mRNA and protein expression of key rate-limiting enzymes and metabolites in the serotonin synthesis pathway between highly seasonal women and controls. **Conclusion:** Collectively, our data suggest that placental 5-HT does not decrease markedly with the onset and progression of hypo-serotonergic symptoms during the fall and winter period in highly seasonal women, though much larger sample sizes are needed.

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ROBUST GENE MARKERS OF NORMAL VILLOUS MATURATION AND THEIR EXPRESSION IN PLACENTAS WITH MATURATIONAL PATHOLOGY

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Introduction: The placenta demonstrates a recognized sequence of histomorphologic maturation throughout pregnancy, and in some cases, shows pathologically advanced (AVM) or delayed (DVM) villous maturation. While AVM and DVM have important clinical implications, it is unknown whether they truly represent a state of altered maturation. **Objective:** To identify a placental age gene set signature and investigate placental ageing pathologies. **Methods:** A total of 142 placentas, previously evaluated by gene expression microarray, were reviewed histologically and classified as normal maturation (NM), AVM, or DVM. Expression data from healthy NM placentas underwent Pearson correlations with gestational age (GA) and network/pathway analysis, and candidate gene markers of normal GA were validated in an independent microarray dataset. Validated gene markers were used to calculate “molecular GAs” of placentas with maturational pathology. **Results:** Analysis of NM placentas yielded 17 candidate gene markers of normal villous maturation, of which 11 were successfully validated. Genes with expression increasing across gestation were associated with transcription and metabolism, and genes demonstrating decreasing expression were involved in cell cycle and division. Molecular GA was 5.3 weeks older than true GA among AVM placentas ($p < 0.001$), and 1.1 weeks younger among DVM placentas ($p = 0.149$). **Conclusion:** DISCUSSION: We have completed the first genome-wide search for molecular markers of villous maturation, and revealed strong evidence of advanced molecular GA in AVM placentas,

while molecular alterations in DVM placentas were merely suggestive of delayed maturation. These findings are important for understanding villous maturation and maturational pathology, and should be investigated as potential (1) placental tissue biomarkers for post-partum diagnosis, (2) serologic markers for intra-partum diagnosis, and (3) functional drivers of placental maturation.

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IN-UTERO LOW DOSE IRRADIATION EFFECTS ON POST-NATAL GROWTH AND BLOOD PRESSURE IN C57BL MICE.

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Introduction: Ionizing radiation exposure during pregnancy presents a two-fold problem: concern for the mother and the unborn child. This is of relevance due to the prevalence of fetal exposures to ionizing radiation (the majority at very low doses) through diagnostic radiography or occupational exposures of the pregnant mother. Ionizing radiation is known to result in the production of secondary free radical species at the cellular level. Developmental programming (permanent changes in offspring phenotype due to a stressor experienced in-utero) has been reported to involve a mechanism of oxidative stress. Therefore, the role of prenatal ionizing radiation exposure on offspring cardiovascular health and disease following birth is of relevance, even at low doses. **Objective:** To study the effects of ionizing radiation exposure at gestational day 15 in mice by characterizing growth and cardiovascular physiology in offspring through measurements of growth and blood pressure. **Methods:** Pregnant wildtype C57Bl/6J mice were irradiated on gestational day 15 with whole body 137Cs gamma radiation at doses of 5, 10, 50, 100, 300 or 1000 mGy. Mothers were allowed to deliver, and offspring were followed. Post-natal measurements of weight and blood pressure (mean arterial pressure, measured using tail-cuff plethysmography) were completed weekly until 16 weeks of age. **Results:** Significant reduction in body weight was observed in female pups consistently over the course of post-natal development at higher doses (100, 300, and 1000 mGy) compared to sham-irradiated female pups, with the greatest reduction in weight at 1000 mGy. A significant increase in mean arterial pressure was also observed at 8 weeks of age in female pups at the same higher doses. Consistent, significant increase in male pup weights was observed over the course of post-natal development at lower doses (5, 10, and 50 mGy) relative to sham-irradiated male pups. **Conclusion:** Gender-specific effects of prenatal ionizing radiation exposure with evidence of growth restriction and hypertensive phenotype in female pups and increased growth at low doses in male pups. Further investigation into the effects of ionizing radiation exposure during pregnancy (particularly at low doses and exposure at other times during gestation) is important due to evidence of programming effects with prenatal exposure to ionizing radiation

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SALMONELLA ENTERICA SEROVAR TYPHIMURIUM INFECTION IN MOUSE PREGNANCY

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Introduction: Salmonella are Gram-negative, facultative, intracellular bacteria that cause adverse pregnancy complications including spontaneous abortion, chorioamnionitis and preterm labour. In pregnant mice, Salmonella enterica serovar Typhimurium (S.Tm) infection is reported to cause placental bacterial replication, inflammation, placental necrosis, and fetal loss by unknown mechanisms. Necroptosis, or programmed necrosis mediated by RIPK3 (receptor-interacting protein kinase3), is implicated in S.Tm pathogenesis in non-pregnant mice but its roles during pregnancy are undefined. **Objective:** To evaluate the role of necroptotic cell death in S.Tm-infection-mediated pregnancy losses in vivo. **Methods:** Gestation day (GD) 12 susceptible C57BL6/J (B6) mice or resistant B6 mice expressing functional Slc11a1 (encodes the natural resistance associated macrophage protein1) gene (B6.Slc11a1+/+) with or without the expression of Ripk3, a key mediator of necroptosis, received 103 CFUs S.Tm i.v. At GD 14 and 15,

mice were euthanized and implantation sites (IS) were harvested, fixed and paraffin-embedded. IS from all litter members of infected dams were sectioned and stained for histopathology (H&E). S.Tm localization was determined by immunohistochemistry using an anti-Salmonella Typhimurium LPS antibody using 2 mid-placental sections/IS. Immunostaining for leukocytes was conducted to determine immune infiltration. Matched GD 14 and GD 15 naïve (non-infected) pregnancies served as controls. **Results:** In Slc11a1 incompetent mice, S.Tm localized primarily to labyrinthine trophoblasts and yolk sac (YS) within 48h of infection. In Slc11a1 competent mice, S.Tm localized to the decidua, spongiotrophoblast of the junctional zone and YS regardless of Ripk3 status within 72h post-infection. Areas with S.Tm infection showed heavy immune cell infiltratration and tissue damage. **Conclusion:** Slc11a1 status dictates trophoblast susceptibility to S.Tm while Ripk3 and thus necroptosis does not appear to have critical roles. We hypothesize that the rapid fetal death seen by 96h in this model of S.Tm infection is due to disruption of YS hematopoiesis, failure of fetal oxidative processes and fetal bacteremia and is independent of decidual and placental responses.

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THE IMPACT OF MATERNAL DIABETES ON FETAL-PLACENTAL SIZE AT BIRTH AND UMBILICAL CORD OXYGEN VALUES

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Introduction: Studies of diabetic mothers show increased maternal glucose as a cause for fetal macrosomia with enhanced placental growth and up-regulation of placental substrate transporters as nutritional cues for macrosomia. However, whether fetal oxygenation is also increased through enhanced placental diffusion thereby facilitating fetal growth, or is instead decreased with growth-related utilization, is unknown. **Objective:** To examine associations between maternal diabetes and fetal weights at birth, placental weights and birth/placental weight ratios as measures of placental development, and umbilical vein and artery PO2 as measures of placental oxygen diffusion and fetal oxygen utilization, respectively. **Methods:** A tertiary hospital database was used to obtain maternal diabetes status, birth and placental weight, umbilical cord gases, and other pregnancy-related information for all patients delivering more than 34 completed weeks between Jan 1, 1999 to Dec 31, 2010 (N=34,086). The effect of maternal diabetes status on birth weight category, birth/placental weight ratios, and umbilical cord PO2 values was examined controlling for interactions and confounders. Data are presented as grouped means±SD. **Results:** There were 32,296 non-diabetic (ND), 1387 gestational-diabetic (GD), and 403 overt insulin dependent diabetic (IDDM) patients available for study. Diabetic patients had increased body-mass index, were older, had increased hypertensive disorders of pregnancy and preterm birth, and increased cesarean deliveries (all p<.05 or .01). GD and IDDM patients had a stepwise increase in large for gestational age (LGA) infants at 17.8% and 37.7% vs the NDs at 7.0% (all p<.01); and a decrease in the birth/placental weight ratio at 4.94±0.84 (p<.01) and 4.90±0.84 (NS) and indicating disproportionally large placentas vs the NDs at 5.20±0.87. IDDM patients had lower umbilical vein PO2 at 25.2±6.9 mmHg vs the NDs at 27.4±6.6 mmHg (p<.05) and lower umbilical artery PO2 at 14.4±6.0 mmHg vs the NDs at 15.3±5.5 mmHg, although NS, while GD values were little changed. **Conclusion:** GD and IDDM patients had more LGA infants and disproportionally large placentas consistent with enhancement of nutrient supply to the placenta leading to up-regulation in nutrient transport and thereby placental growth and that of the fetus. While unchanged in the GDs, umbilical vein and artery PO2 were decreased in IDDM infants and likely involving aberrant placental development with diffusional impairment of oxygen and increased utilization with the larger size in these infants, respectively. As such, oxygen is unlikely to be a primary promotor for fetal growth in these pregnancies.

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PRENATAL MATERNAL STRESS IS ASSOCIATED WITH ALTERATIONS IN PLACENTAL GLUCOCORTICOID SYSTEM: A QF2011 STUDY.

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Introduction: Prenatal maternal stress (PNMS) is linked to adverse fetal development and alterations in child outcome.

There is growing evidence linking the mother's hypothalamic–pituitary–adrenal (HPA) axis and its end product, cortisol, to fetal programming. To counterbalance the effect of a higher circulating cortisol level, the placenta expresses the type 2 11beta-hydroxysteroid dehydrogenase (11β-HSD2, HSD11B2 gene) enzyme. This enzyme converts cortisol into inactive cortisone. The placenta also expresses glucocorticoid receptors (GR, NR3C1 gene) α and β as well as the cortisol producing enzyme 11β-HSD1 (HSD11B1 gene). Glucose, the primary fetal energy source, is transported across the placenta by the glucose transporters. The main placental glucose transporter isoform is GLUT1 (SLC2A1 gene). GLUT1 has been shown to be reduced in animal models with induced stress. **Objective:** The objective is to link PNMS from a natural disaster to alterations in the cortisol system and glucose transport in the human placenta. These alterations could be linked to adverse child development. **Methods:** 96 Placentas were collected from participants in the QF2011 Queensland Flood Study who were pregnant at the time of the flood. Detailed questionnaire results for objective hardship and for subjective distress were obtained to assess stress level. mRNA level of placental genes was obtained by RT-qPCR. Hierarchical multiple linear regression was used to assess the effect of specific stress measures on placental mRNA. Timing of the stressor event and fetal sex were assessed for their moderating effect. Child development was assessed by Bayley's cognitive and motor tests as well as the autism spectrum rating scale. **Results:** Subjective distress was significantly associated with a reduction in placental NR3C1-β mRNA for the total sample and even more significantly for boys only ($p \leq 0.05$). Objective hardship was associated with a decrease in SLC2A1 for girls' placentas ($p \leq 0.10$). Timing was a significant moderator of the effect of subjective distress on placental mRNA level for NR3C1-α and HSD11B1 in boys' placentas: for both NR3C1-α and HSD11B1, higher subjective distress is associated with higher placental mRNA levels if the stressful event occurred later in gestation ($p \leq 0.05$) **Conclusion:** While results did not show any alterations in placental 11β-HSD2 mRNA, we showed a reduction in placental NR3C1-β, as well as the moderating effect of gestational timing on placental NR3C1-α and HSD11B1.

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EFFECTS OF PRENATAL HYPOXIA ON FETAL CARDIOMYOCYTE PROLIFERATION

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Introduction: Intrauterine growth restriction (IUGR) is known to decrease fetal cardiomyocyte proliferation. TNF-related weak inducer of apoptosis (TWEAK) induces cardiomyocyte proliferation through activation of the fibroblast growth factor-inducible molecule 14 (Fn-14) receptor. The TWEAK/Fn-14 pathway has not being studied in offspring born growth restricted after a hypoxic insult. Thus, we hypothesized that IUGR offspring will exhibit reduced cardiomyocyte proliferation due to reduced Fn-14 expression. **Objective:** To determine the cardiac Fn-14 protein expression in control and IUGR offspring, and to assess cardiomyocyte proliferation from control and IUGR offspring in the presence of recombinant TWEAK (r-TWEAK). **Methods:** Pregnant Sprague Dawley rats were exposed to control (21% oxygen) or hypoxic (11% oxygen, IUGR) conditions from gestational day 15 to 21. Ventricular cardiomyocytes were isolated from female and male, control and IUGR offspring at postnatal day 1 (PND 1). Proliferation and protein expression of Fn-14 were determined. Cardiomyocyte proliferation was also assessed in the presence or absence of r-TWEAK (72-hours, 100 ng/mL) and the Fn-14 receptor antibody (100µg/mL). **Results:** Being born growth restricted was not associated with differences in the Fn-14 protein expression or cardiomyocyte proliferation at PND 1 in either male or female offspring. After being in culture for 72-hours, cardiomyocytes from IUGR male offspring had a decreased proliferation compared to controls. The addition of r-TWEAK increased proliferation in both groups. Moreover, Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (164.4% vs. 47.1%; p=0.04), and IUGR (208.5% vs. 70.03%; p=0.02) male offspring. Interestingly, in female offspring, being born growth restricted was not associated with decreased proliferation. The addition of r-TWEAK increased proliferation in both control and IUGR offspring. The Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (175.9% vs. 76.8%; p=0.007), and IUGR (224.4 % vs. 39.9%; p=0.02) female offspring. **Conclusion:** Only male IUGR offspring had a decreased cardiomyocyte proliferation compared to controls, but this was not due to changes in the Fn-14 pathway. Thus proliferation is altered in a sexual dimorphic manner in IUGR offspring and studies addressing other mechanisms of proliferation that may be compromised in growth restricted offspring should be addressed.

THEME: Neonatology I – Respiration/Ventilation/Cardiology

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PARENTAL PROJECTION OF QUALITY OF LIFE DOES NOT REFLECT CLINICAL RISK OF NEURODEVELOPMENTAL SEQUELAE IN CHILDREN ADMITTED TO THE NEONATAL INTENSIVE CARE UNIT

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Introduction: Newborns born prematurely or with congenital malformations are at risk of neurologic sequelae. Critical decisions are frequently taken by the healthcare professionals (HPs) with the family based on predictions of functional impairments and their impact on future quality of life (QOL). No known study has examined how parents predict this future QOL. **Objective:** To delineate parental perspective of the future quality of life of infants hospitalized in the NICU, and having high risk of neurodevelopmental sequelae. **Methods:** Prospective multicentre study conducted using a questionnaire validated from previously identified qualitative themes of parental projection of QOL. Perspectives from a cohort of parents of neonates at risk of severe neurodevelopmental outcome as defined by follow-up referral criteria (<29 weeks, Sarnat ≥2, IVH ≥3, PVL, severe neurological condition, severe genetic abnormality, exchange transfusion, ROP ≥3, diaphragmatic hernia or any condition having significant neurological impact) were compared with a control group including parents of all other neonates admitted to the NICU. Questions include likert scales (1 to 7) and yes/no answers. Variables were analyzed using Chi2 test. **Results:** 107 questionnaires were returned (88%). 58 (54%) cohort group and 49 (45%) control. Both groups had similar income and level of education. Parents of cohort group projected more long term financial impact on the family (p=0.012). There were no statistical differences between the groups on projections of: physical and mental difficulties, pain and discomfort, longevity of life, having a chronic condition, feeling of difference and ability to cope, happiness and QOL, role in society, having friends and a family, ability to live alone and emotional impact on the family. Both group scored low on risk of long term physical and mental difficulties, pain or child feeling different (mean score 1.7-2 out of 7), and scored high on child's happiness, QOL and ability to cope (mean score 6.4-6.6 out of 7). Cohort and control had moderate scores on emotional impact on the family (mean score 2.4-3.2 out of 7). 100% parents projected that their child would be self-sufficient for activities of daily living and able to find employment. **Conclusion:** Parental projection of future QOL of infants hospitalized in NICU is not associated with known risks of neurodevelopmental sequelae. Most parents predict overall a good future quality of life. Parental concerns focused more on the impact on the family. Other factors may influence if a parent projects a positive or negative future QOL.

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OUTCOMES OF PRETERM INFANTS IN PREGNANCIES COMPLICATED BY HYPERTENSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Pregnancy-induced hypertension (PIH) is commonly associated with preterm birth affecting neonatal mortality and morbidity. However, the relative contributions of prematurity and auxiliary effects of PIH in relation to neonatal outcomes remain unclear. **Objective:** To determine the clinical outcomes of preterm infants < 37 weeks GA born to mothers with and without PIH. **Methods:** A systematic review of the literature was conducted using pre-specified search terms in four databases (MEDLINE, EMBASE, CINAHL, PsycINFO) from January 2000 through October 2016. The risk of bias of included studies was performed using a modified Newcastle-Ottawa scale. Meta-analyses for pre-specified outcomes were performed with RevMan 5.3 when appropriate using a random-effects model and unadjusted and adjusted (when available) odds ratios (ORs) were pooled. **Results:** Of 4765 articles screened, 36 studies were included in the systematic review of which 26 were deemed to have low to moderate risk of bias and considered satisfactory for metanalysis. Among all preterm infants, PIH was associated with a lower pooled adjusted odds of

mortality and severe retinopathy of prematurity (ROP). Severe brain injury (SBI) was also significantly lower in PIH, but no adjusted data were available. No significant association was found between PIH and bronchopulmonary dysplasia (BPD) or necrotizing enterocolitis (NEC) from both adjusted and unadjusted data. Short term respiratory outcomes were not different (data not shown). Subgroup analyses were performed for all outcomes among infants < 29 weeks GA, and BPD was found to be significantly higher with PIH (adjusted OR 1.15 [1.06, 1.26], 3 studies; I2 =0%). **Conclusion:** PIH reduces the odds of mortality, SBI and ROP for all preterm infants, increases the odds of BPD in preterm infants < 29 weeks GA, and does not influence odds of NEC. There is very little, albeit conflicting, data on the impact of PIH on short-term respiratory outcomes, and further research is required for this, as well as long-term outcomes.

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PORACTANT ALFA VERSUS BOVINE LIPID EXTRACT SURFACTANT FOR INFANTS 24+0 TO 31+6 WEEKS GESTATIONAL AGE: A RANDOMIZED CONTROLLED TRIAL

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Introduction: A meta-analysis comparing poractant alfa (Curosurf), a porcine-derived surfactant, to beractant, a bovine-derived surfactant, report less need to repeat dosing, less mortality and shorter duration of oxygen requirements in infants who received poractant alfa. In Canada, bovine lipid extract surfactant (BLES), which is similar to beractant, is the most commonly used surfactant; poractant alfa is not currently available. Reports of severe airway obstruction during administration of BLES have been published. No study to date has compared BLES and Curosurf. **Objective:** To compare the efficacy and safety of bovine lipid extract surfactant and poractant alfa in preterm infants. **Methods:** Randomized, partially-blinded, multicenter trial. Infants <32 weeks needing surfactant before 48 hours were randomly allocated to receive poractant alfa or bovine lipid extract surfactant. The primary outcome was being alive and extubated at 48 hours post-randomization. Secondary outcomes included need for re-dosing, duration of respiratory support and oxygen, bronchopulmonary dysplasia, mortality and complications during administration. **Results:** Three centers recruited 87 infants (mean 26.7 weeks and 906 grams) at a mean age of 6 hours, between March 2013 and December 2015. 21/42 (50%) were alive and extubated at 48 hours in the poractant alfa group vs 26/45 (57.8%) in the bovine lipid extract surfactant group; OR 0.76 (95% CI 0.30 – 1.93) (p=0.56). No differences were observed in the need to re-dose. Duration of oxygen support (41.5 vs 64 days; OR 1.69 95% CI 1.02-2.80; p=0.04) was reduced and BPD among survivors was less frequent (48.5% vs 69.1%; OR 0.27 95%CI 0.10-0.71; p<0.01) in infants who received poractant alfa. Twelve infants died before discharge, 9 in the poractant alfa group and 3 in the bovine lung extract group (p=0.06). Two deaths were related to respiratory failure: one pulmonary hypoplasia/pulmonary hypertension in the poractant alfa group and one bronchopulmonary dysplasia in the bovine lipid extract surfactant group. The leading causes of death were late onset sepsis or NEC for the remaining 10 infants. Severe airway obstruction following administration was observed in 0 (poractant alfa) and 5 (bovine lipid extract surfactant) infants (p=0.07). **Conclusion:** Poractant alfa may be more effective and associated with fewer acute complications after administration than bovine lipid extract surfactant. Larger studies are needed to determine the effect on survival and whether the benefits we observed translate in shorter hospital admissions, or other long term benefits.

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EFFECT OF VASOPRESSIN IN HYPOXIC PPHN

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Introduction: Persistent pulmonary hypertension of the newborn (PPHN) is a rapidly progressive vasculopathy marked by failure of pulmonary vascular relaxation. Vasopressin, used clinically as a pulmonary vasodilator in PPHN, systemic vasoconstrictor acting on the smooth muscle V1R receptor, thought to cause vasodilation in pulmonary and cerebral circulations via endothelial V1R/oxytocin receptor stimulation causing nitric oxide release. **Objective**: To determine the effects of vasopressin infusion on pulmonary and systemic hemodynamics in an animal model of hypoxic PPHN, using 2D echocardiography. Hypothesis: Vasopressin will acutely reduce pulmonary arterial resistance and improve right ventricular filling in hypoxic PPHN piglets, without altering systemic blood pressure. **Methods:** PPHN was induced in newborn piglets by exposure to FiO2 10% x 72 hours. Controls were age-matched. Acute experimentation was

randomized using a crossover design. Animals were intubated, anesthetized with propofol, and ventilated. After a 15 min stabilization period, following confirmation of PPHN by baseline ECHO, PPHN and control animals were randomized to start in Block 1 or 2: Block 1: Normoxic ventilation [N] for 30 min, then ECHO-N; Vasopressin [NV] infusion 0.0012 units/kg/min x30 min, then ECHO-NV. Washout period of no vasopressin x 45 min. Block 2: Hypoxic ventilation [H] for 30 min, then ECHO-H; Vasopressin [HV] infusion for 30 min, then ECHO-HV. Washout period of no vasopressin x 45 min. ECHO parameters analyzed: Pulmonary VTI [velocity time interval], [RVO] right ventricular output, AT/ET [acceleration time/ejection time]; FAC [fractional area change], TAPSE [tricuspid annular plane systolic excursion], RV end-diastolic volume [RV-EDV], TR [tricuspid regurgitation], SVC [superior vena cava] VTI, interventricular septum flattening in systole and diastole. **Results:** We studied 7 controls and 6 PPHN piglets. PPHN piglets had increased TR compared to controls [p 0.014], lower pulmonary VTI (p 0.002), and lower RVO (p 0.009); flattened IVS in systole [p 0.0005] and diastole [p 0.02]. PPHN animals had no difference in RV-EDV compared to controls, nor in SVC flow. Control HV animals had a small decrease in pulmonary VTI. In PPHN piglets, vasopressin increased the blood pressure during N only. Vasopressin decreased TAPSE in PPHN animals under N and H ventilation [p 0.003]. There was a non-significant effect of vasopressin on RVO, and no change in RV-EDV or pulmonary AT/ET ratio. **Conclusion:** We conclude that vasopressin administration to PPHN piglets has no direct pulmonary vasodilator effect within the time frame of this study. We accept the null hypothesis, that vasopressin does not decrease pulmonary arterial resistance in hypoxic PPHN. We speculate vasopressin may improve right ventricular preload

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MEASURE OF RESILIENCE CORRELATES TO PARENTAL PROJECTION OF QUALITY OF LIFE IN CHILDREN ADMITTED TO THE NEONATAL INTENSIVE CARE UNIT.

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Introduction: In neonatology, many decisions regarding benefits of invasive treatments are based on a prediction of the future quality of life (QOL) of the neonate by the parents and the healthcare team. The Salutogenic Model of Health questions how individuals respond to situations of stress and use available resources in a health promoting way. The Sense of Coherence scale (SOC) is a validated questionnaire that measures how one sees the structure in the environment (comprehensibility), how predictable (manageability) and explicable (meaning) it is. A strong SOC has been shown to positively affects one's QOL. **Objective:** Is a resilient response to stress correlated with a more positive parental projection of future QOL of children hospitalized in NICU? **Methods:** Parents of hospitalized high risk newborns were recruited prospectively in 3 university affiliated centres from 2014-2016 with a questionnaire validated with QOL themes (development and pain, differences and role in society, autonomy, happiness and quality of Life, coping, impact on the family and sanctity of life) and an anxiety scale, the Brief Symptom Inventory (BSI). SOC-13 version was used. Statistical significance was determined by Pearson correlation for $p<0.05$. **Results:** 107 questionnaires were completed (88%). Results are described in table. A low SOC correlated with a high anxiety score on the BSI. The SOC did not correlate with other projected aspects of QOL such as child's happiness, lack of pain or discomfort, lack of physical and mental difficulties, resiliency, ability to participate in social life (friends, school, family) or ability to look after themselves. **Conclusion:** Parental SOC may impact the prediction of the future QOL of their children. Parents with stronger resiliency capabilities project a positive general QOL while parents will less coping skills predict that their child may remain ill, and have financial and emotional repercussions on the family. However, SOC does not relate to all aspects of QOL. Anxiety may also play a role in those predictions. SOC may be used in clinical setting to screen parents requiring more support and understand how they envision the future in a decision making process.

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NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE INFLUENCES BOTTLE-FEEDING AFTER PRETERM BIRTH

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Introduction: In preterm infants, the time from initiation to full oral feeding can take weeks, which represents one of

the most worrisome problems in neonatal medicine. Though current knowledge strongly suggests that oral feeding should be introduced as soon as possible, this is often delayed due to the need for prolonged nasal respiratory support. Indeed, most caregivers fear that nasal continuous positive airway pressure (nCPAP) could disrupt sucking-swallowing-breathing coordination and in turn induce tracheal aspiration and/or apneas. We have previously shown that bottle-feeding with nCPAP is safe and does not alter swallowing-breathing coordination in full-term lambs (Bernier A, 2012). **Objective:** The objectives of the present study were to assess the impact of nCPAP on the introduction of bottle-feeding in preterm lambs and to determine how it evolves over 24 hours. **Methods:** Seventeen lambs (8 control and 9 nCPAP 6 cmH2O) born 14 days prematurely were instrumented to record sucking, swallowing and respiration as well as ECG and oxygenation. Preterm lambs were fed via a nasogastric tube until introduction of bottle-feeding. Thereafter, standardized bottle-feeding was introduced every 4 hours for 24 hours. **Results:** Results revealed that nCPAP increased bottle-feeding efficiency while maintaining higher oxygenation without any deleterious cardiorespiratory events. However, coughs were more frequent in lambs under nCPAP immediately following bottle-feeding. **Conclusion:** nCPAP positively influences bottle-feeding in preterm lambs by increasing oxygenation and feeding efficiency. We hypothesize that the increase in coughs following bottle removal under nCPAP is mainly related to the very high milk flow in preterm lambs feeding from a bottle. Further studies documenting the presence or not of laryngeal penetration and/or tracheal aspiration are needed before recommending bottle-feeding attempts in preterm infants under nCPAP.

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COMMUNICATION DURING THE ANTENATAL CONSULTATION FOR ANTICIPATED BIRTH OF AN EXTREMELY PREMATURE INFANT A SYSTEMATIC REVIEW

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Introduction: Parental distress associated with anticipated delivery of an extremely preterm infant necessitates tactful communication by healthcare professionals. The antenatal consultation (ANC) to facilitate decision-making is filled with parental fear, anxiety, and questions regarding the future of their child. **Objective:** We performed a systematic review of the literature to synthesize parental expectations on how healthcare professionals should interact with them during an ANC. **Methods:** Electronic searches of Medline, CINAHL, PsycInfo, Embase and grey literature were conducted. We included studies that explore parent perspectives and experiences with the ANC. Two independent reviewers reviewed 526 titles, of which 103 abstracts then 25 full text articles were reviewed. Fourteen articles were included for final data abstraction. We pre-determined six topics of interest (setting, timing, preferred healthcare professional, information, resources or aids, parents-physician interaction) to facilitate thematic analysis. Quality appraisal was conducted using Walsh and Downe's guide. **Results:** In addition to the six pre-determined topics of interest, overarching themes such as perception of support, degree of understanding, hope, spirituality and faith and decision-making emerged from the review. Studies suggest the quality of the ANC is not purely about information content, but also the manner in which that information is provided and how the healthcare provider builds trust. There is no 'one-size-fits-all' standard; the evidence indicates that parents may want different information in different ways with variation in physician and nursing roles. Finally, the ANC is not a one-time event; studies suggest parents want multiple opportunities for information gathering and discussion. **Conclusion:** These findings will help guide communication during the ANC in a way that should increase parental engagement and satisfaction. The results were used to generate proposed strategies to facilitate communication that may inform clinical practice guidelines.

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A NOVEL PROGNOSIS BASED GUIDELINE FOR INFANTS BORN AT THE LIMIT OF VIABILITY: BARRIERS AND FACILITATORS TO IMPLEMENTATION AND USE

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Introduction: While survival of extremely premature infants born between 22-25 weeks has improved, the decision to attempt resuscitation or provide palliative care at birth remains complex. To address the need for a high quality guideline to inform practice in our region, our multi-disciplinary working group created a novel clinical practice

guideline, based on the AGREE-II and GLIA guideline appraisal tools. The guideline was implemented in one hospital in September 2015. **Objective:** To identify facilitators and barriers to use of the guideline following pilot implementation. **Methods:** A purposeful sample of health care providers (neonatologists, maternal fetal medicine specialists, obstetricians, fellows, residents, birthing unit and neonatal nurses) was identified based on their involvement in the care of at least one of five cases involving extremely premature infants during the pilot implementation. Healthcare providers were invited to participate in an individual semi-structured interview by phone or in-person to share their views on the guideline content, implementation process, and facilitators and barriers encountered. The interviews were audio-recorded and transcribed verbatim. Qualitative content analysis was used to code, categorize, and thematically describe the data. **Results:** Between October-November 2015, 25 key informants (16 physicians, 9 nurses) were interviewed about their experiences following guideline implementation. Participants described varying levels of knowledge of the guideline, and different means of learning about it including e-mail, presentations, and in-services. Facilitators to guideline implementation included the healthcare team: (1) believing in the importance of the guideline, specifically the importance of engaging the family in the decision process; (2) perceiving that the guideline contains relevant and evidence-based information that can be used to inform practice; and (3) having easy access to the guideline on the units. Identified barriers to guideline implementation included: (1) attitudes and emotions of the healthcare team related to the value-laden nature of the decision surrounding management of these infants; (2) lack of awareness about the guideline and its content; and (3) lack of resources required to care for infants newly born at 22 weeks. **Conclusion:** This evaluation has identified facilitators and barriers to implementation of our guideline. This information will inform the development of tailored strategies for improved local and future broader implementation, including: diverse communication strategies, increased staff training opportunities, improved resource planning.

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NEED ASSESSMENT OF MEDICAL ETHICS AND COMMUNICATION TEACHING FOR NEONATAL PERINATAL MEDICINE TRAINEES IN CANADA.

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Introduction: Advances in neonatal care routinely pose ethically challenging clinical situations which require neonatologists able to tactfully communicate with parents and their colleagues. To master these critical competencies, they need comprehensive training. However, national consensus on the content and educational strategies to support their learning is lacking. **Objective:** To determine the ethics education needs, as perceived by learners and teachers. The results will assist in building a foundation for teaching and evaluation of neonatal ethics training in Canada. **Methods:** This is an exploratory study using two distinct cross-sectional electronic surveys. The first survey targeted the recently graduated neonatologists (RGNs) who completed at least 2-years' training in a Canadian Neonatal Perinatal Medicine (NPM) program between June 2010 and July 2015. The second survey was sent to NPM program directors (PDs) who were listed in the 2015 Royal College Physicians and Surgeons of Canada website. The domains of interest were: perception of education; topics to be included; educational strategies to facilitate learning; assessment of trainees' competencies and barriers to neonatal ethics education. **Results:** Forty-eight out of 106 RGNs completed the on-line survey (45.2% response rate). Twelve PDs completed the survey from the 13 NPM residency program. Both RGNs and PDs agreed that training is important (91.5 vs 91.7% respectively). A quarter of PDs felt that trainees may not be fully competent by the end of their training compared to 10.6% of the RGNs. PDs and RGNs highly valued training on communication with parents (90.9% vs 81.8%), discussing the goals of care with families (81.8% vs 61.4%) and breaking bad news (90.9% vs 72.7%). PDs valued training more than the RGNs for the following topics: theoretical bioethics (100% vs 51.3%), landmark ethics cases (100% vs 52.2%), medical decision-making (100% vs 54.6%), and limitations of parental authority (100% vs 60.3%). Preferred teaching strategies for PDs and RGNs were observation and feedback. Ethically sensitive case discussions were preferred by PDs and reflecting on ethically challenging situations less important for RGNs. Faculty engagement and availability facilitate training in neonatal ethics and communication. Challenges are financial resources to pay for actors and teachers (21.1%), physical space (21%) as well as faculty training in patient-physician communication (14%). **Conclusion:** Training in communication with parents during ethically sensitive situations including discussing goals of care and breaking bad news are very important for learners and teachers. Education on theoretical bioethics, me

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IMPROVING NEONATAL CARE WITH THE HELP OF VETERAN PARENTS: AN OVERVIEW OF CURRENT PRACTICES

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Introduction: Recently, veteran NICU (Neonatal Intensive Care Unit) parents have become increasingly involved to provide peer-to-peer support to parents of sick neonates. This unique form of support optimizes the integration of families in neonatal care. **Objective:** to review the literature and engage in benchmarking to examine how veteran parents are involved in Neonatology internationally. To examine parental perspectives. **Methods:** A review of the literature was performed to examine how veteran parents are involve in Neonatology, either in clinical care, teaching or research. Participating "veteran parents" in Canada were also surveyed to examine their perspective regarding participation. Clinicians and researchers who had worked with veteran parents were also surveyed to examine the impact of veteran parents in Neonatology. **Results:** Veteran NICU parents also assume many roles in clinical care, research, administration and/or teaching, but those roles are not described in detail in the literature. More than 70 activities were examined and classified according to the location of involvement (hospital or not), the presence of direct interaction with families and providers (with or without) and the topic of involvement (clinical care, research, administration or teaching). We have also identified gaps in knowledge relative to recruitment and training, development and evaluation of programs, primary responsibility and remuneration. Parents mainly participate to "give back" and optimize care for neonates and their families. **Conclusion:** Future research is needed to measure the impacts of veteran parents on the care of neonates and their families.

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POSTNATAL PREDICTION OF GESTATIONAL AGE USING NEWBORN FETAL HEMOGLOBIN LEVELS

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Introduction: Knowledge of newborn gestational age is critical to guiding appropriate care, yet in many parts of the developing world, gestational age may not be readily determined due to lack of access to dating ultrasound and poor ascertainment of date of last menstrual period. **Objective:** We set out to develop and validate a prediction model for postnatal gestational age estimation utilizing the relative levels of newborn and adult hemoglobin types, in addition to a panel of other newborn screening analytes from heel-prick blood spot samples. **Methods:** A retrospective cohort analysis of 159,215 infants born January 2012–December 2014 in Ontario, Canada who underwent routine newborn screening. Multivariable linear and logistic regression analyses were used to evaluate the precision of postnatal gestational age prediction models derived from newborn fetal and adult hemoglobin levels, and maternal/neonatal characteristics. **Results:** Prediction models derived from a combination of hemoglobin ratios and birthweight were more precise at predicting gestational age (RMSE1·23 weeks) than models limited to birthweight (RMSE1·34). Addition of other newborn screening analytes to the prediction model improved model performance, accurately estimating gestational age to ±2 weeks in 95·3% of the cohort. Models including birthweight, hemoglobin ratio, TSH and 17-OHP were able to discriminate ≤34 versus >34 weeks gestational age with a c-statistic of 0·98, and performed well in small for gestational age infants (c-statistic, 0·998; PPV at 80% sensitivity, 0·831). **Conclusion:** A streamlined model incorporating hemoglobin ratios or non-mass spectrometry derived metabolites provides reasonable prediction of gestational age. The development of a point-of-care mechanism to allow widespread implementation of a postnatal gestational age estimation tool could serve as an alternate to antenatal ultrasound dating in areas where this technology is not routinely available.

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DOES MULTIPLE ATTEMPTS FOR TRACHEAL INTUBATION AT BIRTH INCREASE THE RISK OF INTRAVENTRICULAR

HEMORRHAGE IN VERY PRETERM INFANTS?

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Introduction: Intraventricular hemorrhage (IVH) is common morbidity of prematurity. Severe IVH is associated with high mortality and is an independent predictor of adverse long term outcome. Adverse responses occur commonly during tracheal intubation (TI) including; bradycardia, desaturation and change in systemic and cerebral blood pressures. All of which are known as pathologic predisposing factors to IVH. However, little is known about the relationship between multiple TI attempts during resuscitation in the delivery room and the development of IVH in very preterm infants. **Objective:** To examine the rate of all grades IVH in very premature infants < 31 weeks gestation that had multiple TI attempts at birth as compared to those who had a single successful TI attempt. Secondary outcomes include; severe IVH (IVH with ventricular dilatation or parenchymal bleeding), death before 28 days of age and the composite outcome of death or IVH. **Methods:** We conducted a retrospective review of all inborn very preterm infants (220 - 306 weeks gestation) who were born between 2006 and 2015 and were admitted to NICU at the IWK Health Centre. Infants who received TI during delivery room resuscitation were reviewed. We excluded those with congenital anomalies and those in whom palliative care was decided during the antenatal period. Antenatal and perinatal risk factors were compared between preterm infants who received single versus multiple TI during delivery room resuscitation. **Results:** A cohort of 378 very preterm infants born during the study period was reviewed. The mean gestational age was 27 weeks (SD ± 2) and the mean birth weight was 950 grams (SD ±290). During delivery room resuscitation, 165 infants (44%) received single TI and 213 infants (56%) received multiple TI attempts. The demographics characteristics and perinatal factors of both groups are shown [table 1]. There was no significant difference between both groups in any of the primary or secondary outcomes, adjusted for extreme low gestational age (< 26 weeks) [table2]. **Conclusion:** This study reports no significant difference between preterm infants who received single vs multiple TI during delivery room resuscitation in relation to IVH, mortality or the composite outcome of death or IVH.

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ASSESSMENT OF PERFLUBRON PULMONARY DISTRIBUTION DURING THE FILLING PHASE OF TOTAL LIQUID VENTILATION

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Introduction: Total liquid ventilation (TLV) provides gas exchange by filling the lungs with liquid perfluorochemical (PFC) and insuring liquid tidal volume. TLV has shown promising results for the management of neonatal respiratory distress. INOLIVENT, a dedicated liquid ventilator developed in Canada, now allows for precise control of ventilation parameters. Refinement of ventilation techniques, such as the initial lung filling, is a necessary step towards clinical use. **Objective:** To assess PFC distribution within the lungs during the filling phase of TLV using fluoroscopy and electrical impedance tomography (EIT) in a neonatal lamb model of induced surfactant deficiency. **Methods:** Six lambs were anaesthetized (propofol/ketamine) and ventilated in supine position. Electrodes were placed around the chest to acquire EIT data. Lambs were placed under fluoroscopy, using a lateral beam. After paralysis, a surfactant deficit was induced by repeated lung lavage (10ml/kg, warm normal saline) until PaO2/FiO2<100mmHg for 20min. The lambs were then disconnected from the conventional ventilator (PEEP 0cmH2O) for at least 10sec to allow for lung deflation. INOLIVENT was connected and lungs were filled with 25ml/kg PFC over 18s, and then TLV was started. Fluoroscopy and EIT signals were recorded during filling and after 1, 5, 10 and 120min. For fluoroscopic image analysis, four regions of interest of equal height were determined along the antero-posterior axis of the thorax. Absolute mean pixel values were measured at end expiration. Friedman and Wilcoxon signed rank sum test were used for comparisons. **Results:** At mid-filling, fluoroscopy shows no significant filling of PFC in the anterior quarter of the lung; conversely, the rest of the lung fills well(p=0,03), reaching a plateau by the end of filling (p>0,4). The anterior quarter of the lung is progressively recruited during the 2-hour TLV(p=0.03), but mostly during the first 10min. Fluoroscopy suggests air is evacuated during the first few expirations. Preliminary results from EIT show an increase in overall lung volume during filling that returns to baseline values after the first expirations, confirming air evacuation with PFC cycling. EIT shows a more homogeneous PFC distribution from

10min onwards. **Conclusion:** These evidence suggest air trapping occurs in the non-dependent regions of the lungs during filling and potential for lung overdistension. To avoid this overdistention, we recommend a filling strategy using the lowest possible initial PFC volume (25 ml/kg), with small increments over the following 10 minutes. EIT bedside monitoring could help the clinician in TLV management.

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THE NEXT GENERATION LONGITUDINAL STUDY: INVESTIGATING THE LINKS BETWEEN MATERNAL TYPE 2 DIABETES AND INFANT HEALTH

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Introduction: The Next Generation Cohort is a longitudinal birth cohort of children born to mothers with pre-gestational type 2 diabetes (T2D). The incidence rate of childhood-onset T2D is increasing every year and disproportionately affects the Manitoba Indigenous population. We have previously reported an increased risk for the development of childhood-onset T2D in this cohort (13% by the age of 12 years), with the youngest child being diagnosed at age 6. Most (28 of 29) of the children diagnosed were born to mothers with pre-gestational T2D. **Objective:** The objective of this project is to report early prenatal and neonatal outcomes. **Methods:** Data was extracted from the maternal pregnancy record (including fetal losses) and infant birth record for mothers with pre-gestational T2D. Descriptive statistics were used to describe the outcomes reported. **Results:** Of the 206 children currently followed in the Next Generation Study, 80 (39%) child-mother pairs had complete medical records available and were included. Median maternal age at delivery was 22.7 years (15.3 – 35.1 years). Median first trimester maternal body mass index (BMI) was 28.2kg/m2 (18 – 45.2kg/m2) and the median glycated hemoglobin (HbA1c) during pregnancy was 8.2% (5.1% –12.0%). Of 128 pregnancies, there were 48 (38%) fetal losses. Of the 80 live births, 27 (34%) were preterm (<37 weeks), 10% were small for gestational age (<2500g), 73% appropriate for gestational age (2500g – 3500g), and 18% were large for gestational age (>4000g). The majority of infants (n=62, 81%) had a neonatal complication (e.g. jaundice, hypoglycemia) and 29 (38%) had a structural anomaly (e.g., cleft palate, ventricular septal defect, microtia). **Conclusion:** In-utero exposure to T2D is associated with pregnancy loss and neonatal complications. With a median maternal HbA1c of 8.2% during pregnancy, a high rate of neonatal complications was seen. This included a 6% rate of stillbirths and neonatal death. Further follow-up of this cohort will provide insight into the risks of in-utero T2D exposure on offspring. Recently, this study has expanded to follow mothers through their pregnancy and to collect cord blood at birth. By obtaining these samples, we can explore the inherent health risk of newborn before post-natal environmental factors play a role. We are investigating liver function, insulin, glucose, and inflammatory markers on these samples.

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RETINOPATHY OF PREMATURITY PRACTICES: A NATIONAL SURVEY OF CANADIAN NEONATAL INTENSIVE CARE UNITS

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Introduction: Retinopathy of prematurity (ROP) accounts for significant morbidity in preterm infants. Early detection and treatment helps prevent adverse sequelae. **Objective:** The objective of this study was to survey the current screening inclusion criteria, treatment options, supportive care and post screening events for ROP in tertiary level Neonatal Intensive Care Units (NICU's) in Canada. **Methods:** The study was designed as a prospective observational study where a survey was sent out to all 29 level three NICU's across Canada. **Results:** Twenty-two level three nurseries responded to the survey (76 % response rate). Ten different ROP screening inclusion criteria were found to be in use with significant variation in gestational age and birth weight criteria. Many other national variations also exist regarding the supportive and procedural protocols surrounding ROP screening as well as mode of treatment for ROP. **Conclusion:** Despite national guidelines, there exists significant variation in ROP screening inclusion criteria practices among neonatal units in Canada. For the many other aspects of ROP screening and treatment, for which there are no national guidelines there also exists significant variations in practice patterns. There is therefore an urgent need for better evidence based screening guidelines as well as a need to standardize supportive measures surrounding ROP screening and treatment, followed by efforts to encourage national uptake of these recommendations.

THEME: Neonatology II – Neurosciences

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LONG-TERM ATTENTION DEFICITSCOMBINED WITH SUBCORTICAL AND CORTICAL STRUCTURAL CENTRAL NERVOUS SYSTEMALTERATIONS IN YOUNG ADULTS BORN SMALL FOR GESTATIONAL AGE

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Introduction: Being born Small for Gestational Age has been associated with neurodevelopmental disabilities and smaller gray matter volumes and cortical thickness in childhood. However, specific impact of being born small for gestational age on cortical gray matter anatomy, in correlation to comprehensive neurocognitive evaluation, has rarely been studied in adults. **Objective:** The goal of this study was to evaluate gray matter anatomy (cortical and subcortical volumes, cortical thickness and cortical surface areas) and cognitive function in adults born Small for Gestational Age at term (SGA), compared to adults born Appropriate for Gestational Age at term (AGA) **Methods:** This prospective follow-up study at age 20 years from the Colombian "Kangaroo cohort", included 39 term-born SGA (birth weight below the 10th percentile for gestational age, mean: 1817 g) and 37 term-born AGA controls (mean birth weight: 3032 g). IQ, attention and memory were evaluated. Gray matter anatomy was investigated with magnetic resonance imaging, which was successfully obtained in 38 SGA and 37 AGA. Anatomical images were analyzed using two complementary structural neuroimaging approaches: a whole brain Voxel-Based-Morphometry procedure with SPM12 and a region of interest FreeSurfer procedure with SPSS. **Results:** Adults born small for gestational age had lower performances in some subtests assessing attention. The cerebral regions with significant differences were the same with the two methods used: VBM and FreeSurfer. Adults born small for gestational age showed smaller total intracranial volume; smaller volumes and surface areas in the frontal lobe, inferior/middle parietal and temporal gyrus; smaller cerebellum, thalamus and basal ganglia volumes with both methods (all ps < 0.05, FWE-corrected and Bonferoni corrected, respectively). All these structures correlated with attention subtests (all ps < 0.05). **Conclusion:** These results highlight the importance of determining consistent brain regions and persistent cognitive impairments that neuroprotective strategies should target.

P108

ADDED VALUE OF INTERLEUKIN-1 BLOCKADE TO HYPOTHERMIA IN NEONATAL ENCEPHALOPATHY DUE TO INFLAMMATORY-SENSITIZED HYPOXIA-ISCHEMIA: A PRECLINICAL STUDY.

Mathilde Chevin, Clémence Guiraut, Guillaume Sébire

Introduction: Background: NE and subsequent cerebral palsy (CP) resulting from hypoxia-ischemia (HI) or inflammatory-sensitized HI remain very prevalent and lead to significant mortality and morbidity. Few neuroprotective treatments are available against NE: they are limited to symptomatic care and HT, leaving about 50% of patients with neurological sequelae. We recently showed that HT fails to counteract the IL-1 system (Chevin et al., Int J Dev Neurosci, 2016), which play a key role in NE. This supports a potential neuroprotective benefit of IL-1Ra as targeted add-on therapy to HT **Objective:** We tested the added value of interleukin-1 (IL-1) receptor antagonist (IL-1Ra) administration to the neuro-protective effect of hypothermia (HT) in neonatal encephalopathy (NE). **Methods:** We used a rat model of lipopolysaccharide (LPS)+HI-induced NE at postnatal (P) day 12. Inflammation was induced by injecting intraperitoneally (ip) 50 µg/kg of LPS from E.coli. Four hours (h) later, the right common carotid artery was ligated, then hypoxia was induced (8% O2, 1 h 30 min). Pups were submitted (or not) to HT (32° ± 0.5°C, 4 h). IL-1Ra (12.5 - 200 mg/kg q12 h) vs saline was injected ip from P12 to P14. **Results:** HT alleviated brain injury in the ischemic penumbra (neocortex and hippocampus), but not core injury, of LPS+HI-exposed pups. This neuroprotective effect did not result from a down-regulation of the neuroinflammatory response mediated by IL-1β or TNF-α. IL-1Ra treatment (50 mg/kg) was well

Conclusion: Our results demonstrate that IL-1Ra (50mg/kg) has an added value to the neuroprotective effect of HT in LPS+HI-induced NE. This project could open new therapeutic avenues to prevent CP.

P110

IS THERE A DARK SIDE OF MATERNAL ANTIBIOTHERAPY IN GROUP B STREPTOCOCCUS CHORIOAMNIONITIS?

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Introduction: Almost 20% of pregnant women have a rectovaginal Group B Streptococcus (GBS) colonization, which is one of the leading microorganism responsible of chorioamnionitis and preterm birth. Recent preclinical models of chorioamnionitis uncovered neurodevelopmental impairments predominantly affecting male offspring in utero-exposed to maternal immune activation induced by either alive or inactivated GBS. The latest Cochrane database review assessed the prophylactic antibiotherapy in preterm labour with intact membranes and found no evidence of its benefit. Moreover, this review suggested an increase of neonatal death and cerebral palsy associated with maternal antibiotherapy. Our hypothesis is that maternal antibiotherapy using ampicillin triggers a fetal inflammatory response syndrome affecting the placenta and the newborn brain **Objective:** Using an established preclinical model (rat) of GBS infection of the placenta we will assess the impact of the antibiotic administration on the level of maternofetal immune activation, the pattern of subsequent blood brain barrier injuries, and the occurrence of perinatal death. **Methods:** At gestational day (G) 19, Lewis dams will undergo an intraperitoneal injection of 10^8 CFU of live serotype Ia GBS. An antibiotic treatment by ampicillin (2 injections of 200 mg/kg) will be given at G21. Caesarian sections will be performed at G22 to collect placentas, fetal brains, maternal and fetal blood samples. **Results:** We anticipate to find increases of pro-inflammatory cells' infiltration and cytokines' expressions in the placenta and fetal blood exposed to GBS plus ampicillin compared to sole GBS. We also anticipate to uncover a more severe disruption of GBS-induced blood brain barrier within the fetal brains exposed to antibiotic. **Conclusion:** These results will provide the rational and the way to design further preclinical studies aiming to test the placento- and neuro-protective roles of targeted anti-inflammatory treatments to prevent GBS-induced chorioamnionitis and inherent mortality and neuromorbidities.

P112

PLACENTAL GROUP B STREPTOCOCCUS INFECTION: SEX SPECIFIC INFLAMMATORY RESPONSE AND AUTISTIC-LIKE TRAITS IN MALE OFFSPRING

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Introduction: Group B Streptococcus (GBS) infection is one of the major causes of chorioamnionitis, which is a risk factor for preterm birth and autism spectrum disorder (ASD). Chorioamnionitis affects the placental synthesis of neurotrophic factors, and triggers the release of neurotoxic inflammatory mediators, such as interleukin-1 (IL-1), which might disrupt myelinated neuroglial fiber tracts. We previously showed, using a new rat model, that GBS-induced maternal infection leads to sex-specific forebrain injuries and ASD-like traits in the offspring (Allard et al., Autism Research, 2016). Our hypothesis is that maternal exposure to GBS impacts the placenta through an IL-1 driven inflammatory response leading to brain injuries and ASD in the offspring. **Objective:** To characterize GBS-induced inflammation on the placenta, and its effect on the offspring' brain. **Methods:** Dams were inoculated intraperitoneally on gestational day (G) 19 with serotype 1a GBS (10^8 CFU). Caesarian-sections were performed at G20, G21 and G22 to collect placental, maternal and fetal blood samples. The maternofetal infectious/inflammatory responses were characterized by Gram staining, immunohistochemistry and ELISA. Offspring born naturally performed ASD-oriented behavioral tests, and their brains were collected at postnatal day (P) 40 for histological studies. **Results:** Placentas of GBS-exposed dams were infected, but did not result in pups' infection. GBS-exposed dams displayed chorioamnionitis characterized by a higher infiltration of polymorphonuclear cells in male than female placentas. Following GBS infection, increased titers of IL-1β were detected in maternal blood, male placentas, and male fetuses' blood, vs control tissues. Forebrain injuries were

observed in the male offspring exposed to GBS compared to controls: enlarged lateral ventricles adjacent to thinner external capsules and corpus callosum, and increased thickness of cingulum and larger area of the left hippocampus. **Conclusion:** Our findings pave the way towards the use of IL-1 blockade in therapeutic trials aimed to prevent ASD arising from GBS infection, a common and modifiable gestational environmental factor.

P114

PREECLAMPSIA AND HUMAN FETAL BRAIN: ANATOMICAL, VASCULAR, FUNCTIONAL AND COGNITIVE IMPACTS.

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Introduction: Individuals (PE-F1s) born from preeclampsia (PE) complicated pregnancies have elevated risks for cognitive impairment and stroke. **Objective:** We hypothesize that fetal brain blood vessel & nervous tissue development are deviated in PE-F1s & PE-associated structural deviations are linked with impaired cognitive functions. We also hypothesized that PE-F1s exhibit a brain functional connectivity pattern that differs from controls. **Methods:** Ten matched pairs of PE-F1 or control children aged 7-10 were analysed for cognitive function (psychometrics, eye tracking) & brain structure using MRI, MRA, Diffusion Tensor Imaging (DTI) and Resting State Functional MRI (rsfMRI). To perform DTI, whole brain analysis made unbiased comparisons in Fractional Anisotrophy (FA) and Mean Diffusivity (MD). Six brain regions of interest (ROIs) were identified for subsequent analysis by tractography (middle occipital gyrus, caudate nucleus & precuneus, cerebellum, superior longitudinal fasciculus and cingulate gyrus). During rsfMRI, seed-based analysis assessed whether differences in resting-state functional connectivity (rs-FC) were present between PE-F1s and controls. The bilateral amygdala, bilateral hippocampus, and the medial prefrontal cortex (MPFC) were selected as ROIs for the seed-based analysis. Data were analyzed by custom MATLAB scripts for voxel-by-voxel comparisons. **Results:** PE-F1s showed impairment in working memory and deficits in saccades to visual targets. While total brain volumes were similar, five specific PE-F1 brain subregions were larger: cerebellum, temporal lobe, left & right amygdala, brain stem. Vascular diameters were globally shorter in occipital & parietal lobes. In DTI, statistical differences were present between groups for fractional anisotropy in the caudate nucleus (PE-F1>Control), volume of tract for superior longitudinal fasciculus (PE-F1>Control), and caudate nucleus (PE-F1>Control), and for parallel diffusivity in cingulate gyrus (PE-F1>Control). In rsfMRI, PE-F1 children compared to controls, had increased rs-FC between the right amygdala & left frontal pole, the left amygdala & bilateral frontal pole, and the MPFC & precuneus. PE-F1 children additionally had decreased rs-FC between the MPFC & the left occipital fusiform gyrus. **Conclusion:** These pilot study outcomes are the first reported in-depth-brain-study data for PE-F1s of any age. They suggest that PE alters fetal development of brain neuroanatomy, vessel radii, and brain functional connectivity. These results justify a fully powered study to better understand impacts of PE during fetal brain development.

P116

EVIDENCE OF ABNORMAL VISUAL FUNCTION IN ASPHYXIATED NEWBORNS TREATED WITH HYPOTHERMIA

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Introduction: Brain injury following birth asphyxia is an important cause of pediatric visual impairments. However, we previously demonstrated in a rat model of term neonatal encephalopathy that, following hypoxia-ischemia, there is also direct injury to the retina, which may also play a significant role in these visual impairments. The effects of birth asphyxia on the retinal function in human newborns have not been studied. **Objective:** To assess visual function in term asphyxiated newborns treated with hypothermia. **Methods:** We recruited 32 term asphyxiated newborns treated with hypothermia and 6 healthy term infants. Flash electroretinogram (ERG; assessment of retinal function), and flash visual evoked potential (VEP; assessment of retino-cortical function) were performed binocularly on day of life (DOL) 10, 30,

and/or 90. Brain injury was assessed on the DOL10 brain MRI. ERG and VEP of the asphyxiated newborns treated with hypothermia were compared to those of the age-matched healthy newborns in terms of morphology, amplitudes and peak times. For further comparisons, the asphyxiated newborns were subdivided into groups depending on whether they displayed brain injury or not. **Results:** 16 out of 32 asphyxiated infants had brain injury. Abnormal ERG peak time or amplitude were found in 25% and 20% of the asphyxiated newborns with and without brain injury on DOL10, and in 30% and 45% of those newborns on DOL30; no abnormal ERGs were found on DOL90. Abnormal VEP peak time or amplitude were found in 46% and 36% of the asphyxiated infants with and without brain injury on DOL10, in 25% and 38% on DOL30, and in 67% and 33% on DOL90. **Conclusion:** Our findings suggest that retinal function in term asphyxiated newborns treated with hypothermia may be impaired with or without associated structural damage to the brain. Follow-up exams are required in these infants to evaluate potential long-term complications.

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APPLICATION OF RESTING-STATE OPTICAL IMAGING OF INTRINSIC SIGNALS TO THE STUDY OF FUNCTIONAL CONNECTIVITY IN AN ANIMAL MODEL OF WHITE MATTER INJURY

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Introduction: Inflammatory white matter injury (WMI) is a leading cause of neurocognitive and neurodevelopmental impairment in very preterm newborns. The development of sensitive and quantitative tools for the assessment of WMI is an important step towards the development of an effective neuroprotective therapy. Resting-state networks (RSNs) have been shown to be altered in preterms, with reduced signal amplitude and spatial extent. When working with animal models, resting-state optical imaging of intrinsic signals (rs-OIS) offers an alternative to functional MRI with increased spatial (hundreds of microns) and temporal resolution (Tr=200ms). **Objective:** This study aims at characterizing the RSNs in an animal model of WMI using rs-OIS **Methods:** METHOD: 13 Sprague-Dawley rats were injected with LPS (1mg/kg; n=5) or saline (sham, n=8) in the left corpus callosum at P3. Three weeks later, resting state activity was recorded using multi-spectral rs-OIS. Functional connectivity (fc) seed-based analyses were performed on different cortical regions. Spatial extent of the networks was assessed. HbO2 and HbR contrasts were considered in the analyses. Two machine learning techniques, support vector machine (SVM) and artificial neural networks (ANN), were applied to assess the use of fc measurements for classification (SVM) and predicting the injury extent (ANN). **Results:** The fc seed-based analyses showed impaired fc in the motor and cingulate cortex of the injured group, but not in the retrosplenial region. Moreover, the number of positive correlations between cortical regions was reduced in the LPS group. These effects were more strongly observed with the HbR contrast. The spatial extent of the RSNs decreased in the motor, cingulate, somatosensory and retrosplenial cortex for both contrasts ($p=0.0452$ for HbO2 and $p=0.0036$ for HbR, after false discovery rate correction). The classification of the SVM demonstrated high accuracy (92.3%) and the ANN predictions strongly correlated ($r=0.9431$, $p=0.0020$ and a RMSEP=2.25%) with the ventricular dilatation caused by the inflammation. **Conclusion:** In agreement with previous results in preterm infants with WMI, neonatal LPS injection caused a long-lasting disruption of the RSNs, particularly in the motor and cingulate networks. This disruption is quantified by a reduction in their spatial extent and number of positive correlations. SVM accuracy suggests a potential use of rs-OIS measurements for therapeutic assessment. Moreover, the high prediction correlation of the ANN shows that fc measurements reflect the injury level.

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DOES MULTIPLE ATTEMPTS FOR TRACHEAL INTUBATION AT BIRTH INCREASE THE RISK OF INTRAVENTRICULAR HEMORRHAGE IN VERY PRETERM INFANTS?

A Aslam, M Vincer, W El-Naggar, J Afifi

Introduction: Tracheal intubation (TI) of preterm infants may cause bradycardia, oxygen desaturation and change in systemic and cerebral blood pressures. All of these factors have been associated with intraventricular Hemorrhage (IVH). Little is known about the relationship between multiple TI attempts during resuscitation of very preterm infants in the

delivery room and the development of IVH. **Objective:** To examine the rate of all grades IVH in very preterm infants (< 31 weeks gestation) that had multiple TI attempts at birth as compared to those who had a single successful TI. Secondary outcomes include; severe IVH (IVH with ventricular dilatation or parenchymal bleeding), death before 28 days of age and the composite outcome of death or IVH. **Methods:** We conducted a retrospective review of all inborn very preterm infants (220 weeks– 306 weeks) who were intubated at birth between 2006 and 2015 and were admitted to the Neonatal Intensive Care Unit at the IWK Health Centre, Halifax, Nova Scotia. We excluded those with major congenital anomalies. Antenatal and perinatal characteristics, neonatal morbidities and short-term outcomes were compared between infants who received single TI attempt and those who received multiple attempts during delivery room resuscitation. All grades of IVH detected on cranial ultrasound were compared between both groups. **Results:** A total of 378 very preterm infants were included. The mean gestational age (+/- SD) was 27 weeks (2) and the mean birth weight (+/- SD) was 950 grams (290). During delivery room resuscitation, 165 infants (44%) received single TI while 213 infants (56%) received multiple TI attempts. The maternal and infants characteristics of both groups are shown in table 1. No significant differences were found between both groups in any of the primary or secondary outcomes after adjustment for potential confounders)[table2]. **Conclusion:** Multiple intubation attempts during resuscitation of very preterm infants in the delivery room were not associated with increased all grades IVH, severe IVH or mortality before hospital discharge.

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Introduction: Tracheal intubation (TI) of preterm infants may cause bradycardia, oxygen desaturation and change in systemic and cerebral blood pressures. All of these factors have been associated with intraventricular Hemorrhage (IVH). Little is known about the relationship between multiple TI attempts during resuscitation of very preterm infants in the delivery room and the development of IVH. **Objective:** To examine the rate of all grades IVH in very preterm infants (< 31 weeks gestation) that had multiple TI attempts at birth as compared to those who had a single successful TI. Secondary outcomes include; severe IVH (IVH with ventricular dilatation or parenchymal bleeding), death before 28 days of age and the composite outcome of death or IVH. **Methods:** We conducted a retrospective review of all inborn very preterm infants (220 weeks– 306 weeks) who were intubated at birth between 2006 and 2015 and were admitted to the Neonatal Intensive Care Unit at the IWK Health Centre, Halifax, Nova Scotia. We excluded those with major congenital anomalies. Antenatal and perinatal characteristics, neonatal morbidities and short-term outcomes were compared between infants who received single TI attempt and those who received multiple attempts during delivery room resuscitation. All grades of IVH detected on cranial ultrasound were compared between both groups. **Results:** A total of 378 very preterm infants were included. The mean gestational age (+/- SD) was 27 weeks (2) and the mean birth weight (+/- SD) was 950 grams (290). During delivery room resuscitation, 165 infants (44%) received single TI while 213 infants (56%) received multiple TI attempts. The maternal and infants characteristics of both groups are shown in table 1. No significant differences were found between both groups in any of the primary or secondary outcomes after adjustment for potential confounders)[table2]. **Conclusion:** Multiple intubation attempts during resuscitation of very preterm infants in the delivery room were not associated with increased all grades IVH, severe IVH or mortality before hospital discharge.

THEME: Perinatal Epidemiology

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STILLBIRTH RISK DURING HIGH OUTDOOR TEMPERATURES IN CANADA

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Introduction: Risks factors for stillbirth are poorly understood, including the possible impact of high outdoor temperature. Elevated temperatures may stress pregnant women, particularly at term, and be a risk factor for stillbirth. **Objective:** We assessed the relationship between elevated temperature and risk of preterm and term stillbirth, including cause of death, in a temperate Canadian province during warm months. **Methods:** We performed a case-crossover analysis of 5,047 stillbirths in the province of Quebec, Canada, between the months of April and September from 1981-2011. We obtained maximum daily temperatures from Environment Canada. We estimated the association (odds ratio; 95% confidence interval, CI) between maximum daily temperature and stillbirth adjusted for relative humidity, comparing temperature on the day of death with nearby days. We modeled temperature continuously using cubic splines, with 20°C as the reference. The main outcome measure was stillbirth according to week of gestation (preterm, term), and cause of death (undetermined, maternal complications, placenta/cord/membranes, birth asphyxia, congenital anomaly, other). **Results:** Elevated outdoor temperatures were associated with greater odds of stillbirth at term, but not preterm. Maximum daily temperatures of 30°C the day before death were associated with 1.22 times greater odds of term stillbirth (95% CI 1.02-1.46) relative to 20°C, and the associations strengthened with higher temperatures. Outdoor temperature was associated with stillbirth due to maternal complications and undetermined causes, but not other causes. Compared with 20°C, maximum temperatures of 30°C were associated with 1.72 times the odds of stillbirth due to maternal complications (95% CI 1.06-2.80) and 1.28 time the odds of stillbirth due to undetermined causes (95% CI 1.02-1.59). **Conclusion:** Elevated outdoor temperature maybe a novel risk factor for term stillbirth, and for stillbirths related to maternal complications or with undetermined cause. As global temperatures rise, further investigation is warranted to study how heat stress affects the health of pregnant women in temperate climates.

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UMBILICAL CORD BLOOD LEVELS OF LEPTIN AND ADIPONECTIN AND THEIR ASSOCIATION WITH CHILD GROWTH MEASURES

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Introduction: Obesity in children has increased dramatically over the past few decades. The physiologic role of adipokines (e.g., leptin and adiponectin) in metabolic function and regulation in adults is recognized, but the association between fetal concentrations of these adipocyte-produced hormones and measures of adiposity in early childhood is poorly understood. **Objective:** To examine the association of cord blood levels of leptin and adiponectin with weight and height measures in early childhood. **Methods:** Between 2008 and 2011, 2001 women were recruited during the first trimester of pregnancy from 10 Canadian cities in the Maternal-Infant Research on Environmental Chemicals (MIREC) Study. In 2013, families were invited to undergo follow-up assessments in the MIREC-Early Childhood Biomonitoring and Neurodevelopment (CD) Plus Study. Live-born singleton infants who participated in the MIREC-CD Plus Study and had a cord blood sample, were included. Age and sex specific z-scores for body mass index (BMI) were calculated as the primary outcome using WHO reference standards; weight and height z-scores were considered secondary outcomes. We used linear regression models to examine the association between measures of cord blood adipokines and anthropometric z-scores. We used logistic regression models to assess the relationship between high (≥90th percentile) and low (≤10th percentile) adipokine levels, and adiposity according to overweight/obesity (defined as BMI z-score >1). Leptin and adiponectin models were run separately and adjusted for a common set of confounders (e.g., maternal and paternal BMI, maternal age, parity, gestational weight gain). **Results:** There were 301 males and 278 females (median age 3.3 years) at follow-up. After adjustment, no significant associations were observed between leptin and BMI z-score,

weight z-score, or height z-score. In an adjusted model, higher levels of adiponectin (≥90th percentile) were positively, and significantly associated with BMI z-score compared to moderate levels (10th-90th percentile). Similarly, children who had higher levels of adiponectin had higher odds of being overweight or obese compared with those with moderate levels (OR 1.7, 95% CI 0.9- 3.3). **Conclusion:** Cord blood leptin concentrations were not associated with weight or height measures in early childhood. In contrast, elevated adiponectin concentrations were associated with the development of adiposity in young children. Fetal adiponectin may be a useful biomarker to understand the impact of intrauterine hormones on metabolic dysfunction later in childhood.

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CAESAREAN SECTION AND HEALTH CARE UTILIZATION IN THE OFFSPRING

Alexander Nikolas MacLellan, Christy G. Woolcott, Linda Dodds, Bryan Maguire, Sarah McDonald, Stefan Kuhle

Introduction: The rates of Caesarean section (CS) delivery have increased over the past decades, and a quarter of all deliveries in Canada are now by CS. The microbiome hypothesis suggests that offspring delivered by CS lack exposure to the maternal vaginal flora, which may increase their risk for immune system-related conditions in childhood. Epidemiologic studies have associated CS with adverse childhood outcomes such as asthma, allergies, obesity, and inflammatory bowel disease, suggesting that children born by CS may have higher health care utilization and costs but this association has not been investigated yet. **Objective:** To examine the association between CS and health care utilization and costs in offspring from birth until age 18. **Methods:** A retrospective cohort study of births in Nova Scotia between 1989 and 1993 was conducted using data from the Nova Scotia Atlee Perinatal Database and administrative health data. The main exposure was mode of delivery (CS vs. vaginal delivery (VD)); CS was further categorized based on whether it was performed before or after the second stage of labour. Outcomes were the number of physician visits, number of hospital stays, and physician costs during the first 18 years of life. Associations were modeled using multiple regression adjusting for maternal pre-pregnancy weight and socio-demographic factors. **Results:** A total of 35,090 births was included in the analysis. Compared to children born by VD, children delivered by CS had 6% more physician visits (95%CI 4-7) and 12% more hospital stays (95%CI 10-15) in the adjusted model. Physician costs were 8% (95%CI 6-9) higher for children delivered by CS compared to VD. Excess physician costs from 0-18 years following CS delivery were 342 per delivery. The differences in physician visits and costs between CS and VD were highest during the first month of life (IRK 1.24 and 1.41, respectively). In children born by CS, health care utilization and costs did not differ significantly between those born before or those born after the onset of the second stage of labour. **Conclusion:** CS compared to VD is associated with only small increases in health care utilization and physician costs in children and youth. The excess physician costs over the first 18 years of life for a child born by CS are negligible. The total excess health care costs for children born by CS can be expected to be higher but we were unable to measure hospital and drug costs in our analysis.

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THE INFLUENCE OF PERINATAL CONDITIONS AND OUTCOMES IN A FIRST PREGNANCY ON SMOKING STATUS IN THE SECOND PREGNANCY

Kimberley Nix and Linda Dodds

Introduction: Smoking during pregnancy is a serious health problem with significant risks for both the mother and the developing fetus. Most women do not change their smoking status between first and subsequent births, but it is not clear whether adverse pregnancy outcomes in a pregnancy will influence decisions about smoking in a subsequent pregnancy. Addressing factors associated with smoking during second pregnancy may inform smoking cessation interventions. **Objective:** To explore, among women who smoked in pregnancy 1 (P1), the rates of prenatal smoking during second pregnancy (P2) , and to determine whether adverse pregnancy conditions and outcomes from P1 affect the likelihood of smoking in P2. **Methods:** A population-based retrospective cohort study of first and second singleton births among women in Nova Scotia, Canada who smoked in P1 was conducted. Data was obtained from the Nova Scotia Atlee Perinatal Database and included all women who had first and second consecutive deliveries between 2003 and 2014 with an infant of 500 grams or more. Women were included if they smoked during the first pregnancy. Women were excluded if information was missing for smoking status in either pregnancy, or if birth weight or gestational age were not recorded. The primary outcome was smoking status in the second pregnancy and the primary independent

variables were adverse pregnancy conditions or outcomes in P1. Data was analyzed using logistic regression, and adjusted for maternal socio-demographic variables. **Results:** Overall, 3441 (20.4%) of women smoked in P1, and 2606 (75.7%) of these women continued to smoke in P2. Among pregnancy conditions, only a diagnosis of gestational hypertension in P1 was associated with a reduced likelihood of smoking in P2 (OR=0.47, 95% CI 0.2-0.91). Of possible infant outcomes in P1, having an infant that was small for gestational age was significantly associated with smoking in P2 (OR 1.91, CI 1.43-2.54) compared to women whose babies who were not small for gestational age. **Conclusion:** Aside from gestational hypertension, adverse maternal or neonatal conditions in the first pregnancy did not result in a reduction in smoking in pregnancy 2. It is concerning that having had an infant who was small for gestational age in P1 increased the likelihood of smoking in P2. More research is necessary to understand the women's decision to smoke in P2 after having had an adverse outcome in a first pregnancy.

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ASSOCIATION OF REDUCING RESIDENT ON-CALL DUTY HOURS, LEVEL OF TRAINING, AND AVAILABLE RESIDENTS AT ADMISSION WITH NEONATAL OUTCOMES.

Marc Beltempo, Karin Clement, Guy Lacroix, Sylvie Bélanger, Anne-Sophie Julien, Bruno Piedboeuf

Introduction: Working more than 16 consecutive hours has been associated with an increased risk of medical errors and harm to patients. In 2011, the collective agreement was amended to reduce the maximum number of consecutive hours worked by pediatric residents in Quebec from 24 to 16 hours. **Objective:** To assess the impact of reducing resident consecutive hours worked on-call, residents level of training, and the number of residents present at admission on neonatal mortality and morbidity. **Methods:** A 6-year retrospective cohort study of all infants admitted in a Level-3 NICU (n=8159). Adjusted odds ratios (AOR) were estimated for mortality with respect to Epoch [Epoch 1 (2008-2011, 24-hour shifts) versus Epoch 2 (2011-2014, 16-hour shifts)], level of training of residents and number of residents present at admission. Mortality and major morbidly in patients born <29 weeks with regards to admission was also assessed (n=436). **Results:** There was no association of resident duty-hour restrictions with mortality in all patients (AOR, 0.73; 95% CI, 0.50-1.07; Epoch 2 vs Epoch 1). Number of residents present at admission was not associated with mortality in all patients (AOR, 0.43; 95% CI, 0.16-1.14; Q4 vs Q1) neither was the level of training of residents present at admission (AOR, 1.37; 95% CI, 0.92- 2.04; junior vs senior). In the subgroup of newborns <29 weeks of gestational age, there was no significant different in odds of mortality or major morbidity (AOR, 0.65; 95% CI, 0.37-1.15; Epoch 2 vs Epoch 1). Level of training and number of residents present at admission were not associated with mortality of major morbidity. Furthermore, in this population there was an increased in mortality or major morbidity with admissions in the evening compared to the day (AOR, 2.28, 95% CI, 1.18-4.42), and during the summer compared to rest of the year (AOR 2.98, CI 1.51- 5.85). **Conclusion:** This study did not show that the reduction in resident consecutive on-call duty hours, level of training or number of residents' present have a significant impact on neonatal mortality and morbidity. The observed increase in mortality and morbidly in patients admitted on evenings and in the summer may be associated with other organizational factors that require further investigation.

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VARIATION IN MATERNAL COMORBIDITIES ACROSS AREA-LEVEL SOCIOECONOMIC STATUS: A CROSS-SECTIONAL STUDY

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Introduction: Area-level socioeconomic status (SES) has a substantial effect on maternal health. Although the presence of one comorbidity during pregnancy relates to a 6-fold increase in risk of severe maternal complications, the influence of area-level SES on maternal comorbidities has not been examined. **Objective:** To examine the variation in maternal comorbidities across area-level SES. **Methods:** The Discharge Abstract Database was used to identify women who delivered a live-born infant in Alberta hospitals between 2005-2007 (n:120,285). Maternal comorbidities, such as pre-eclampsia and multiple gestation were identified using validated case definitions. The Material Deprivation Index, a measure of area-level SES comprising census reported income, education, and employment, was obtained for each dissemination area and linked to hospitalization data. Dissemination areas were aggregated into quintiles ranging from

the least deprived (quintile 1) to the most deprived (quintile 5). Multilevel logistic regression was used to analyze the data adjusting for maternal age and parity. **Results:** The overall prevalence of maternal comorbidities varied significantly across area-level SES (p-value: 0.028), ranging from 7.02% (95% CI: 6.78%, 7.39%) in the least deprived areas to 7.80% (95% CI: 7.49%, 8.12%) in the most deprived areas. The prevalence of some individual comorbidities such as asthma, drug abuse, and previous caesarean delivery were significantly higher in the most deprived areas; whereas gestational hypertension and multiple gestation were significantly lower in the most deprived areas (p-values<0.05). The association of area-level SES with overall comorbidities (i.e., presence of at least one comorbidity) and individual comorbidities remained significant after adjusting for age and parity. For example, overall comorbidities (adjusted OR: 1.28; 95% CI: 1.18, 1.39), asthma (adjusted OR: 1.83; 95% CI: 1.29, 2.58), drug abuse (adjusted OR: 2.67; 95% CI: 1.95, 3.65), and HIV (adjusted OR: 3.62; 95% CI: 1.44, 9.11) were all significantly more likely to occur in the most deprived areas. In contrast, multiple gestation (adjusted OR: 0.55; 95% CI: 0.30, 0.98) was significantly less likely to occur in the most deprived areas. **Conclusion:** The occurrence of maternal comorbidities varies across the spectrum of area-level SES. The higher prevalence of maternal comorbidities in specific SES groups may help to identify groups at greater risk for severe maternal complications and poor birth outcomes. In order to promote improved maternal health outcomes, the vulnerabilities of specific SES groups should be considered when allocating health

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OXYGEN SATURATION TARGETING USING MANUAL VERSUS AUTOMATED CONTROL OF INSPIRED OXYGEN IN PRETERM INFANTS:A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Preterm infants have immature lungs at birth and due to their inherent lung pathology, their spO2 is often found to fluctuate widely necessitating frequent changes to the FiO2. This often leads to variable periods of time spent outside the intended O2 saturation targets. It is known that in preterm infants, hyperoxia is associated with increased incidence of ROP and chronic lung disease(CLD) whereas hypoxia is associated with increased mortality. There have been a number of recent studies comparing control of FiO2 using an automated algorithm versus manual control by health care professionals. **Objective:** To conduct a systematic review of RCTs and quasi-RCTs exploring the following question:In O2-dependent preterm infants who are on ventilator support(invasive or non-invasive), does automatic control of FiO2 compared to manual control lead to improved spO2 targeting, reduction in hypoxic events & mortality and improvement in long-term outcomes(CLD, ROP, major neurodevelopmental morbidities)? **Methods:** MEDLINE, Embase, CENTRAL, conference proceedings and results of unpublished trials were searched. The risk of bias(ROB) of eligible studies was assessed according to a modified version of the Cochrane Collaboration's ROB tool. We assessed the confidence in the estimates for each outcome across the studies using the GRADE approach. **Results:** 274 potentially relevant studies were identified. 10 studies including 274 infants met the inclusion criteria and were included in the final analysis. 8 studies were cross-over RCTs, 1 parallel design and 1 quasi-randomized cross-over trial. Automated FiO2 control resulted in significantly higher time being spent within the target spO2 range [Mean difference: 12.8%;95%CI:6.5to19.2%;I2=90%].Periods of hyperoxia(↓8.8%), severe hypoxia(spO2<80%) (↓1%),& hypoxic events(↓5.6), were significantly reduced with automated control, however, there was no difference in time spent below the target spO2 range or FiO2 exposure in the two groups. Sensitivity analysis exploring the heterogeneity sources revealed type of RCT and type of automated control algorithm significantly contributed to statistical heterogeneity. GRADE assessment showed that all outcomes had very low quality of evidence except for time spent in severe hypoxia and FiO2 exposure which were of moderate quality. **Conclusion:** Automated FiO2 control significantly improves spO2 targeting and reduces periods of hyperoxia, severe hypoxia and hypoxic events in O2-dependent preterm infants. In view of the very low to moderate quality of evidence, further RCTs, preferably parallel-design and blinded, looking at long term outcomes are needed to establish a stronger evidence to routinely promote the use of automated FiO2 control for preterm infants.

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TRENDS AND DETERMINANTS OF EARLY INITIATION OF BREASTFEEDING IN LOW AND MIDDLE INCOME COUNTRIES

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Introduction: More than one third of deaths in children under-five occur within the first month after birth. Infections are one of the leading causes of newborn deaths, especially in low income countries. Recent studies have indicated that early breastfeeding initiation (within 1 hour of birth) was associated with a 45% reduction of risk of death from infection-related neonatal mortality. During the early hours after birth, the mammary glands produce colostrum (first milk) which contains a high concentration of antibodies that help protect neonates from infectious diseases. To our knowledge, no studies have looked at the trends and determinants of early initiation of breastfeeding in multiple countries. **Objective:** The objectives of this study are to examine the (i) trends in breastfeeding initiation in low- and middle-income countries (LMIC), and (ii) factors associated with early initiation of breastfeeding in LMIC. **Methods:** Data from 211 Demographic and Health Surveys in 70 LMIC conducted between 1990 and 2015 were used for this study. Standardized questionnaires were used to collect information on early breastfeeding, cesarean delivery, antenatal care, and other maternal socioeconomic and demographic characteristics. Survey data were pooled and weights re-scaled to achieve equal weighting between countries and years. Trends were analyzed in 5-year intervals. Linear regression models were specified to capture adjusted absolute differences in rates of early breastfeeding. Models were adjusted for survey design effects and included covariates for year of survey, between country differences, prenatal care [at least 1 visit with skilled provider], skilled attendant at delivery [doctor/nurse/midwife vs others], place of delivery [hospital/health facility vs home], child sex, maternal education, and household wealth. **Results:** Over 1.12 million birth records were analyzed. Rates of early breastfeeding have increased in LMIC from 29% in 1990 to 52% by 2015; equivalent to a 15% (95% CI: 14.7-15.5) increase comparing 2005-15 vs 1990-2004 adjusted for maternal and child characteristics and country level fixed effects. Access to prenatal care and delivery in a health facility were associated with an absolute increases in early breastfeeding of 4.3% (95% CI: 3.9-4.8) and 4.5% (95% CI: 3.9-5.1). Delivery by cesarean section was associated with 24% lower rate of early breastfeeding (95% CI: 23.9-25.0). **Conclusion:** Rates of early breastfeeding have increased substantially in recent years. Access to quality prenatal care was strongly associated with increased rates of in early breastfeeding, but cesarean section impacted negatively on early breastfeeding in LMIC.

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WOMEN WITH A HISTORY OF ABUSE BEFORE PREGNANCY HAVE INCREASED RISK FOR ADVERSE PREGNANCY OUTCOMES. A SYSTEMATIC REVIEW

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Introduction: Preterm birth (PTB) is the leading perinatal health problem. Research indicates a maternal history of abuse is associated with PTB, but no systematic review of the abuse and PTB literature has been conducted. **Objective:** To perform a systematic review of the world literature to assess the association between maternal abuse (physical, emotional, and sexual) and PTB. **Methods:** Step 1. The Medical Subject Headings and keywords for exposure (abuse) and the outcome (PTB) were searched through MEDLINE, EMBASE, Cochrane Library, Central, Psycho info, CINAHL, Scopus, Pilots, and Web of Science. Reference lists of the included articles were manually examined to find other relevant literature. Also, relevant researchers or organizations were approached for published or unpublished studies not retrieved by our search. Step 2. Identified citations were appraised using structured inclusion/ exclusion form. The Newcastle-Ottawa Quality Assessment Scale was used to assess the methodological quality of the included studies. Two independent reviewers performed the selection; their agreement with that of the senior author was required for the final inclusion of the studies. Step 3. Meta-analysis was conducted. Odds ratios (OR) with 95% Confidence Interval (CI) were calculated for those included articles that did not report these measures. Statistical heterogeneity was assessed using I- squared statistics. **Results:** Out of 6,404 citations that were obtained through online search and manual reference list search, fifteen studies that were recognized as high or moderate quality studies were included in this review. These studies reported an association between maternal histories of abuse in different points of life before pregnancy and PTB. Consequently, three subgroups of childhood abuse, anytime abuse, and recent abuse were created, and analysis was conducted within each group. Having an experience of sexual abuse during childhood increases the odds of PTD by 73% compared to women who did not have that experience. However, the odds ratio decreased to 22% when sexual or physical abuse occurred in adult women any time during their married life before pregnancy. In addition, when maternal abuse was experienced within 6 to 12 months before pregnancy the odds of PTD increased by 35%.

Conclusion: This review suggests that it is necessary to screen women for a history of abuse before pregnancy as a part of normal and adequate prenatal care, as this screening is not currently performed consistently or thoroughly in Canada. We also recommend more original research on the impact of childhood abuse on pregnancy outcomes, especially in low and middle income countries. Last, we recommend a systematic review focused on the impact of childhood abuse on pregnancy outcomes.

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ADVERSE BIRTH OUTCOMES IN RELATION TO MATERNAL MARITAL AND COHABITATION STATUS IN CANADA

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Introduction: Marital status is an important demographic variable that is associated with a range of health outcomes and is frequently considered as a potential confounder or effect modifier of exposure-outcome associations. However, an increasing percentage of children in Canada are born to couples who cohabit but are not legally married. The associations of marital and cohabitation status with adverse birth outcomes in Canada have not been measured at the national level. **Objective:** To estimate associations of maternal marital and cohabitation status with preterm birth (PTB), small- and large-for-gestational-age (SGA and LGA) birth, stillbirth and infant mortality in a representative Canadian sample. **Methods:** Data were from the 2006 Canadian Birth-Census Cohort, with births from May 2004 to May 2006, created by linking birth registration data with the 2006 long-form census. Marital and cohabitation status were determined based on census data. Outcomes were assessed from linked birth and infant death registrations. Log-binomial regression was used to estimate risk ratios for adverse birth outcomes associated with being single or living with a common-law partner, with married women as the reference group. Analyses controlled for maternal age and education. **Results:** Data on marital and cohabitation status were available for 130,931 mothers with singleton births. Approximately two-thirds were married, one-fourth were cohabiting, and one in eight were single. Compared to married mothers, single mothers had a moderately higher adjusted risk of PTB (RR = 1.36, 95% CI = 1.27-1.46) and SGA birth (RR = 1.31, 95% CI = 1.22-1.39), while cohabiting mothers had a slightly higher adjusted risk of PTB (RR = 1.09, 95% CI = 1.03-1.15) and a marginally increased adjusted risk of SGA birth (1.05, 95% CI = 0.99-1.10). Crude rates of LGA birth were slightly higher among married women (11.4%) than among single and cohabiting women (10.5% in both groups), but these differences persisted only marginally after adjustment for other maternal characteristics (RR = 0.95, 95% CI = 0.90-1.01 for single women, RR = 0.96, 95% CI = 0.92-1.00 for cohabiting women). Stillbirth rates were substantially higher in single vs. married mothers (adjusted RR = 1.92, 95% CI = 1.51-2.42) and did not differ significantly between cohabiting and married mothers (adjusted RR = 0.93, 95% CI = 0.74-1.16). Crude infant mortality rates were highest among single mothers (8.7 per 1000) but did not differ substantially between married and cohabiting mothers (4.2 and 4.4 per 1000, respectively). **Conclusion:** In a nationally-representative Canadian birth cohort, cohabiting and legally-married women experienced similar birth outcomes, but single women's outcomes were substantially worse. These findings have important implications for research, targeting public health interventions and care.

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VALIDITY AND RELIABILITY OF PARENT-REPORTED CHILDHOOD IMMUNIZATION STATUS IN THE ALL OUR BABIES COHORT

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Introduction: Accurate measurement of childhood immunization uptake is important for assessing vaccine coverage of a population. Previous studies have assessed the validity of parent report at only one point in time, which does not enable determination of the ideal time point for valid reporting. An ongoing longitudinal cohort study, All Our Babies (AOB), provides an opportunity to validate parent-reported data on vaccination status across varying time points, using public health records as a gold standard. **Objective:** To assess the validity and reliability of parent-reported data on child immunization status for scheduled immunizations at three time points. **Methods:** Parents' report of vaccination status of children at ages 12, 24, and 36 months was obtained from survey data from the AOB cohort and linked to electronic

records of vaccination status as provided by public health records (PHANTIM) in the Calgary zone. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated. Consistency of parent report was measured using kappa statistics. **Results:** Parent report showed high sensitivities (98.7% to 99.9%) and lower specificities (11.6% to 94.5%). PPV ranged from 94.6% to 99.9%, while the NPV ranged 66.0% to 96.7%. Parents accurately recalled their child's vaccination status more consistently for 18 month vaccinations (kappa = 0.78) than for 2 month vaccinations (Kappa= 0.44). **Conclusion:** Parents' report of vaccine completion is generally valid, but their report of non-vaccination is less so. A longer time delay between when the vaccine was administered and when the parent reported on vaccination status may decrease validity of the parent report.

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PERINATAL MENTAL HEALTH SERVICE DELIVERY MODELS: A SCOPING REVIEW.

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Introduction: Evidence supports the efficacy of a range of treatment modalities for perinatal mental health conditions, and early detection and treatment are considered ideal for the health and well-being of young families. However, timely access to appropriate services remains a challenge in many Canadian settings, suggesting a need to examine optimal perinatal mental health service models. **Objective:** S: Our objectives were to identify the state of the research evidence regarding the effectiveness and cost-effectiveness of, and patient satisfaction with, service models for perinatal mental health services, and to describe the characteristics of models that achieve favourable outcomes. **Methods:** We conducted a scoping review using the methods described by Arksey & O'Malley. Two team members conducted literature searches using pre-determined search terms in three databases. Search results yielded: 707 articles on Medline; 3,485 articles in SCOPUS, and 3,645 in CINAHL. Abstracts for these studies were assessed based on pre-determined inclusion criteria establishing the population, intervention, comparison, and outcomes of interest. Both English and French publications were included. To verify their relevance, full publications were read for all studies that appeared to meet the inclusion criteria, which resulted in the identification of 126 articles from which data was charted. **Results:** Of 126 charted articles, only five studies reported outcomes related to effectiveness, cost-effectiveness, or patient satisfaction associated with perinatal mental health service models. Features of successful care service models included: community based clinics, multi-disciplinary teams, service providers in advocacy/ advisory roles, education and outreach to primary care providers, multi-pronged approaches to maximize accessibility, and collaboration and partnership between existing service providers. **Conclusion:** There is limited high quality research evidence to guide the organization and structure of perinatal mental health services to optimize clinical effectiveness, cost effectiveness, and patient satisfaction. The development of innovative service models should take into account what is known from the literature regarding barriers and facilitators of timely access to appropriate care, and evaluation of any such innovations is warranted.

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COMPARING MATERNAL SERUM SCREENING MARKERS AMONG IVF AND SPONTANEOUS CONCEPTIONS IN ONTARIO

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Introduction: Multiple marker prenatal screening uses maternal serum markers combined with nuchal translucency measurement to estimate risk of Down syndrome or a number of other aneuploidies. This algorithm incorporates corrections for ethnicity, smoking, diabetes and in vitro fertilization (IVF) for specific maternal serum screening markers. In Ontario, only PAPP-A, total, and µE3 have an IVF correction factor applied. **Objective:** The objective of this study was to investigate the accuracy of IVF identification on the prenatal screening record and to compare the screening markers in IVF and non-IVF pregnancies in the population of Ontario **Methods:** The Better Outcomes Registry & Network (BORN) Ontario collects comprehensive information on prenatal screening from all prenatal screening centres and information on the use of IVF from all fertility clinics in Ontario through CARTR Plus. Prenatal screening data and fertility data were merged to create a linked dataset. For each MSS marker and NT measurement, log10 transformations were performed in order to account for the skewed distributions. Linear regression models were produced for both of these scenarios.

New adjustment factors were developed for each MSS marker. These adjustment factors were applied to all IVF records with prenatal screening results. **Results:** When identification of the use of IVF from the prenatal screening record was compared to the gold standard for fertility treatment in Canada (the CARTR Plus database), the sensitivity was 95.8% and the specificity was 98.9%, however the positive predictive value was 68.8%. The largest differences in mean MoM for the prenatal screening Ontario (PSO) and CARTR Plus models were seen for PAPP-A, total hCG and µE3, which was appropriate given that these three MSS markers were the ones that currently have adjustment factors for IVF applied. When we compared the same population of patients, we found that the new adjustment factor for IVF improved the mean MSS marker MoMs to a greater extent than the current PSO IVF adjustment factors. Slight differences were observed among IVF and FET cycles. **Conclusion:** Interestingly, the current PSO IVF adjustment factor for total hCG adjusted the mean MoM in the wrong direction. This strengthens the rationale for modifying the current MSS marker adjustment factors for IVF in the Ontario population. The majority of MSS markers would benefits from an IVF adjustment. Additionally, identification of conception method would be more appropriate for implementing correction factors if ascertained from CARTR Plus.

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DO NEONATAL FACTORS PREDICT RISK OF IMPAIRED GLUCOSE TOLERANCE AMONG YOUNG ADULTS BORN PRETERM?

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Introduction: Preterm birth is associated with an increased risk of lower insulin sensitivity and metabolic abnormalities later in life. However, little is known about relationship between neonatal factors, growth, and parents' health status with metabolic outcomes in young adulthood. **Objective:** To compare metabolic outcomes between very preterm and term born young adults and to examine neonatal factors, growth and parents' metabolic health status associated with glucose metabolism in adults born preterm. **Methods:** 82 adults (18-29 years) born <29 weeks of gestation and 82 sex-, race- and age-matched term born controls underwent physical examination including blood pressure, waist circumference measurement, blood lipid and glucose profile. Criterions of metabolic syndrome were based on the harmonized metabolic syndrome definition from IDF, NHLBI, AHA, WHF, IAS, and IASO published in 2009. The definition of pre-diabetes was based on Clinical Practice Guidelines published by Canadian Diabetes Association in 2013. Neonatal charts were reviewed. Weight in z-score at discharge, 1 and 2 years old were collected from medical charts or health booklet. Parents' metabolic health data were collected using questionnaires answered by parents or by participants. Group comparison was performed with independent t-tests and Chi-square test. **Results:** Mean GA was 27.2±1.4 weeks and birth weight 990±240 g for the preterm group. Metabolic results were similar among the two groups except a significant higher prevalence of impaired glucose tolerances in the preterm group (29%) compared to the control (11%). No difference was found in neonatal factors, growth and parents' metabolic health among preterm with impaired glucose tolerance compared to preterm without. **Conclusion:** We did not detect any differences between preterm vs term born participants for the number of components of metabolic syndrome. However, young adults born preterm have greater risk of impaired glucose tolerance in absence of dyslipidemia and this is not associated with neonatal factors, growth, and parents' metabolic health status. Relationship between impaired glucose metabolism and factors that happen later on in life, such as lifestyle and environment, could be investigated in future studies.

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THE EFFECT OF AN ELECTRONIC AUDIT AND FEEDBACK SYSTEM ON SIX KEY PERFORMANCE INDICATORS IN ONTARIO: THE BORN MATERNAL NEWBORN DASHBOARD

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Introduction: In November 2012, the Better Outcomes Registry & Network (BORN Ontario) launched an audit and feedback (A&F) system in hospitals providing maternal-newborn care in Ontario. The Maternal Newborn Dashboard (MND) provides feedback about six key performance indicators (KPIs). **Objective:** To assess the effect of the MND on rates of 6 KPIs in the province of Ontario. **Methods:** BORN registry datasets covering 2009 through 2015 were used. The study time period included 3 years pre-MND implementation and 2 years post-implementation. Using segmented regression models, we carried out an interrupted time series analysis to assess the effect of MND implementation on rates of 6 KPIs in Ontario hospitals. The effect of the intervention was measured at 30 months post-MND implementation as the absolute difference between observed KPI rates and predicted KPI rates based on pre-implementation temporal trends. Two internal control and four external control indicators were included. **Results:** At 30 months post-implementation, there was a statistically significant change in rates of 4 of the 6 KPIs. We report a decrease of 1.5% (95% CI: -2.4, -0.6, p<0.001), in the rate of episiotomy, a decrease of 10.4% (95% CI: -11.5, -9.3, p<0.001) in the rate of repeat cesarean section in low risk women performed before 39 weeks, a decrease of 11.7% (95% CI: -16.0, -7.4, p<0.001) in the rate of induction for post-dates in women who were less than 41 weeks at delivery and an increase of 2.8% (95% CI: 2.2, 3.5, p<0.001) in the rate of group B streptococcus screening. MND implementation did not affect the rate of unsatisfactory blood samples sent to Newborn Screening Ontario, nor did it affect the rate of formula supplementation at discharge. No effect of MND implementation was observed on any of the control indicators. **Conclusion:** These results demonstrate that an A&F program implemented in maternal-newborn hospitals led to improvements at the provincial level in the majority of targeted behaviors.

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ADVANCED NEONATAL MEDICINE IN CHINA: A NATIONAL BASELINE DATABASE

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Introduction: Previous surveys of neonatal medicine in China have not collected comprehensive information on workforce, investment, health care practice, and disease expenditure, yet it is necessary to know the situation. **Objective:** The goal of the present study was to develop a national database of neonatal care units and compare present outcomes data in conjunction with health care practices and costs. **Methods:** We summarized the above components by extracting data from the databases of the national key clinical subspecialty proposals issued by national health authority in China, as well as publicly accessible databases. **Results:** Sixty-one newborn clinical units from provincial or ministerial hospitals at the highest level within local areas in mainland China, were included for the study. Data were gathered for three consecutive years (2008-2010) in 28 of 31 provincial districts in mainland China. Of the 61 newborn units in 2010, there were 4,948 beds (median=62 [IQR 43-110]), 1,369 physicians (median=22 [IQR 15-29]), 3,443 nurses (median=52 [IQR 33-81]), and 170,159 inpatient discharges (median=2,612 [IQR 1,436-3,804]). During 2008-2010, the median yearly investment for a single newborn unit was US344,700 (IQR 166,100-585,800), median length of hospital stay for overall inpatient newborns 9.5 (IQR 8.2-10.8) days, median inpatient antimicrobial drug use rate 68.7% (IQR 49.8-87.0), and median nosocomial infection rate 3.2% (IQR1.7-5.4). For the common newborn diseases of pneumonia, sepsis, respiratory distress syndrome, and very low birth weight (<1,500 grams) infants, their lengths of hospital stay, daily costs, hospital costs, ratios of hospital cost to per-capita disposable income, and ratios of hospital cost to per-capita health expenditure, were all significantly different across regions (North China, Northeast China, East China, South Central China, Southwest China, and Northwest China). The survival rate of extremely low birth weight (ELBW) infants (Birth weight <1,000 grams) was 76.0% during 2008-2010 in the five hospitals where each unit had more than 20 admissions of ELBW infants in 2010; and the median hospital cost for a single hospital stay in ELBW infants was US8,613 (IQR 8,153-9,216), which was 3.0 times (IQR 2.0-3.2) the average per-capita disposable income, or 63 times (IQR 40.3-72.1) the average per-capita health expenditure of local urban residents in 2011. **Conclusion:** Our national database provides baseline data on the status of advanced neonatal medicine in China, gathering valuable information for quality improvement, decision making, longitudinal studies and horizontal comparisons.

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TRENDS IN NEONATAL MORTALITY AND MORBIDITY FOLLOWING SPONTANEOUS AND IATROGENIC PRETERM DELIVERY

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Introduction: After a decade of increase, preterm birth rate in the US declined from 10.4% in 2007 to 9.6% in 2015. The largest decline occurred at late preterm gestation (34-36 weeks). We conducted a study to examine concomitant changes in adverse neonatal health outcomes. **Objective:** To examine temporal trends in neonatal mortality and severe morbidity among infants born preterm following premature rupture of membranes (PROM), spontaneous birth and iatrogenic delivery. **Methods:** We used information from birth certificates and linked hospitalization data on all singleton live births in Washington State, USA from 2004-2013 (n = 737,711). Types of preterm delivery included PROM (>12 hours), iatrogenic delivery (labour induction and caesarean delivery without labour), and spontaneous birth (all other delivery). Severe adverse outcome included neonatal death or severe neonatal morbidity consisting of any of the following: bronchopulmonary dysplasia, intraventricular haemorrhage grade ≥3, or periventricular leukomalacia. Cochran-Armitage test for trends was used to assess statistical significance of temporal trends, and rates were contrasted between years 2004-06 vs. 2011-13. **Results:** The overall preterm birth rate declined from 7.3% in 2004-06 to 7.0% of live singleton births in 2011-13. Preterm birth following PROM declined from 1.3% to 1.1%, and spontaneous preterm birth declined from 3.2% to 3.0% while iatrogenic preterm birth increased from 2.7% to 2.9%; all trends were statistically significant ($p<0.01$). The overall neonatal mortality/severe morbidity rate remained unchanged among preterm infants (3.5%). The rate of neonatal mortality/severe morbidity declined significantly only in infants delivered following PROM from 5.4% in 2004-06 to 4.0% in 2011-13 ($p<0.01$). Neonatal mortality/severe morbidity was unchanged in iatrogenic (4.4%) and spontaneous (2.2%) preterm delivery. Late preterm birth rates declined significantly from 5.8% in 2004-06 to 5.3% in 2011-13 ($p<0.01$); the decline occurred in all delivery categories (all p-values <0.05). However, the neonatal mortality/severe morbidity increased in late preterm infants from 0.4% to 0.6% ($p=0.04$) mainly due to an increase among infants with spontaneous late preterm delivery (from 0.1% to 0.4%; $p<0.01$). **Conclusion:** The rate of preterm birth following PROM and spontaneous birth declined in Washington State between 2004 and 2013 while iatrogenic preterm birth rate increased. Neonatal mortality/severe morbidity rate declined among preterm infants born following PROM. Late preterm birth rate declined in all types of delivery. However, neonatal mortality/severe morbidity increased among infants born spontaneously at late preterm

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THE EFFECT OF MATERNAL AGE ON SEVERE MATERNAL MORBIDITY AND PERINATAL OUTCOMES

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Introduction: Although average maternal age continues to rise in industrialized countries, potentially life-threatening maternal morbidity associated with maternal age has been understudied. **Objective:** To examine the association between maternal age and severe maternal morbidity. The secondary objective was to examine the association with adverse fetal/infant outcomes. **Methods:** We carried out a population-based retrospective cohort study, including all singleton births to women residing in Washington State, USA, 2003-2013 (N=828,269). We compared age-specific rates of maternal mortality/severe morbidity (e.g., obstetric shock, acute renal failure, etc.) and adverse fetal/infant outcomes (e.g., perinatal death); logistic regression was used to adjust for parity, body mass index, assisted conception, and other potential confounders. We compared crude odds ratios (OR) and adjusted odds ratios (AOR) and risk differences (RD) and their 95% confidence intervals (CI). **Results:** Severe maternal morbidity was significantly higher among teenage mothers versus those 25-29 years (crude OR=1.5, CI: 1.5-1.6) and increased exponentially with maternal age over 39 years, from OR=1.2 (CI: 1.2-1.3) among women aged 35-39 years to OR=5.4 (CI: 2.4-12.5) among women aged ≥50 years. The elevated risk of severe morbidity among teen mothers disappeared after adjustment for confounders, except for sepsis (AOR=1.3, 95% CI: 1.2-1.5). Adjusted rates of severe morbidity remained increased among mothers ≥35 years; namely the rates of amniotic fluid embolism (AOR=7.2, CI: 2.4-21.6) and shock (AOR=3.5, CI: 1.6-7.7) among mothers

≥40 years; and renal failure (AOR=12.4, CI: 4.2-36.7), complications of obstetric surgery (3.9, CI: 1.9-7.9), and ICU admission (5.9, CI: 2.7-12.7) among those ≥45 years. The adjusted risk difference in severe maternal morbidity between mothers 25-29 and 40-44 was approximately 1% (adjusted RD=0.94, 95% CI: 0.7-1.2), 1.5% (95% CI: 0.7-2.7) for mothers 45-49 years, and 2% for those over 50 (95% CI: -0.3-10.5). Similar associations were observed for fetal and infant outcomes; neonatal mortality was elevated in teen mothers (AOR=1.4, 95% CI: 1.2-1.7), while mothers over 29 years had higher risk of stillbirth. **Conclusion:** Maternal age-specific incidence of severe morbidity varied by outcome. Older women (≥40 years) had significantly elevated rates of some of the most severe outcomes, including renal failure, shock, acute cardiac morbidity, serious complications of obstetric interventions, and ICU admission.

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SHOULDER DYSTOCIA: RATES AND OUTCOMES OVER TIME IN NOVA SCOTIA

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Introduction: Shoulder dystocia occurs when, after delivery of the fetal head, delivery arrests and additional obstetric manoeuvers are needed to complete delivery. The rate of shoulder dystocia as recorded in the Nova Scotia Atlee Perinatal Database (NSAPD) has increased over the past three decades, and is presently higher than other published rates. **Objective:** To determine if variation in the prevalence of risk factors accounts for the increase in shoulder dystocia rates, and to estimate the rates of complications associated with shoulder dystocia by time period. **Methods:** A population-based retrospective cohort study was conducted using the NSAPD including all singleton vaginal cephalic deliveries to residents of Nova Scotia between 1988 and 2015. Shoulder dystocia was defined by maternal and neonatal codes specific to the condition. Year of delivery was represented in five epochs within which rates were approximately stable. A set of risk factors was identified using backward stepwise regression. Shoulder dystocia rates in each epoch were standardized to the distribution of these risk factors observed in the overall time period using a regression-based method. Rates of shoulder dystocia with a complication (brachial plexus palsy, or fracture of the clavicle or humerus) were similarly examined. **Results:** Included were 205,094 singleton vaginal cephalic deliveries. Rates of shoulder dystocia as recorded in the NSAPD were 1.4% in 1988-1992, 2.4% in 1993-1998, 3.4% in 1999-2005, 4.6% in 2006-2010, and 5.2% in 2011-2015. Standardization of these rates (to account for shifts in the distribution of pre-pregnancy weight, gestational weight gain, diabetes, fetal sex and birthweight, use of regional anesthesia and other risk factors) did not reduce the magnitude of increase over time. The rate of complications (brachial plexus palsy, or fracture of the clavicle or humerus) co-occurring with shoulder dystocia increased significantly ($p<0.001$) over time (per 1000 singleton vaginal cephalic deliveries: 0.13, 0.14, 0.27, 0.38, and 0.29 in 1988-1992, 1993-1998, 1999-2005, 2006-2010, and 2011-2015, respectively). The total rate of these complications that occurred both with and without recorded shoulder dystocia, however, has not increased to the same extent ($p=0.052$) **Conclusion:** The increased rate of shoulder dystocia as recorded in the NSAPD cannot be explained by changes in the distribution of risk factors. Increases in the rate of complications co-occurring with shoulder dystocia could reflect a real increase in severe shoulder dystocia, or could be due to increased documentation when complications occurred.

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SEVERE ILLICIT DRUG USE AND DEPENDENCE AND CONGENITAL HEART DEFECTS IN OFFSPRING

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Introduction: Congenital heart defects (CHD) are one of the birth defects that are most associated with maternal factors. Despite recent substantial decline in congenital heart defects overall, mild subtypes changed little, and instead, atrial septal defect (ASD) substantially increased in Canada. **Objective:** This study aimed to determine the prevalence of major subtypes of CHD in offspring of women with severe illicit drug use and dependence. **Methods:** Using Discharge Abstract Data from the Canadian Institute for Health Information, we carried out a population-based study of mother-newborn dyads (N=3 209 474) including singleton livebirths and stillbirths who delivered at hospital (at ≥20 weeks of

gestation) in Canada (except Quebec) from 2003 to 2014. Presence of any CHD was detected and diagnosed prenatally and/or at birth. Critical CHDs including tetralogy of Fallot, endocardial cushion defects, univentricular hearts truncus arteriosus, or transposition complexes or atrial septal defects (ASD) or ventricular septal defects (VSD) were also categorized for analysis. Mother's use of and dependence on illicit drug including cannabinoids, cocaine, opioids or other illicit drugs was identified using ICD-10 codes (i.e., mental and behavioural disorders due to use of specified illicit drug) as fetal exposure. Maternal age, comorbidities such as pre-gestational diabetes type 1, type 2 or hypertension, early onset preeclampsia (<34 weeks), morbid obesity, alcohol or tobacco addiction, geographic area and 2-year period of infant's birth are all included as covariates. Associations of CHD overall and the above three categories with maternal illicit drug use were separately examined using multivariable Poisson regression analysis adjusting for the individual covariates. **Results:** The absolute prevalence of congenital heart defects was higher for infants of women with illicit drug use than those without it (17.8 vs 7.0 per 1000 total births). Relative to non-exposure, infants exposed to drug use had higher prevalence of any heart defect (adjusted prevalence ratio (aPR), 1.49; 95% confidence interval (CI) 1.39–1.59, but differed substantially by selected subtype. In particular, prevalence of ASD was significantly associated with women with use of opioids (aPR, 2.44; 95% CI 1.72-3.45), cocaine (aPR, 1.66; 95% CI 1.14–2.42) and miscellaneous drugs (aPR, 1.33, 95% CI 1.16-1.52) though non-significantly of cannabinoid (aPR, 1.27; 95% CI 0.87-1.85). Prevalence of VSD was significantly associated with women with use of opioids (aPR, 2.23, 95% CI 1.64–3.29), and of cocaine (aPR, 95% CI 1.58, 1.08-2.30), while use of cannabinoid was associated with critical CHDs.

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ASSOCIATION OF RESIDENT CALL-HOUR REFORM WITH MORTALITY OR MAJOR MORBIDITY AMONG PRETERM INFANTS

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Introduction: In July 2011, the collective agreement of all medical residents working in the province of Quebec was amended to reduce the maximum number of consecutive hours worked from 24 to 16 hours. Concerns were raised that higher number of handoffs required due to change in work schedule may affect outcomes adversely, whereas reduced resident fatigue may lead to improved outcomes. However, no study has evaluated the safety or benefits of these changes on the outcomes of preterm infants. **Objective:** To evaluate the association of the 2011 Quebec resident call-hour reform with mortality or major morbidity of infants born 32 weeks gestation in Quebec **Methods:** A 7-year retrospective observational study of all infants born between 23 and 32 weeks admitted at 5 Quebec neonatal intensive care units participating in the Canadian Neonatal Network. The primary outcome was a composite adverse outcome defined as mortality or major morbidity (bronchopulmonary dysplasia, severe neurological injury, necrotizing enterocolitis or retinopathy of prematurity). Multivariable analyses were used to adjust for patient characteristics and timing of admission and to calculate adjusted odds ratios (AOR) comparing the outcomes before (2008-2011) and after the call-hour reform (2011-2015). **Results:** The study population included 4721 infants born 23-32 weeks (2598 in pre and 2123 in post era), comprising 85% of all infants born 32 weeks gestation in the province during this period. The mortality rate was 8.4% (218/2598) before the resident call-hour reform and 8.6% (182/2123) after the reform (Risk difference = 0.2%, 95% CI = -1.4 to 1.8, P=0.82). The incidence of the composite outcome was 32.0% (830/2598) before the call-hour reform and 29.0% (615/2123) after the reform (Risk difference = -3.0%, 95% CI = -5.6 to -0.3, P=0.03). In the adjusted analyses, the resident call-hour reform was not associated with a significant change in mortality (AOR = 1.17, 95% CI = 0.91-1.50) or in the composite outcome (AOR = 0.87, 95% CI = 0.74 -1.03). **Conclusion:** Among infants born 32 weeks, there was no significant difference in the rate of mortality or major morbidity after the 2011 Quebec medical resident call-hour reform compared to before. This suggests that the reduction in fatigue was not associated with improvements of neonatal outcomes and at the same time the increased number of patient handoffs were not associated with worsening outcomes

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CESAREAN SECTION WITHOUT MEDICAL INDICATION AND CHILDHOOD ASTHMA IN SHANGHAI, CHINA:

EPIDEMIOLOGIC STUDIES AND MECHANISTIC RESEARCH

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Introduction: CS has been associated with childhood asthma. But it remains unclear whether this association was due to the underlying CS indications or CS itself. **Objective:** To examine whether CS without medical indication increases the risk of asthma, and what are the possible biological mechanisms. **Methods:** We conducted three epidemiologic studies: a population-based cross-sectional survey with cluster random sampling in primary school students in Shanghai (N=17,571) and a hospital-based case-control study (697 asthma cases and 1099 non-asthma controls aged 6 to 11 years) to examine the association between CS and asthma. We also conducted a prospective cohort study (N=1,182) to examine how CS impacted fetal hormone, methylation in fetal white blood cells at birth and microbione at 1 year of age. **Results:** The Survey and case-control study both showed that CS without medical indications was associated with significantly increased risks of asthma (aOR=1.63, 95%CI: 1.17 - 2.27 and aOR=1.52, 1.14 - 2.03 in the Survey and case-control study, respectively). Cortisol and estradiol levels in the cord blood were significantly higher in vaginal births than CS (cortisol 69.3 vs. 32.0 μg/dl; estradiol 10387 vs. 7854 pg/ml, respectively, both p<0.01). CS was associated with a lower level of DNA methylation, particularly at HLA loci and asthma-related genes. No significant difference was observed in microbione (16S rDNA sequence) between CS and vaginal births at 1 year of age **Conclusion:** CS itself increases the risk of childhood asthma. Changes in the levels of relevant hormones and DNA methylation may be the underlying mechanisms. CS without medical indication should be performed with caution.

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UNIVARIATE PREDICTORS OF MATERNAL CONCENTRATIONS OF ENVIRONMENTAL CHEMICALS: THE MIREC STUDY

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Introduction: The developing fetus and pregnant woman can be exposed to a variety of environmental chemicals that may adversely affect their health. Moreover, environmental exposure and risk disparities are associated with different social determinants, including socioeconomic status (SES) and demographic indicators. **Objective:** Our aim was to investigate whether and how maternal concentrations of a large panel of persistent and non-persistent environmental chemicals vary according to sociodemographic and lifestyle characteristics in a large pregnancy population. **Methods:** Data were analyzed from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, a cohort of pregnant women (N = 2,001) recruited over four years (2008 – 2011) in 10 cities across Canada. In all, 1,890 urine and 1,938 blood samples from the first trimester (1st and 3rd trimester for metals) were analysed and six sociodemographic and lifestyle indicators were assessed: maternal age, household income, parity, smoking status, country of birth and pre-pregnancy body mass index (BMI). **Results:** We found these indicators to be significantly associated with many of the chemicals measured in maternal blood and urine. Women born outside Canada had significantly higher concentrations of di-2-ethylhexyl and diethyl phthalate metabolites, higher levels of all metals except cadmium (Cd), as well as higher levels of polychlorinated biphenyls (PCBs) and legacy organochlorine pesticides (OCPs). Nulliparity was associated with higher concentrations of dialkyl phosphates (DAPs), arsenic, dimethylarsinic acid (DMAA), perfluoroalkyl substances (PFASs) and many of the persistent organic pollutants. Smokers had higher levels of bisphenol A, Cd and perfluorohexane sulfonate, while those women who had never smoked had higher levels of triclosan, DMAA, manganese and some OCPs. **Conclusion:** Our results demonstrated that inequitable distribution of exposure to chemicals among populations within a country can occur. Sociodemographic and lifestyle factors are an important component of a thorough risk assessment as they can impact the degree of exposure and may modify the individual's susceptibility to potential health effects due to differences in lifestyle, cultural diets, and aging

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DOES THE AMOUNT OF WEIGHT GAINED DURING PREGNANCY MODIFY THE ODDS OF CAESAREAN DELIVERY IN OBESE WOMEN?

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Introduction: Obesity during pregnancy is associated with a variety of adverse pregnancy outcomes, including caesarean delivery. The Institute of Medicine (IOM) has developed guidelines for optimal gestational weight gain (GWG) by pre-pregnancy BMI, with the aim of improving pregnancy outcomes. However, the IOM guidelines only provide one recommendation (11-20 lbs) for all obese women, although there are 3 classes of obesity: I (BMI 30-34.9 kg/m2), II (BMI 35-39.9 kg/m2), and III (BMI ≥ 40 kg/m2). Studies suggest that this recommendation should not apply to all obese women and that weight gain less than the amount recommended in these guidelines (and weight loss) resulted in lower rates of caesarean delivery for obese women. However, previous studies have been small and lacked information on women among the highest class of obesity. **Objective:** To determine the odds of caesarean sections for class I, II and III obese pregnant women who either: lose weight during pregnancy, gain less weight than recommended, or gain more weight than recommended, compared to women who gain the recommended amount of weight. **Methods:** Using publicly available 2014 USA birth certificate data on obese women (N= 767,337), descriptive statistics were used to characterize the population, stratified by obesity class. Chi square tests examined the bivariate association between categories of GWG and caesarean sections for women with class I, II and III obesity. Logistic regression models were built to examine the odds of caesarean sections by GWG categories adjusted for maternal age, education, marital status, parity, medical insurance, and race. **Results:** The rate of caesarean delivery for obese class I, II, and III were 36.5% (36.3–36.6), 42.5% (42.3–42.8), and 51.2% (50.9–51.5). Bivariate analyses showed GWG by obese class were associated with caesarean sections in the current pregnancy (p<0.001). Obese women who lost weight during pregnancy (OR (95%CI) I: 0.82 (0.79-0.86); II: 0.78 (0.75-0.82); III: 0.78 (0.75-0.82)) or gained less weight (OR (95%CI) I: 0.89 (0.86-0.92); II: 0.88 (0.84-0.91); III: 0.88 (0.84-0.91)) than IOM recommendations had decreased odds of caesarean delivery compared to women who gained the recommended weight. While weight gain greater than the recommended amount was associated with increased odds of caesarean delivery (OR (95%CI) I: 1.30 (1.27-1.32); II: 1.30 (1.27-1.34); III: 1.20 (1.16-1.24)). **Conclusion:** The patterns of association between gestational weight gain and caesarean delivery was similar for all 3 obesity classes, indicating that a standard recommendation could be used for all obese women; however, the lower odds of caesarean delivery associated with lower weight gain may indicate that the current recommendation is too high.

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THE ASSOCIATION OF MATERNAL PLASMA HOMOCYSTEINE WITH PREECLAMPSIA AND OTHER PLACENTA-MEDIATED COMPLICATIONS: RESULTS FROM THE OTTAWA AND KINGSTON (OAK) BIRTH COHORT

Introduction: Preeclampsia, placental abruption, fetal growth restriction, and fetal loss are placenta-mediated complications (PMCs) that can have serious consequences for maternal and infant well-being. Subsequent to findings in cardiovascular disease research, elevated maternal homocysteine levels are postulated to play a role in alterations of the utero-placental vasculature. Prospective cohort studies have reported conflicting results. Furthermore, larger studies have analyzed homocysteine as a binary or categorical variable, where elevated levels are determined according to various percentile cut-offs for gestational week of blood work. Categorization can result in the loss of important information. **Objective:** To investigate the association between maternal plasma homocysteine concentration and PMCs in a large prospective cohort study using rigorous statistical methodology that explores potential non-linear effects of the homocysteine exposure. **Methods:** Multivariable logistic regression analyses of 7201 OAK participants examined the association of homocysteine and pre-specified predictors of interest with preeclampsia, small for gestational age (SGA), and any PMC (preeclampsia, SGA, placental abruption, pregnancy loss). Model building followed recommended procedures for predictive models. First, a saturated main effects model was fitted where continuous variables were modeled with a restricted cubic spline function. Next, an ANOVA plot of partial associations was generated. For weaker partial associations, continuous variables were reduced to fewer knots or a linear term and categorical variable categories were collapsed. Final model complexity was guided by Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC). Modifying effects of high risk pregnancy and the MTHFR C677T genotype (measured in 3771

participants) were examined. Missing data were handled with multiple imputation. Analyses were performed in RStudio version 0.99.892, R version 3.2.3. **Results:** Higher plasma homocysteine concentration was significantly associated with an increased risk of any PMC (p=0.0016) and SGA (p=0.0015), but not preeclampsia (p=0.2267). ANOVA plots and AIC/BIC led to the decision to model homocysteine as a linear term. A 1-unit change in homocysteine concentration significantly increased the risk of any PMC and SGA (PMC OR 1.096, 95% CI 1.035-1.160 and SGA 1.112, 1.042-1.188). The association did not differ significantly due to high risk pregnancy or MTHFR C677T genotype. Folic acid supplementation and serum folate concentration were not associated with the outcomes. **Conclusion:** Our results suggest that higher maternal plasma homocysteine concentration is linearly associated with an increased risk of any placenta-mediated complication and SGA

THEME: Perinatal Nutrition & the Gut

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VALIDATION OF A WEB-BASED 24-HOUR RECALL AND ASSOCIATIONS WITH NUTRITIONAL RECOMMENDATIONS IN THE FIRST TRIMESTER OF PREGNANCY - PRELIMINARY OF THE «ANGE» PROJECT

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Introduction: Nutritional status during pregnancy is an important factor affecting both the mother's health and the child's development. During this crucial period, accurate assessment of nutrient intakes to detect possible nutrient deficiencies or excesses is essential. The optimal method to assess dietary intakes in pregnant women has not yet been determined. **Objective:** 1) To validate the use of a Web based 24-hour dietary recall (R24W) during pregnancy and 2) to compare dietary intakes to current nutritional recommendations. **Methods:** Sixty pregnant women will be recruited and will complete, between their 9th and 13th week of pregnancy, three R24W and one 3-day food record. Participants' weight and height will be measured in the first trimester and pre-pregnancy weight will be self-reported. Various Web questionnaires on attitudes and behaviors towards food and physical activity and on socioeconomic status will also be completed by the participants. **Results:** To date, 45 pregnant women aged 32.1 ± 3.9 years old with an average pre-pregnancy BMI of 24.8 ± 4.9 kg/m2 were recruited. Significant correlations were observed between the two dietary assessment tools for energy (r=0.58), protein (r=0.52), fat (r=0.38), carbohydrates (r=0.52), vitamin D (r=0.39), calcium (r=0.53), iron (r=0.35) and folate (r=0.36) intakes. Average vitamin D intakes from food (223.3 ± 127.6 IU) was below the Estimated Average Requirement (EAR) of 400 IU, but reached 649.9 ± 698.1 IU when dietary supplements were considered. Including foods and supplements, 40% of women had vitamin D intakes within or above the Recommended Dietary Allowance (RDA) of 600 IU, while 87% and 82% of women met the RDA for folic acid (600mg) and iron (27mg), respectively. Average energy intakes were higher than the estimated needs for 76% of the women while the average protein intakes reached 1.61 ± 0.30g/kg of body weight, thus exceeding the recommendation of 1.1g/kg of body weight for 98% of the women. **Conclusion:** Preliminary analysis in the first trimester demonstrated the potential validity of the R24W in a population of pregnant women. So far, 98% of the women exceeded protein needs, while 60% of them did not reach the vitamin D RDA, even when prenatal supplements were considered.

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EVALUATION OF DIETARY INTERVENTION AND PREGNANCY OUTCOMES AMONG FOOD INSECURE WOMEN ATTENDING THE MONTREAL DIET DISPENSARY PROGRAM

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Introduction: The Montreal Diet Dispensary has been aiming to reduce health inequalities among pregnant women with low-income economic status through a nutrition support program named the Higgins' intervention. The program, which is composed of biweekly nutritional consultation during late gestation, food supplementation (milk, eggs and mineral/vitamin supplements) and social support, was shown to be successful in reducing the rate of low-birth weight (LBW) as well as preterm births (PTB). **Objective:** To compare the proportion of pregnancy complications in the clientele of the Montreal Diet Dispensary against local and national statistics; and to describe these complication rates in the Dispensary's changing demographic population predominantly composed of visible minority and newly immigrated women. **Methods:** Pregnancy complications were evaluated using an electronic database from June 2013 to December 2015 (n=1387 pregnancies). Demographic information, including country of birth, time of arrival in Canada, marital status and maternal education, were self-reported at patient's registration at 20.4 ± 7.0 weeks gestation. Pregravida weight was self-reported, weight was then measured at biweekly visits until birth. Anemia, gestational diabetes (GDM) and gestational hypertension (HTN) were ascertained using copies of medical reports. Infant birth weight was collected from the vaccination booklet and Kramer's growth curve reference (Pediatrics, 2001) was used to assess size at birth. Women who were eligible to participate in the program had lower family income than the determined budget for basic

needs established by the Dispensary. **Results:** Descriptive statistics revealed that more than half of the participants were White (58.0%) and 33.5% were Black. Most of the women were born abroad (90.2%) and were living in Canada for less than 5 years (65.8%). The rate of LBW was 4.18% (95% confidence interval (CI): 3.13, 5.24), small-for-gestational age (SGA) 5.47% (95% CI: 4.28, 6.68) and PTB 4.76% (95%CI: 3.64, 5.88); these were significantly lower than Canadian statistics (Table 1). Large-for-gestational age (LGA) rate was 10.60% (95%CI: 8.98, 12.22) which was significantly higher than in Montreal, but similar to the Canadian rate. Prevalence of maternal outcomes were 17.15% (95%CI: 15.05, 19.25) for GDM and anemia was 44.88% (95%CI: 41.90, 47.86) which both were significantly higher than the Canadian rates. HTN rate was 3.82% (95%CI: 2.81, 4.83) which was similar than Canadian rates. **Conclusion:** This study suggests that the Higgins' intervention contributed to supporting infant health as evidenced by lower infant complications than national statistics. Earlier nutritional intervention, prioritization of high risk groups of women and adaptation of the intervention to better prevent adverse maternal pregnancy outcomes would be needed for this vulnerable population.

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PROPHYLACTIC PROBIOTICS FOR PRETERM INFANTS: A NATIONAL RETROSPECTIVE COHORT STUDY

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Introduction: The use of probiotics to prevent necrotizing enterocolitis (NEC) has not yet been widely embraced across the neonatal intensive care units (NICUs) in North America. Recently, an increasing number of Canadian NICUs (17 CNN centers) have started routine probiotic prophylaxis in preterm infants using one of two products: Florababy (Bifidobacteria and Lactobacillus Rhamnosus GG) or BioGaia (Lactobacillus reuteri Protectis). **Objective:** To compare the incidence of NEC in preterm infants who received probiotic prophylaxis to those who did not receive probiotics. The secondary objectives included comparing the incidence of surgical NEC, mortality, late onset sepsis (LOS), and parenteral nutrition days. **Methods:** We conducted a retrospective review of all preterm infants 20 or not receiving breast milk. The incidence of NEC, mortality and a composite outcome of NEC or death were significantly lower in the probiotic group after adjusting for confounders. There were no significant differences in the incidence of surgical NEC, LOS, or parenteral nutrition days (Table 2). **Conclusion:** Routine prophylactic probiotic administration was associated with reduction in NEC and mortality in extremely premature infants. There is a need for trials comparing efficacy of different probiotic strains.

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DURATION OF GESTATION IN MICE: TOWARD A NEW ROLE FOR THE INTESTINAL MICROBIOTA.

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Introduction: It is now established that the microbiota ("the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space" Lederberg and McCray 2001) has an impact on human health. While multiple roles for the microbiota have been described (maintenance of the intestinal barrier, nutrient host metabolism, protection against pathogens...), few studies focused on its function during gestation. Physiological changes during pregnancy (immunological, endocrine and metabolic adaptations) are associated with temporal variations of the vaginal and intestinal microbiota in healthy woman. To better understand the role of the microbiota during the normal pregnancy, further investigations need to be performed. **Objective:** Objectives: The aim of our project is to determine a role for the intestinal microbiota on gestation and labor initiation, using a mouse model of fecal transplant (FT). Here we tested the hypothesis that the intestinal microbiota could be involved in labor onset. **Methods:** Method: At gestational day (GD) 17 and 18, CD1 pregnant mice received by gavage fecal sluries collected from donor mice at GD-17 (group 1; n=19); or from donor mice at GD19,5 (group 2; n=17); or they received saline (control group; n=15). GD-19,5 represents a phase of labor initiation and GD-17 corresponds to a uterine quiescent phase. After the first gavage, mice were monitored until delivery. Feces were collected before and after each FTs for the determination of the intestinal microbiota with high-throughput sequencing of 16S ribosomal RNA. **Results:** We found that FT is well tolerated and no adverse effects were observed. Mice from group 2 (GD-19,5) delivered earlier compared to control mice (mean delivery

time: 19,6 days). Fifty hours following the first FT, the risk of delivery was 3.5 higher compared to group 1 (not significant p value=0.5). On the contrary, mice from group 1 (GD17) appeared to deliver later than both group 2 and control mice. Determination of the gut microbiota composition by sequencing of the 16S rRNA gene is underway and will shed light on microbial changes that could possibly explain our observations. **Conclusion:** Conclusions : We reported that FT can modify the duration of gestation in mice. More interestingly, we showed the possibility of extending the gestational period by maintaining uterine quiescence with appropriate FT. These results suggest that the gut microbiota could be associated with labor initiation and/or delivery. In order to reach statistical significance, we plan to repeat the experiment with younger mice and to perform 4 FTs. To our knowledge, this is the first report of a pregnant mouse model developed to study the effects of intestinal microbiota and FT on the duration of gestation.

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THE IMPACT OF A HISTORY OF ADVERSE CHILDHOOD EXPERIENCES ON BREASTFEEDING INITIATION AND EXCLUSIVE BREASTFEEDING: FINDINGS FROM A NATIONAL POPULATION HEALTH SURVEY

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Introduction: Exclusive breastfeeding is strongly recommended by the World Health Organization (WHO). Given the low rate of exclusive breastfeeding in Canada and the increasing reports of a history of adverse childhood experiences, this study sought to investigate the association between a history of adverse childhood experiences and breastfeeding initiation and breastfeeding. **Objective:** To explore any associations between a history of adverse childhood experiences and breastfeeding initiation and breastfeeding. **Methods:** Data used for this study were based on the 2011-2012 Canadian Community Health Survey (CCHS), collected using a cross-sectional survey. The outcome measures were breastfeeding initiation and exclusive breastfeeding for 6 months or more. History of adverse childhood experiences was the main explanatory variable. Multivariable logistic regression models were developed to investigate the effect of on breastfeeding initiation and on exclusive breastfeeding in women who gave birth within 5 years prior to when the surveys were conducted. **Results:** The study sample included 697 and 633 women for analyses on breastfeeding initiation and breastfeeding respectively. The proportion of women with breastfeeding initiation and exclusive breastfeeding for up to 6 months in this study were 96.8% and 42.8% respectively. After controlling for age and highest level of education, having a history of adverse childhood experiences was not significantly associated with breastfeeding initiation (OR 0.46, 95% CI 0.10-1.87) but mothers with such history were less likely to exclusively breastfeed for up to 6 months compared with those without (OR 0.53, 95% CI 0.31, 0.90). **Conclusion:** These findings suggest the need for more breastfeeding monitoring programs beyond the hospital environment to provide more support to Canadian mothers, especially those who have experienced adverse childhood experiences or trauma in the past.

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THE EFFECTS OF DIETARY PATTERNS ON GLYCAEMIC OUTCOMES DURING PREGNANCY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: Evidence to support dietary modifications to improve glycaemia during pregnancy is limited, and it is unclear whether dietary advice provides benefit beyond limiting gestational weight gain (GWG) advice. **Objective:** We conducted a systematic review and network meta-analysis of randomized controlled trials to compare the effects of various common diets on fasting blood glucose and blood insulin, HbA1c, and HOMA-IR in pregnant women with diabetes or at increased risk of gestational diabetes mellitus. **Methods:** We searched MEDLINE, EMBASE, Cochrane database, and reference lists of published studies from inception through February 2016. Randomized controlled trials directly comparing two or more diets for ≥two-weeks were eligible. Two reviewers extracted data independently. A

Bayesian network meta-analysis was performed for fasting blood glucose. Owing to a lack of similar dietary comparisons, we conducted a standard pairwise meta-analysis for the other glycaemic outcomes. The certainty of the pooled effect estimates was assessed using the GRADE tool. **Results:** Twenty trials (n= 2,349 participants) were included. When given alongside advice to manage GWG, several diets improved fasting blood glucose compared with a high-fibre diet. This effect on fasting blood glucose was not observed in our analyses limited to dietary patterns with no GWG advice or to GWG advice only. However, we did observe that in the absence of GWG advice, the DASH-style diet compared to standard of care improved fasting blood insulin and HOMA-IR, and a dietary approach to limit GWG improved fasting blood insulin. The GRADE quality of evidence ranged from moderate to very low. **Conclusion:** Our findings suggest that dietary patterns in conjunction with advice to limit GWG improved fasting blood glucose. We did not see significant improvements on FBG in trials where only dietary patterns with no GWG advice or only GWG advice was given. This suggest that the most effective approach to manage FBG during pregnancy is via a combination of dietary and GWG advice. However, the systematic review identified a small number of trials and most dietary comparisons were underpowered to detect differences in glycaemic outcomes. There is a need for more large high-quality trials.

P193

EXAMINING INTERACTIONS OF THE OBESE MATERNAL MICROBIOME AND PLACENTAL FUNCTION – A ROLE FOR MICROBIAL METABOLITES AND PLACENTAL MACROPHAGE POLARIZATION.

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Introduction: Globally, 1 in 2 women enter pregnancy overweight or gain excess weight during gestation. This greatly increases their child's risk of developing metabolic disease later in life, including obesity and type 2 diabetes. Experimental studies have shown that consumption of a high-fat diet prior to and throughout pregnancy can induce changes in placental growth and function, with concomitant changes in the maternal gut microbiota. The placenta contains immune cells capable of responding to alterations in the abundance of bacterial products, including short-chain fatty acids (SCFAs), suggesting an interplay between maternal gut microbiome metabolites and placental development, metabolism, and immunity. **Objective:** To ascertain the effects of a high-fat diet (HFD) on maternal microbial metabolite production, placental development, and inflammation **Methods:** Three-week-old female C57BL/6J mice were fed a control purified standard diet (CD; 17% kcal/g fat) or a HFD (60% kcal/g fat) for 6 weeks prior to mating and throughout pregnancy. Pregnant mice were sacrificed at term (GD18.5) and maternal cecal contents and placentae were collected. Placental mRNA levels of signaling pathways involved in inflammation, apoptosis and immune function were analysed using Nanostring technology (n=4/sex/group). Maternal cecal contents were analyzed for SCFA levels using gas chromatography mass spectroscopy (n=10/group). **Results:** HF females displayed a modest reduction in maternal cecal butyrate levels ($p = 0.06$), while levels of acetate and propionate were unchanged compared to control. In placentae of HF females, a significant reduction was identified in STAT3 ($pdiet = 0.009$), Bif-1 ($pdiet = 0.049$), and VEGF ($pdiet = 0.0078$), mRNA levels. Notable decreases were observed in Arginase ($pdiet=0.066$) and Beclin-1 ($pdiet=0.0583$) mRNA levels in placentae of HF females. Conversely, HFD resulted in higher IL-10 mRNA levels ($pdiet=0.0167$). **Conclusion:** Maternal obesity results in modestly decreased levels of butyrate, an immunomodulatory metabolite known to influence macrophage polarization. This decrease is associated with decreased placental expression of arginase, a key mediator of macrophage polarization, suggesting possible placental immune modulation by maternal SCFA production. Macrophages of the placenta influence its growth and vascularization, markers of which (STAT3, VEGF) are also altered by maternal obesity along with apoptotic markers (Bif-1, Beclin-1), suggesting a link between maternal bacterial metabolites and placental macrophage polarization.

THEME: Reproductive Immunology

P201

A POTENTIAL ANTAGONIST PEPTIDE OF NEUROMEDIN U RECEPTOR 2 (NMU-R2) TO PREVENT PRETERM LABOR.

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Introduction: 3 out of 4 preterm births (before 37 weeks of gestation) are due to preterm labor, in which myometrial contractions are induced by uterine activation proteins greatly expressed in the presence of inflammation. Furthermore, premature babies are at a higher risk of neonatal mortality and morbidity and/or long-term complications. To date, tocolytics (agents inhibiting uterine contractions) are not efficient enough to prolong gestation for more than 48hrs and cause numerous maternal and/or fetal side effects. Recently, we discovered that a neuropeptide called neuromedin U (NmU) favors uterine contraction by inducing an intracellular release of calcium via neuromedin U receptor 2 (NmU-R2). This uterotonic system involved in preterm labor has been well studied in our laboratory. **Objective:** We aim to characterize five small antagonist peptides of NmU-R2, developed in our laboratory, in order to choose the best candidate to develop a new tocolytic agent. **Methods:** We performed ex vivo contraction assays of uterine segments in tissue baths, with or without the different peptides and murine NmU (10-7 or 10-8M). We assessed the inhibition of intracellular release of calcium in vitro using isolated murine primary myometrial cells to perform calcium assays with the five NmU-R2-antagonists. Also, we pre-incubated myometrial primary cells with several doses of best performed peptides (chosen from the ex vivo assay) or vehicle for 30 minutes followed by a stimulation with 10-7M of NmU and incubation of 10 minutes at 37°C. Afterwards, we analyzed by Western Blot the phosphorylation of kinases (Erk and Akt). **Results:** 1) peptides 3 and 5 inhibit more strongly uterine contraction ex vivo (40-50% inhibition) and the release of calcium in vitro (50-60% inhibition); 2) these peptides can inhibit the release of calcium in a dose-dependent manner (IC50 of dose-response curves: 0.63nM for peptide 3 and 23nM for peptide 5); 3) phosphorylation of Erk and Akt is dose-dependently inhibited by these peptides. **Conclusion:** Our results show that two out of five peptides hold better antagonist properties against NmU-R2. However, our results are more consistent with peptide 5, suggesting it as the best candidate for a potential tocolytic agent targeting NmU-R2 to prevent preterm labor.

P202

STERILE INFLAMMATION AT THE MATERNAL-FETAL INTERFACE: ROLE OF HMGB1

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Introduction: Sterile inflammation plays an important role in early pregnancy and at the onset of labor. However uncontrolled inflammation between these events represents a major problem strongly associated to poor pregnancy outcomes. Our lab previously showed increased levels of “high-mobility group box 1” (HMGB1) in the maternal circulation, in association with placental inflammation/dysfunction in pathological pregnancies. HMGB1 is a nuclear protein that regulates transcription but, when in the extracellular space, act as a pro-inflammatory inducer. However, its role and mechanisms of action at the maternal-fetal interface is mostly unknown. **Objective:** The objective of this work was to investigate the role of HMGB1 at the maternal-fetal interface including secretion of HMGB1 by placental cells and its pro-inflammatory abilities. **Methods:** Term placental explants and the trophoblast-like cell line (BeWo cells) were used. HMGB1 secretion and sub-cellular localization were analyzed by IHC and western blot respectively, at several time points during trophoblast differentiation. BeWo cells were differentiated using forskolin and HMGB1 localization modulated with leptomycin (nuclear export inhibitor) and NaB (HDAc inhibitor). Alongside, placentas from women with either term uncomplicated pregnancies or preeclampsia (PE) were used to study the distribution of HMGB1. **Results:** HMGB1 was constitutively release by BeWo cells in association with trophoblast differentiation. In human placental explants, overall levels of HMGB1 were elevated with trophoblast differentiation, with decreased levels in the cytoplasmic fraction reflecting nuclear accumulation. Blocking the nuclear export of HMGB1 interfered with trophoblast differentiation but forcing HMGB1 export from the nucleus did not increased differentiation. In placentas from pregnancies with PE, total HMGB1 levels did not changed but, its sub-cellular localization was affected being mainly localized to the cytoplasm of trophoblast as compared to the typical nuclear localization observed in placentas from

uncomplicated pregnancies. **Conclusion:** We have demonstrated constitutive release of HMGB1 by trophoblasts in a physiological setting. Modulation of HMGB1 levels and localization is associated with trophoblast differentiation although the causal link needs further studies. In pregnancies complicated with PE, HMGB1 is redistributed to cytoplasm which is a first step prior to extracellular release, where it can exert pro-inflammatory deleterious actions. A better understanding of HMGB1 movements during trophoblast differentiation in pregnancy complications is important to prevent the occurrence of the deleterious extracellular HMGB1 action.

P203

SUBCUTANEOUS IMMUNOGLOBULIN TREATMENT FOR IMMUNE MEDIATED REPRODUCTIVE FAILURE: A CASE SERIES

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Introduction: IVIg has been used to improve success rates of IVF in women with suspected IMRF but has been associated with rare serious side effects including viral transmission, hypercoagulability, aseptic meningitis, renal insufficiency and hemolysis. ScIg is an alternative form of IgG, which is administered at home, is associated with a reduction in systemic side effects and has been shown to have similar immunomodulatory properties as IVIg. To our knowledge, there are no studies exploring scIg's role in the treatment of idiopathic RIF and RPL. **Objective:** To evaluate whether scIg is safe, effective and well tolerated as a last resort therapy in a population of women with idiopathic RPL and RIF who cannot receive IVIg. **Methods:** This is a descriptive analysis of women who received scIg for suspected IMRF at the Allergy-Immunology Clinic of the Montreal General Hospital (MUHC) from 08/2014-01/2016. We included patients aged 18-42 with > 4 miscarriages, or > 3 embryo transfer (ET) failures who did not tolerate, refused or could not receive IVIg because of geographical constraints. Hizentra 20% (10g/week if <65 kg or 12.5 g/week if >65kg) was started 1 month before implantation and continued weekly if successful pregnancy ensued until 32-34 weeks. The addition of low dose ASA or LMWH was left to the discretion of the obstetrician. We then prospectively followed these patients every 3 months during gestation and 1 month after delivery to determine the safety of scIg. **Results:** Five patients received scIg. Patient 1 had failed 4 good-quality ET and received 2 doses of IVIg for her 5th ET, but switched to scIg because of ease of administration. She delivered a healthy singleton at term. Patient 2, with 8 early RPL, was started on scIg directly because of geographical issues. She conceived naturally after 1 month of therapy and delivered a healthy singleton at term after being put on bed-rest for PTL at 27 weeks. Patient 3 had 6 early RPL and 2 good quality ET failures. She received 2 doses of IVIg for her 3rd ET but elected to switch to scIg because of ease of administration. She is currently at 32 weeks of an uncomplicated gestation. Patient 4 had 12 early RPL and was started directly on scIg before a double blastocyst transfer because of IVIg refusal. She is currently at 25 weeks of uncomplicated gestation with twins. Patient 5, diagnosed with secondary infertility after an 8 week SA, failed multiple IUI attempts and 10 ET. She had an ET with donor egg under IVIg but developed hypotension and chills during the infusion. She tolerated scIg subsequently and is currently at 16 weeks of gestation. No maternal, obstetrical or fetal complications were reported with scIg. **Conclusion:** ScIg appears to be a safe and potentially effective therapy for patients with idiopathic RIF or RPL who have failed conventional medical therapy and refuse or do not tolerate IVIg. It confers an added benefit with respect to ease of self-administration.

P204

OBESE ENVIRONMENT AFFECTS KILLER IMMUNOGLOBULIN-LIKE RECEPTOR (KIR) EXPRESSION IN DECIDUAL NATURAL KILLER CELLS (DNK)

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Introduction: Obesity is a growing health concern in western countries, affecting half of the women of reproductive age. Maternal obesity associates with a low-grade inflammation and increases the risk of pregnancy complications. dNK play a crucial role in the establishment and maintenance of pregnancy and placental development. Activation of dNK is a

tightly regulated process, controlled by a wide repertoire of surface receptors able to integrate different inputs from the uterine environment. In early pregnancy, the influence of obesity-linked inflammation on dNK activity, are largely unknown. **Objective:** To examine the effects of maternal obesity on dNK cell biology. **Methods:** dNK from lean (BMI 20-24.9 kg/m2; n = 22) and obese (BMI >30 kg/m2; n = 19) women in early pregnancy (6-10 weeks gestation), were characterized by flow cytometry to asses differences in degranulation (via CD107a), cytokine production (TNFa and IFNg) and surface expression of activating (NKp30, NKp44, NKp46, NKG2D, KIR2DS1) and inhibiting (NKG2A, KIR2DL1, KIR2DL4, LILRB1) receptors. KIR2D gene levels were additionally measured by quantitative PCR (qPCR) analysis. Functional assays to examine dNK cell responsiveness against HLA class I negative target cells were done using K562 cell line at a effector:target ratio of 5:1. Moreover, HLA-C2-expressing target cells were co-culture with dNK to measure KIR2DS1/L1 activation. The presence/absence of low-grade inflammation in our patient cohort was assessed in serum using a high-sensitivity CRP (C-reactive protein)ELISA. **Results:** Flow cytometry analysis showed that the inhibiting NKG2A and activating NKp46 receptors were decreased in dNKs of obese women, while KIR2DS1/L1 levels were shown to increase. qPCR analysis demonstrated that mRNA levels of KIR2DL1 remained unchanged between lean and obese dNKs; in contrast KIR2DS1 mRNA levels were higher. Multicolour flow cytometry further revealed increased KIR2DS1 surface expression (as determined by MFI) on obese dNK. On the other hand, the proportion of KIR2DL1 expressing cells was reduced. dNK from obese women showed elevated basal and HLA-C2 KIR2DS1/L1 ligand stimulated activity, as defined by increased surface CD107a expression. However, both cohorts were hypo-responsive to HLA-I negative target cell stimulation. **Conclusion:** Our findings provide insight into how maternal obesity alters dNK function in early pregnancy through alterations in NK cell receptor expression.

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DIET-INDUCED OBESITY MAY ALTER UTERINE NATURAL KILLER CELL BIOLOGY AT MATERNAL-FETAL INTERFACE

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Introduction: Obesity is a state of chronic inflammation, with increasing prevalence among the women of childbearing age. Maternal obesity has been associated with multiple adverse reproductive outcomes, negatively affecting the health of both the mother and the fetus. The mechanisms that link obesity to pregnancy complications remain unclear. Proper development of the placenta and establishment of utero-placental vasculature are essential for optimal fetal growth and survival. Uterine immune cells, particularly uterine natural killer cells (uNKs), play a fundamental role in promoting these events. This work aims to develop a mouse model of obesity in pregnancy to examine the effects of obesity on uterine uNK cell biology and establishment of the fetal-maternal interface. **Objective:** To examine how maternal obesity in mice affects uNK biology at the maternal-fetal interface. **Methods:** A diet-induced mouse model of obesity was established by subjecting 6-week old female C57B-6 mice to a high-fat diet (HFD; n=10) for 13 weeks; control mice (n=10) were fed a low-fat diet for 13 weeks (LFD). Following the 13-week diet regime, mice were mated with C57B-6 male mice, and on day 10 of gestation (gd10) uterine horns were extracted and decidual mononuclear cells (DMCs) were isolated and subjected to multicolor flow-cytometry analysis. Specifically, subpopulations of tissue-resident (tr) and conventional (c) uNK cells were quantified and characterized in their expression of the cytotoxicity receptor (NCR1). For comparisons, one-tailed non-parametric t-tests were performed. **Results:** Total DMCs from 8 control and 5 HFD mice were analyzed. Diet-induced obesity resulted in an increase in proportion of total uterine leukocytes; this increase was reflected by a subtle increase in tr-uNK cells. Notably, a HFD also associated with a higher proportion of total uNK cells expressing the NCR1. We did not detect differences in the proportions of total uNK or c-uNK populations. **Conclusion:** A HFD model of maternal obesity resulted in subtle alterations in sub-populations of uNK cells at GD10 in mice, characterized by increased proportions of tr-uNK cells and uNK cells expressing the NCR1. As tr-uNK cells produce angiogenic factors in early pregnancy, the cellular alterations identified in this study suggest that maternal obesity may lead to alterations in neo-vascularization in the uterus. Further, an increase in the uNK cell NCR1 population suggests that maternal obesity may also result in alterations in uNK cell cytotoxicity/activity. Further work is required to dissect the importance of these obesity-linked immunological changes in pregnancy.

P206

RAPID CHANGES IN THE MATERNAL IMMUNE SYSTEM FOLLOWING DELIVERY ARE ABROGATED IN WOMEN WITH ANTE AND POSTPARTUM PREECLAMPSIA

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Introduction: Preeclampsia (PE) is a leading cause of maternal-fetal mortality and morbidity worldwide. The placenta plays a key role in PE with its delivery being the only curative treatment. Classically, PE occurs during pregnancy but by an unexplained mechanism, it can develop in the postpartum period where the placenta cannot be the cause. The maternal immune system could be the link between pregnancy and PPPE since the immune system is strongly altered during pregnancy and the how the maternal immune system goes back or not to non-pregnant status following delivery is unknown. **Objective:** The aim was to understand the dynamic changes occurring in the maternal immune system in the perinatal period (before and after delivery) in women with normal term pregnancies, pregnancies complicated with PE or normal term pregnancies that will later developed PE. **Methods:** Women were recruited at the Sainte-Justine Hospital with uncomplicated term pregnancies (Ctrl, N=20), PE (PE, N=20) or normal pregnancies with postpartum PE (PPPE, N=20). Blood samples were collected prior and 24h after delivery in all patients and at the time of diagnosis (for PPPE). **Results:** Delivery was associated with rapid (within 24h) and strong changes in the maternal circulating immune system with an elevation in the number of total leukocytes and neutrophils with decreased proportion of lymphocytes and monocytes in Ctrl pregnancies. However, in pregnancies complicated with PE, leukocytes and neutrophils count were already elevated prior to delivery as compared to Ctrl and did not change 24h after delivery. Lymphocytes levels, on the other hand were similar to Ctrl prior to birth and were significantly elevated after delivery. For PPPE, leukocytes and neutrophils count were the same as Ctrl prior to delivery but, contrary to Ctrl pregnancies, they did not raise following birth and were significantly lower at the time of PPPE diagnosis. Furthermore, the percentage of lymphocytes was significantly elevated at PPPE diagnosis. **Conclusion:** Altogether, these results strongly suggest that changes in the immune system occur rapidly following delivery and that these changes are abrogated, or might take longer, in PE. Also, women with seemingly normal pregnancies that later develop PPPE have altered immune system. The lack of immune activation could be used to identify women at high-risk of PPPE and detailed understanding of the immune changes in the perinatal period is of high importance.

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SPHINGOSINE-1-PHOSPHATE MEDIATED VASCULAR ADAPTATIONS AND THE IMPACT OF TNFA ON VASCULAR TONE IN PREGNANCY

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Introduction: Vascular adaptations during pregnancy deal with increased blood volume and regulate fetal blood supply. Sphingosine 1-phosphate (S1P) is a bioactive lipid that may contribute to increased vasodilatory capacity in pregnancy, but has not yet been investigated. S1P generates nitric oxide (NO), an important vasodilator. However, S1P can also induce constriction and permeability depending on which receptors and cell types it binds to. TNFα, a proinflammatory cytokine that doubles in preeclampsia, is reported to induce constriction and increase permeability. Signaling through TNFα receptors generates S1P, but whether the vascular effects of TNFα are mediated by SIP is unknown. **Objective:** To determine the contributions of S1P to the increased vasodilatory capacity that occurs during pregnancy. To determine if TNFα increases constriction and permeability through the S1P pathway. **Methods:** Vascular tone in uterine arteries from nonpregnant (NP) and day-18 pregnant mice were measured using a pressure myograph system after intraluminal infusion of S1P (1μM) or TNFα (10ng/mL) in the presence or absence of NOS inhibitor LNAME (100μM) or Sphingosine Kinase I inhibitor (SK-II; 1μM). Some arteries were pre-constricted with addition of a thromboxane mimetic to the bath prior to infusion of S1P or S1P+LNAME. **Results:** Infused S1P alone did not alter vascular tone in arteries from pregnants (1.97±2.37%) or NP (-0.582±1.99%). However, S1P-induced constriction was significantly increased in arteries from pregnants when LNAME was co-infused (35.2±3.66%) compared to those from NP (2.43±2.96%), indicating the

importance of S1P-induced NO in maintaining vascular tone in pregnancy. This was confirmed by 44.8±12.3% dilation when S1P was infused in pre-constricted arteries from pregnants, whereas co-infusion of S1P+LNAME resulted in 19.0±4.29% constriction. Infused TNFα alone did not induce constriction in arteries from pregnants or NP (0.870±1.16; -2.90±0.562%). However, when co-infused with LNAME, TNFα now induced significant constriction that was greater in arteries from pregnants (28.4±1.38%) compared to NP (5.50±1.86%). However, these TNFα effects may not be via the S1P pathway, as co-infusion of TNFα+SK-II did not produce the same effect (-1.99±1.70%). **Conclusion:** Our novel evidence shows that S1P plays an important role in the increased vasodilatory capacity in pregnancy in part through S1P-induced NO. TNFα induces greater constriction in arteries from pregnants when NO production was prevented. Thus, under conditions of low NO bioavailability such as occurs in preeclampsia, elevated levels of TNFα may therefore induce constriction and contribute to the pathophysiology of this pregnancy disorder.

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GROUP B STREPTOCOCCUS-INDUCED CHORIOAMNIONITIS: IL-1B-DRIVEN INFLAMMATORY RESPONSE AND IMPACT OF FETAL SEX

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Introduction: Chorioamnionitis (CA) increases the risk of the newborn to suffer from long term sequelae, including autism spectrum disorders (ASD). CA is assumed to mostly arise from ascending genitourinary tract infections caused by pathogens such as group B streptococcus (GBS), one of the most common bacteria colonizing pregnant women. As interleukin (IL)-1β up-regulation plays a pivotal role in GBS-induced immune response, we hypothesized that IL-1β is implicated in GBS-induced CA. As there is a sex bias underlying ASD, more boys are affected than girls, we secondly hypothesized that CA induced by GBS is more severe in placentas associated with male than females fetuses. **Objective:** The goal of this study is to uncover the IL-1β driven inflammatory mediators involved in the pathogenesis of GBS-induced CA and to compare the inflammatory response between placentas associated with male versus female fetuses. **Methods:** Dams were injected intraperitoneally with inactivated GBS (109 CFU/100 µL/12 h) or sterile saline (control group) from gestational day 19 to 21. Cesareans were performed at different time points (from 1 h to 72 h) after the first injection to collect placentas, maternal blood, and fetal blood. To assess cells and molecules involved in inflammatory response to GBS, proteins titration (ELISA) and histological analysis (immunohistochemistry and cell counts) were performed. **Results:** Dams showed elevated IL-1β blood titers from 3 to 72 h following the GBS inflammatory challenge. At 72 h post-GBS, IL-1β expression was increased in placentas and fetal blood. Placental histology revealed diffuse polymorphonuclear (PMN) cells infiltrations in the decidua and the labyrinth of placentas 24 h and 48 h after the GBS exposure. Metalloproteinase 10 was also increased in GBS exposed placentas 48 h after inflammatory challenge (Bergeron J et al., 2016). Multifocal areas of IL-1β positive PMN and macrophages were observed at 72 h on the fetal face of the placenta after the GBS challenge and interestingly, these areas of inflammatory cells are larger in placentas associated to male fetuses. Preliminary results on the sex dichotomous placental inflammatory response showed that IL-1β placental expression seems higher in male placentas. **Conclusion:** To our knowledge, this is the first study assessing inflammatory molecular pathways leading to GBS-induced CA. Stronger placental inflammatory response in male than female placentas is an important finding. It could contribute to explain the sex bias observed in neurodevelopmental disorders such as ASD. This provides targets to new therapeutics avenues, such as cytokine blockade, to protect newborns from the adverse effects of CA.

THEME: Paediatric Stem Cells

P209

HUMAN UMBILICAL CORD MESENCHYMAL STROMAL CELLS (HUC-MSCS) IMPROVE SURVIVAL AND BACTERIAL CLEARANCE IN NEONATAL SEPSIS IN RATS

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Introduction: Sepsis is the main cause of morbidity and mortality in neonates. MSCs are potent immune-modulatory cells, but their effect in neonatal sepsis has never been explored. **Objective:** To evaluate the effect of human umbilical cord MSCs (hUC-MSCs) and hUC-MSCs preconditioned with INF-γ in experimental neonatal sepsis. **Methods:** Sepsis was induced in 3-day-old rats by intravenous injection of Escherichia coli (5×105 colony forming units/rat). One hour after the infection, rats were treated intravenously with hUC-MSCs, INF-γ preconditioned hUC-MSCs (107 cells/kg) or normal saline. Animals were observed for survival for 72 hours after E. coli injection. Eighteen hours after the infection, bacterial counts, plasma LL-37 concentration, lung neutrophil and macrophage influx, phagocytosis and apoptosis of splenocytes were measured in each group. **Results:** Treatment with either MSCs or preconditioned MSCs significantly increased survival (hUC-MSCs, 81%; preconditioned hUC-MSCs, 90%; saline, 53%; $p<0.05$). Both, hUC-MSCs and preconditioned hUC-MSCs enhanced bacterial clearance in the blood and decreased lung neutrophil influx. The number of activated macrophages (CD206+) in the spleen was increased with hUC-MSCs and preconditioned hUC-MSCs; preconditioned hUC-MSCs increased the phagocytic activity of CD206+ macrophages. hUC-MSCs and preconditioned hUC-MSCs also decreased splenocyte apoptosis in E. coli infected rats. Furthermore, levels of LL-37 were elevated in the plasma of neonatal rats treated with hUC-MSCs or preconditioned hUC-MSCs. **Conclusion:** hUC-MSCs enhance survival and bacterial clearance in experimental neonatal sepsis. Increased bacterial clearance was associated with higher LL-37 levels in plasma and enhanced phagocytosis activity of activated macrophages in the spleen. hUC-MSCs may be an effective adjunct therapy to reduce neonatal sepsis-related morbidity and mortality.

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EARLY SCREENING FOR IMMUNOLOGICAL EMERGENCIES IN NEONATES:OMENN SYNDROME

Veronica Mugarab Samedi, Amy Shaffey, Nicola Wright, Luis Murguia Favela

Introduction: Healthy looking at birth infants may have SCID, and neonatologist may be the first physician to encounter these patients. **Objective:** In presented case clinical and laboratory findings of erythroderma, severe infection, failure to thrive, eosinophilia, and elevated IgE together with immunodeficiency met the diagnostic criteria of Omenn syndrome. **Methods:** The only effective treatment for this condition is Hematopoietic Stem Cell Transplantation (Bone Marrow, PBSC or Cord Blood Transplant); in case of undiagnosed or untreated SCID majority of patients will die before 1 year of life. **Results:** In our patient' mother found to be 10/10 match donor, and he underwent successful BMT therapy. Omenn Syndrome and other SCID could be detected by special immunodeficiency screening based on quantitative PCR that measures TRECs from a dried blood spot (DBS) after genomic DNA extraction. **Conclusion:** SCID screening is part of routine screening of newborn in USA, and it is included in newborn metabolic screening in Ontario and Maritimes. In term screening has 99.99% specificity for SCID, with no false negatives. In preterm infants screening is less accurate due to lack of standard TREC values in this age group.

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* * *

Molly Towell was a pioneer clinician-scientist in the field of Obstetrical and Perinatal Medicine. Her medical training was in England. After emigrating to Canada and working as a Ship's Surgeon along the British Columbia coast for a year, she accepted a position in the Department of Obstetrics and Gynecology at the University of British Columbia. Her interest in research led her to undertake training with Dr. Karlis Adamsons at Columbia University. She then returned to UBC and subsequently moved to McMaster University.

Her research made important conceptual contributions to fetal heart rate monitoring, mechanisms of preterm birth and nutrition of the fetus and newborn. She died from breast cancer at the age of 60.

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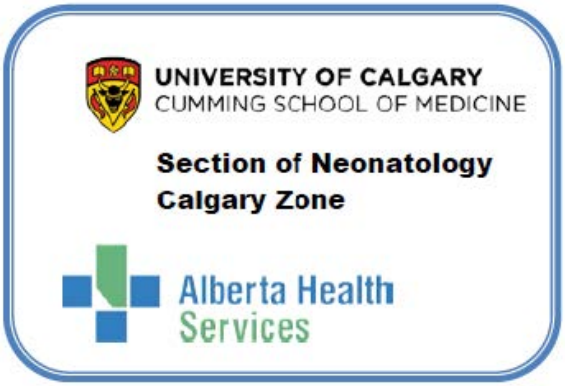

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