2020 WCHRI Research Day website content & abstracts

women & children's health research institute

Registration is now closed!

All registrants should have received a personalized InEvent access code from "WCHRI Research Day 2020". Check your spam folder! If you didn't receive this access code, please let us know at .

Information on how to access and navigate InEvent is below:

InEvent guide for attendees.

InEvent guide for presenters.

InEvent guide for moderators.

Presenters, please use a laptop or desktop when giving your 3MT-style presentation, not a tablet (e.g. iPad, Galaxy Tab, etc.) or mobile device. These devices are fine for attendees but not for presenters.

The Women and Children's Health Research Institute is proud to be hosting its annual Research Day in 2020. For the first time, Research Day will be held virtually!

Due to COVID-19 restrictions, we are launching a new interactive virtual format for Research Day 2020. This will not only allow our trainees to safely present their work but also provide them with the opportunity to develop new presentation skills.

WCHRI's Research Day brings our members and stakeholders together to share common interests and research outputs on women and children's health and is a great venue for our trainees to communicate their recent work, discuss their research and network with colleagues. Presentations for Research Day will be combined into themed sessions and presented in moderated virtual sessions. As well, participants are invited to take part in virtual networking activities!

Research Day will include a presentation and live question and answer session from our keynote speaker, Dr. Cara Tannenbaum. Read more about our keynote presentation.

Important dates:

Registration and abstract submission opens	July 29
Learning Session: "How to prepare your abstract"	July 29
Abstract submission closes	September 15 (4 p.m.)

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Abstract submission closes	September 15 (4 p.m.)
Learning Session: "How to prepare your 3MT-style presentation for WCHRI Research Day"	October 6
Registration closes	November 1 (4 p.m.)
Personalized InEvent access codes emailed	November 2

All attendees must register even if you are not submitting an abstract. Registration numbers are limited. Please register if you plan to attend.

See you on November 4th!

WCHRI Research Day is an open event where photographs of presenters and attendees are taken.

Questions? Contact .

Keynote Speaker

We are delighted to announce our keynote speaker for 2020 is Dr. Cara Tannenbaum of the Université de Montréal and the Canadian Institutes of Health Research Institute of Gender and Health.

Her presentation is entitled: "**From birth to death and everything in between:** *Tackling sex and gender in women's health research across the lifespan.*"

View Dr. Tannenbaum's biography and presentation abstract below.

Biography +

Presentation abstract +

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Biography

Dr. Cara Tannenbaum is a professor at the Faculties of Medicine and Pharmacy at the Université de Montréal. She is also scientific director of the Institute of Gender and Health at the Canadian Institutes of Health Research and currently serves as departmental science advisor for Health Canada.

Dr. Tannenbaum has long been immersed in the field of gender and health, including being involved in the EMPOWER trial, aimed at helping older adults discontinue inappropriate medication. Dr. Tannenbaum also led the international "Dare to Age Well for Women" urinary incontinence trial.

A physician specializing in the fields of geriatrics and women's health, Dr. Tannenbaum's practice is informed by research and she continually strives for improvements in health outcomes.

She has won multiple prestigious awards for her cutting-edge research, including the Betty Havens Prize for Knowledge Translation in Aging by the Canadian Institutes of Health Research (CIHR) Institute of Aging and Women of Distinction Award, Health category, from the YWCA of Montreal. She has also been inducted into the Canadian Academy of Health Sciences.

Dr. Tannenbaum studied medicine at McGill University before specializing in geriatric medicine and older women's health. She received clinical training in women's health and osteoporosis at Mount Sinai Hospital in New York during her CIHR postdoctoral fellowship. She also completed a master's degree in epidemiology and biostatistics from McGill University and research training on sex hormones from the University of California in San Diego.

Presentation abstract

From birth to death and everything in between:
Tackling sex and gender in women's health research across the lifespan

Women's health research has evolved from a focus on reproduction and female anatomy to a more holistic view of women's wellbeing across the lifespan, from cell to society. Attention to both biological sex and multidimensional sociocultural constructs of gender add complexity to research, requiring new methodological and analytical approaches. This presentation will describe how the CIHR Institute of Gender and Health is sparking a paradigm shift in the way sex and gender are incorporated into research, and provide guidance around best practices for applying sex and gender within the fields of women, pregnancy and children's health research. Using examples from her own research, Dr. Tannenbaum will challenge the audience to redefine criteria for excellence across the spectrum of women's health research in Canada.

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Program

This year's program will be from 8 a.m.–noon on November 4. Research Day will be hosted online using the innovative digital event platform, InEvent.

Watch your email on November 2 for your personalized InEvent access code from "WCHRI Research Day 2020". Information on how to access and navigate InEvent is below:

InEvent guide for attendees.

InEvent guide for presenters.

InEvent guide for moderators.

Time		
7:45	8:00	**Virtual Lobby** Join us for some early morning networking and catch up with colleagues!
8:00	8:15	**Welcome** • Sandy Davidge, executive director, Women and Children's Health Research Institute

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8:15	9:00	**Presentations** Watch our top trainees deliver their research in a three-minute thesis (3MT-style) presentation and interact with them during the live question and answer section. Choose from several themed rooms to join: • Children's health and well-being • Pregnancy and developmental trajectories • Lifelong women's health • Knowledge translation and decision-making
9:00	10:15	**Keynote** Join Dr. Cara Tannenbaum, scientific director of Canadian Institutes of Health Research's Institute of Gender and Health, as she speaks on women's health and gender research. Title: **From birth to death and everything in between** *Tackling sex and gender in women's health research across the lifespan* Ask Dr. Tannenbaum your questions during the live question and answer section!
10:15	10:30	**Break** Visit our sponsor rooms to connect with representatives from the Stollery Children's Hospital Foundation and Royal Alexandra Hospital Foundation, or just pop by to say "thanks" for their support!

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		Visit our sponsor rooms to connect with representatives from the Stollery Children's Hospital Foundation and Royal Alexandra Hospital Foundation, or just pop by to say "thanks" for their support! Networking rooms will also be available.
10:30	11:45	**Presentations** Watch our top trainees deliver their research in a three-minute thesis (3MT-style) presentation, and interact with them during the live question and answer section. Choose from several themed rooms to join: • Children's health and well-being • Pregnancy and developmental trajectories • Lifelong women's health • Knowledge translation and decision-making
11:45	12:00	**Wrap Up** Closing remarks from Sandy Davidge, executive director, and Todd Alexander, associate director, Women and Children's Health Research Institute Stop by the Stollery Children's Hospital Foundation and Lois Hole Hospital for Women sponsor rooms. Networking rooms are also available.

Presenters, please use a laptop or desktop when giving your 3MT-style presentation, not a tablet (e.g. iPad, Galaxy Tab, etc.) or mobile device. These devices are fine for attendees but not for presenters.

All abstracts are included below and listed alphabetically. Click on the "presenters" or "supervisors" button to narrow down your search and then choose from the drop-down menu to filter by WCHRI research theme, 3MT-style presenters and abstract winners. When you have found the abstract you want to view, click on the "+" symbol to view the full abstract.

View the abstract winners list.

Every effort to report the abstract as submitted has been made. Questions may be addressed to wcgrants@ualberta.ca.

Presenters | Supervisors

A
B
C
D
E
F
G

All abstracts

Abbasi Dezfouly, Mostafa +

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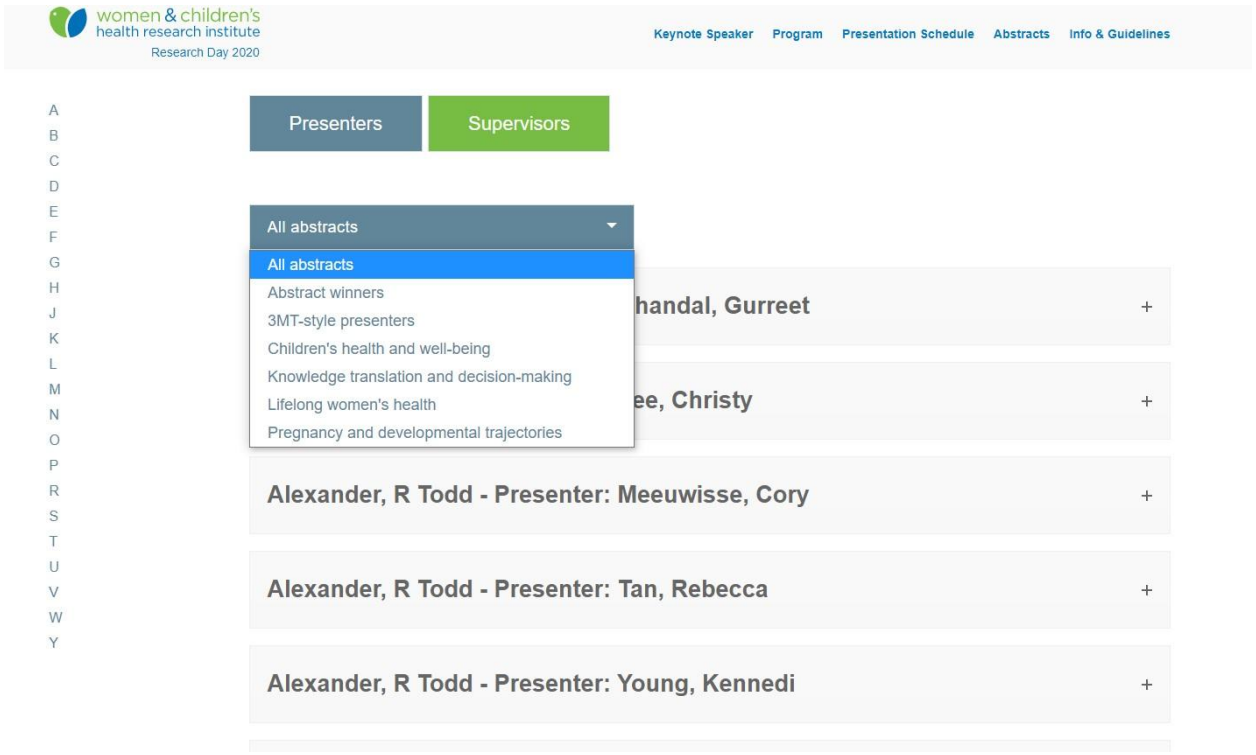

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Promote your research—virtually!

WCHRI Research Day offers trainees under the supervision of WCHRI academic members the opportunity to showcase their research progress. This year, we look forward to interacting virtually with our academic members, their trainees and our funders, the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women!

We have adapted our annual Research Day to provide interactive learning and networking opportunities supported through a virtual event platform.

Other changes for this year include:

- trainees must be supervised by a WCHRI academic member to be eligible to submit an abstract.
- trainees will be judged on their abstract submissions only.
- the trainees who have earned top grades on their abstracts will have an opportunity to present live during Research Day through a three-minute thesis (3MT-style) format.
- top grades will be based on trainee level and will be representative of WCHRI's three research themes: children's health and well-being, pregnancy and developmental trajectories and lifelong women's health.

health research institute
Research Day 2020

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Abstract preparation outline

Before you start your registration and abstract submission, please be familiar with the general expectations regarding your abstract. Please have your completed abstract open as you will be using this as a source document for the abstract submission form.

The purpose of your abstract is to:

- present a large amount of information in a concise manner.
- engage your audience.

Why it's important:

- This will determine whether you are asked to present on virtual Research Day.
- All abstracts will be posted on our website, so it will be a chance to build your professional portfolio.

Structure

For the research itself, key components include:

- a title
- an introduction
- methods
- results
- conclusion

Abstract submission

Eligibility criteria for the WCHRI Research Day 2020 program is as follows:

- Abstract submission is open to trainees under the direct supervision of a WCHRI academic member.
- Trainees who wish to submit an abstract must do so at the time of registration.
- Trainees may submit a single abstract only. Where more than one submission per trainee is provided, WCHRI will accept the submission closest to the deadline.
- All abstracts submitted to WCHRI for research day must align with our WCHRI relevance criteria.

Abstracts must be complete at the time of submission. WCHRI does not modify, amend or edit submitted information.

Abstract review process +

3MT-style presentations +

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Abstract submission +

Abstract review process −

The abstract review process is as follows:

- Abstracts will be assigned and evaluated by reviewers on our Research Day abstract review committee.
- The reviewers will first confirm alignment with WCHRI relevance criteria and then score the abstract.
- The top grades for each trainee level, allocated by WCHRI theme, will be offered the opportunity to make a 3MT-style presentation on November 4.
- All abstracts that have been reviewed and meet WCHRI relevance criteria will be published on our website.
- WCHRI will provide notification to all trainees of the outcome of their abstract submission on or before October 5.
- A listing of the abstracts that have been selected for a 3MT-style presentation will be posted to our website on October 6.

3MT-style presentations +

Please note: iPads and mobile devices are fine for attendees but not for presenters! Presenters, please use a laptop or desktop when giving your 3MT-style presentation.

Trainees who have earned top grades will have an opportunity to present a three-minute thesis (3MT-style) presentation live on Research Day.

Those chosen will have three minutes to explain the breadth and significance of their research to a non-specialist audience, after which there will be three minutes for questions from judges and other audience members.

You may wish to review the following resource for your 3MT-style presentation:

- UAlberta Faculty of Graduate Studies and Research: What is a Three Minute Thesis?

Presentations will be as follows:

- Each three-minute presentation will be **live**.
- Each presenter will be allowed **one, non-animated slide**. Presenters will need to share their own screens in order to use the slide.
- The slide will only be on the main screen for the first 90 seconds of the presentation. After that, the presenter will be on the main screen.
- Presentations will be immediately followed by a live three-minute question and answer component.
- A moderator and two judges will be in the (virtual) audience.
- Be aware that you will have a diverse audience including trainees, faculty and representatives from the Royal Alexandra Hospital Foundation and/or the Stollery Children's Hospital Foundation. We suggest that you tailor your presentation to this mixed audience.

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Learning Sessions

WCHRI hosts two Learning Sessions, the first to help you prepare your abstract and the second to help you complete your 3MT-style presentation.

"How to prepare your abstract"

- Presenters: Eytan Wine and Lesley Wiart
- Event date: July 29, 11:30 a.m.–1 p.m.
- Presentation slides
- Zoom session recording

"How to prepare your 3MT-style presentation for WCHRI Research Day"

- Presenters: Charity Slobod, Chris Schoengut, Martha Ruiz
- Event date: October 6, 11:30 a.m.–1 p.m.
- Presentation slides
- Zoom session recording

Register Now

Deadlines

Abstract submission for WCHRI Research Day closes **September 15** at **4 p.m.**

Applications must be submitted to WCHRI using the WCHRI 2020 Research Day registration form. Late abstracts will not be accepted.

Access to WCHRI 2020 Research Day registration will close for a period of system maintenance between September 15 at 4:01 p.m. through to September 16 at 8:30 a.m.

WCHRI will notify trainees on the outcome of their abstract submission by October 5.

Acknowledgement

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Acknowledgement

WCHRI is supported by the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women. Without their generous support, our institute would be unable to continue to support the research done by you and your colleagues.

It is imperative that you acknowledge funding of your research as all research is supported in some way by a financial commitment. If you are unsure of the source of funding for your project, please ask your supervisor. All research projects funded by or receiving subsidized research services from WCHRI must acknowledge the support of WCHRI and the appropriate Foundation, including using logo(s) on your presentation slides.

Further information on acknowledgement requirements and logo files can be found on WCHRI's acknowledgements and logos webpage.

Additional Acknowledgement Information and Examples

Registration

Registration closes **November 1, 2020, at 4:00 p.m**. Please use this link to register.

All attendees must register. **Registration numbers are limited.** Please register only if you plan to attend!

Abstract #:	66
Presenter:	Mostafa Abbasi Dezfouly
Supervisor:	Conway, Jennifer
Title:	Nutritional Status and Cannula Infections in Pediatric VAD Patients
Authors:	Mostafa Abbasi Dezfouly; Holger Buchholz; Tara Pidborochynski; Kylie Lewis; Osiris Zelaya; Maegan Phinney; Jennifer Conway
Theme:	Children's health and well-being

Introduction:

Ventricular Assist Devices (VADs) have emerged as an effective treatment option to bridge pediatric patients to heart transplant. Paracorpeal VADs require the placement of an inflow and outflow cannula, which can create an environment for infections. We aimed to characterize cannula infections in pediatric VAD patients and examine the impact of nutrition.

Methods:

This was a single center retrospective study (2005-2019) of all patients <20 years old implanted with a VAD using Berlin Heart cannulas. A cannula infection was defined by symptoms in the presence of a positive culture and the need for antibiotic therapy.

Results:

There were 49 eligible for the study. The median age of implant was 0.9 yrs (IQR 0.3, 5.0), 59% were male, and the most common etiology being non-congenital heart disease (69%). The median time on VAD support was 61days (IQR 30, 143). During the study period, 29% of patients developed a cannula infection with a median time to infection of 66 days (IQR 21, 124). There was no difference in terms of pre-VAD weight, height, malnutrition scores, BMI or albumin between patients with and without a cannula infection. However, lower pre-implant pre-albumin levels was associated with cannula infections (p=.022). Seventy-five percent (n= ¾) of the patients with a g-tube developed a cannula infection and almost 80% of patient who developed a cannula infection were malnourished based on their weight z-scores.

Conclusion:

Less than one-third of pediatric VAD patients with Berlin cannulas developed a cannula infection. Pre-albumin levels were associated with the development of a cannula infection and a majority of the children with an infection were malnourished, suggesting that pre-implant nutritional status may an important risk factor. These results suggest a relationship between nutritional status and infection that warrants further study.

Funded By: This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women and has been generously supported by a grant from the MNCY SCN and NACTRC Summer Studentship

Abstract #:	128
Presenter:	Bisi Adewale
Supervisor:	Santos Salas, Anna
Title:	Exploring the Experiences of Family Caregivers of Persons Living with Advanced Cancer in Ghana
Authors:	Authors: Bisi Adewale, Dr. Anna Santos Salas, Dr. Wendy Duggleby
Theme:	Lifelong women's health

Introduction: Cancer is the second leading cause of death worldwide with an estimated number of 9.6 million deaths in 2018, with majority of deaths occurring in low-and-middle-income countries (LMIC). Globally, an estimated 40 million people are in need of palliative care, with 78% of them located in LMICs. In Ghana, approximately 22,823 new cancer cases report annually. Family members are solely responsible for the care of relatives with advanced cancer in Ghana, yet little is known regarding their experiences. The majority of these family caregivers are women in sub-Saharan Africa as well as Ghana. Despite the government of Ghana's continuous effort in collaboration with organizations such as the United Nations, social and cultural prejudice on education still exist, with the girl child usually at the disadvantage. Women are expected to take up the roles as family caregivers, in addition to performing their personal activities such as employment and marital responsibilities. In some instances, some of these women postpone their personal life accomplishments such as education, jobs, or marriage, to care for an ill relative. Unfortunately, women with low socioeconomic status are expected to play the caregivers role, with some ignoring their own personal health care to perform this role. The purpose of this study is to explore the experiences of family caregivers of persons living with advanced cancer receiving palliative care in Ghana. The study is currently underway. In this presentation, we present the study protocol and preliminary findings if possible.

Methods: Interpretive Descriptive approach as delineated by Thorne. 10-15 family caregivers and 4-6 health care professionals will be recruited from a Palliative Care Outpatients Unit located in a major public health care hospital in Ghana. Family Caregivers included in this study will be current caregivers of a person living with advanced cancer receiving palliative care, able to communicate in English or Twi, and 18 years and above. Members of the palliative care team will also be included in the study. Two semi-structured recorded telephone interviews will be conducted with family caregivers, and an online focus group discussion with health care professionals. Data will be analyzed through the process of sorting and organizing data, making sense out of the patterns, and transforming patterns into findings. The NVivo software will be used to manage the data collected during the interviews and focus group discussion.

Results: We will report preliminary findings. We anticipate the majority of family caregivers who take part in the study will be women. We anticipate that findings from the study will assist us to learn from the experiences of family caregivers, in particular, Ghanaian women. In our results, we will discuss how the caregivers' roles performed by these women affect their health, wellbeing, and ability to progress in society. Study findings will serve to inform relevant stakeholders on the experiences of family caregivers of persons living with advanced cancer in Ghana. This will also aid in the development of support programs. In addition, the potential to translate this research into the Canadian experience also exists given pressing cancer inequities in Canada.

Funded By: 1. International Student Go Abroad Program

2. Minton Endowment Fund Student Education Bursary

Abstract #: 76
Presenter: Babak Afsharipour
Supervisor: Gorassini, Monica Ann
Title: Developing a method to estimate the intrinsic activation of motoneurons in children with Cereberal Palsy
Authors: Babak Afsharipour, Nagib Manzur, Jennifer Duchcherer, Keith F. Fenrich, Christopher K. Thompson, Francesco Negro, Katharin A. Quinlan, David J. Bennett, Monica A. Gorassini
Theme: Children's health and well-being

Introduction: Abnormal muscle tone and reflexes are permanent movement disorders that are symptoms of brain injury in children, known as Cerebral palsy (CP), which occurs in the developing fetal or infant brain (2.1-per-1000-live-births). Although changes to the brain are well studied in CP, less is known about the spinal cord. Spinal motoneurons get activated (fire) in response to sufficient amounts of synaptic inputs during a voluntary or reflexive muscle contraction. Intrinsic inward calcium currents (persistent inward currents: PIC) flowing through voltage-sensitive channels on the motoneurons membrane can also provide a depolarizing drive. PIC keep motoneurons active at a lower level of synaptic input compared to the amount needed for a motoneuron to start firing. Excessive activation of spinal motoneurons due to PIC has been considered as a potential source of abnormal muscle tone and reflexes in CP. To estimate PIC amplitude in children with CP, in an ongoing study, we developed a new method to estimate synaptic input and contribution of PIC to self-sustained firing in human motoneurons. We have also investigated if PIC amplitude depends on the size of a motoneuron.

Method: We analyzed the firing frequency profile of active motoneurons during a triangular isometric torque contraction. To obtain firing frequency profiles, we used high-density surface EMG (HDsEMG) electrodes to record from 64 sites arranged in a 5 x 13 grid with 8mm inter-electrode distance on tibialis anterior (TA) and soleus muscles. EMG signals and ankle joint torque were recorded from 10 participants (6 female, 4 male) aged 21 to 58 years during exerted triangular dorsiflexion torque contraction profile at 10%, 20% and 30% of maximum voluntary contraction (MVC) over 2 to 3 trials. We processed the recorded data to isolate motor unit activities (decomposition) during the ascending and descending phase of the contraction to obtain the firing frequency profile of low and high threshold units (represent small and large motoneurons, respectively). We constructed a composite (control) firing profile from the lowest-threshold units that fired linearly with force to estimate synaptic input to the higher-threshold (test) units. The difference in the composite firing rate (synaptic input) at the time of test unit recruitment and de-recruitment was used to measure the PIC amplitude that sustained firing.

Results: From the HDsEMG, we decomposed about 20 motor units per contraction at the 10%, 20% or 30% MVC. The number of control motor units selected for the composite profile was limited by the number of low threshold (< 3% MVC; typically 3 to 6) motor units. Test units with recruitment thresholds 1-30% of maximum had similar DeltaFs; however, the PIC seems to be activated more before firing in low threshold motoneurons compared to higher threshold motoneurons as the later showed more firing rate accelerations near recruitment indicative of simultaneous PIC activation.

Conclusion: Our method provides a more precise estimation of PIC comparing to the previously developed method. Our analysis suggests that the portion of the PIC that sustain firing is similar across a wide range of motoneuron sizes.

Funded By: WCHRI Postdoctoral Fellowship, National Institutes of Health

Abstract #:	42
Presenter:	Malema Ahrari
Supervisor:	Hartling, Lisa
Title:	Short-term Use of Therapeutic Opioids for Children and Future Opioid Use Disorders: a Qualitative Study of Decision-maker Information Needs.
Authors:	Ahrari, M., Ali, S., Dyson, M., Hartling, L.
Theme:	Children's health and well-being

Introduction:

Despite an overall decline in opioid prescriptions in Canada, healthcare visits, hospitalizations, and deaths due to opioid-related harms continue to rise for children. Decision-makers (including patients/parents, clinicians, and policy-makers/influencers) require high quality syntheses to inform decisions regarding opioid use for children. Previous research has found that how systematic review (SR) results are presented may influence uptake by decision-makers. Evidence summaries are a short summary of the best available evidence on a defined question and can be appealing to decision-makers as they provide key messages in a succinct manner.

The objective of this study was to gain perspectives from decision-makers who influence children's health policies, on the usability and presentation of results of a systematic review (SR) through the form of an evidence summary.

Methods:

Decision-makers influencing children's health policies were recruited through purposive and snowball sampling methods. They participated in one-on-one interviews to discuss an evidence summary created for a SR studying the association between short-term therapeutic opioid use in children and youth and future opioid use disorders. Interviews were transcribed and data were analyzed using thematic analysis.

Results:

13 decision-makers participated in interviews. Four major themes emerged from the data: 1) content, 2) format, 3) expertise, and 4) actionability.

Decision-makers shared their preferences for the content and format of evidence summaries, which included having short 'one pagers' in plain language, infographics, bolding, colours, and white space. Tables including details, statistics and links to studies were preferred as an appendix. Decision-makers also shared perspectives on the insufficient evidence that emerged from the SR being unable to prompt any major changes and noted that the lack of actionability is a common observation with SR results in general. Finally, they commented on the role of experts in knowledge synthesis and trusting those who developed the summary, as well as their reliance on content experts for making judgements and decisions in the absence of strong evidence.

Conclusions:

This study provides important information about the needs of decision-makers who influence children's health policies, in terms of the content and format of evidence from systematic reviews, to guide decision-making.

Funded By: Alberta Research Centre for Health Evidence Operational Grant, Maternal Newborn Child & Youth Strategic Clinical Network (MNCY SCN), Emergency Strategic Clinical Network (ESCN) Systematic Review Grant

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Abstract #:	67
Presenter:	Asim Al Balushi
Supervisor:	Mackie, Andrew S
Title:	Angiotensin Converting Enzyme Inhibition and Pre-Glenn Hemodynamics in Infants with Single Ventricle Physiology
Authors:	Asim Al Balushi, Konstantin Averin, Daphne T. Hsu, Andrew S. Mackie
Theme:	Children's health and well-being

Introduction: Preliminary animal and human data suggests that angiotensin converting enzyme inhibition has a role in pulmonary vascular remodelling. We sought to assess the effect of enalapril versus placebo on pulmonary artery pressure and transpulmonary gradient among infants undergoing single ventricle palliation.

Materials and Methods: Using the publicly available Pediatric Heart Network Infant Single Ventricle trial dataset, we compared mean pulmonary artery pressure at pre-Glenn catheterization (primary outcome), transpulmonary gradient, pulmonary to systemic flow ratio, and post Glenn oxygen saturation (secondary outcomes) in infants receiving enalapril vs. placebo.

Results: A total of 179 infants underwent pre-Glenn catheterization, 85 (47%) who received enalapril. There was no difference between the enalapril and placebo group in the primary and the secondary outcomes. Mean pulmonary artery pressure in the enalapril group was 13.1± 2.9 compared to 13.7± 3.4 mmHg in the placebo group. The transpulmonary gradient was 6.7± 2.5 vs. 6.9± 3.2 mmHg in the enalapril and placebo groups respectively. The pulmonary to systemic flow ratio was 1.1 ± 0.5 in the enalapril group vs. 1.0 ± 0.5 in the placebo group and the post Glenn surgery saturation was 83.1 ± 5.0% in the enalapril group vs. 82.2 ± 5.3% in the placebo group. In the pre-specified subgroup analyses comparing enalapril and placebo according to ventricular morphology and shunt type there was no difference in the primary and secondary outcomes.

Conclusion: Enalapril did not impact mean pulmonary artery pressure or transpulmonary gradient among infants with single ventricle physiology prior to Glenn palliation.

Funded By: This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

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Abstract #:	68
Presenter:	Hilal Al riyami
Supervisor:	Escudero, Carolina
Title:	Does a smartphone-based ECG recording system in pediatric patients with palpitations improve diagnostic yield?

Authors: Hilal AL Riyami , Lisa Hornberger, Joseph Atallah, Yashu (James) Coe ,Carolina Escudero

Theme: Children's health and well-being

BACKGROUND

-Palpitations are a common occurrence in children and a frequent indication for referral to pediatric cardiology

-There are several types of diagnostic equipment that can be used to obtain symptom-rhythm correlation

-Event recorders (CardioCall) are most commonly used for documentation of intermittent palpitations but it has some limitations

-AliveCor (Kardia) monitor is a newer generation device which is much smaller and more easily portable than the CardioCall event recorder . Also, it is cheaper.

OBJECTIVES

Primary:

-Determine the diagnostic utility and time to diagnosis using the AliveCor (Kardia) monitor compared to the current standard of care (CardioCall event recorder)

Secondary:

-Compare the use of the AliveCor (Kardia) versus (CardioCall) by examining:

-Proportion of patients obtaining a diagnosis

-Time to first diagnostic transmission

-Incremental cost-effectiveness analysis

METHODS:

Study Design:

- A prospective, randomized trial of patients in the outpatient pediatric cardiology clinic who are being investigated for palpitations

Inclusion Criteria:

-Age 5-18 years

-Parent or patient ownership of a smartphone compatible with use of the AliveCor (Kardia) Application

-Estimated palpitation duration of at least 1 minute

-Consistent symptoms of palpitations with the need for symptom-rhythm correlation using an event recorder, as determined by the consulting pediatric cardiologist

Exclusion Criteria:

-Patients will be excluded for refusal to consent

Protocol:

-Patients will be assigned to either the "standard of care" group or "AliveCor (Kardia)" group

-CardioCall event recorder prescribed for up to 4 weeks

-Patients will be taught how to use the monitor and transmit recordings trans-telephonically

-AliveCor (Kardia) group will be provided the monitor for 3 months, or until sufficient diagnostic recordings have been documented

-The patient will be directed how to download the AliveCor Kardia application to their telephone

-The patient will be shown how to record and send a transmission (via email) by the ECG laboratory personnel

Randomization:

-Stratified block randomization according to frequency of palpitations

-At least once weekly versus less frequently than once weekly with 1:1 patient allocation to each group

-Randomization by opening unidentifiable and opaque sealed envelopes indicating patient assignment

Data Collection:

-Data will be collected using REDCap (Research Electronic Data Capture)

-Patient demographic information will be collected

-Clinical features including the frequency and duration of palpitations will be collected at the time of enrollment

-Baseline ECG abnormalities will be collected

-After each transmission, patients or their parents will be emailed a questionnaire (to a maximum of 4 times) through REDcap regarding their satisfaction with the CardioCall event monitor/AliveCor Kardia

-Responses to the questionnaire items will be on a 5-point Likert scale

-We will investigate the cost to the health care system for diagnosing the etiology of the palpitations

Study Progress:

Started July 2019 and expected to finish on July 2021

Total of 50 patient out of 96 has been recruited so far

CLINICAL IMPACT

They will be a significant impact to our practice if we prove the hypothesis.

Funded By: WCHRI

University of Alberta

Abstract #:	77
Presenter:	Sarah Almas
Supervisor:	Yager, Jerome Y
Title:	A review of transcranial doppler (TCD) values in healthy infants and children
Authors:	Sarah Almas, Oriana Shaw, Janette Mailo, Carol Derksen, Jay Kassiri, Khurshid Khan, Jerome Y. Yager
Theme:	Children's health and well-being

Transcranial doppler (TCD) provides a safe, inexpensive, and readily available technique to record blood flow velocities of cerebral arteries in patients of all ages. Compared to currently employed methods, including angiography that carry risks of radiation exposure, anesthesia, and invasiveness, TCDs have a tremendous diagnostic potential for diseases involving intracranial vessels. The role of TCDs has been observed for the screening of various conditions, including sickle cell disease, brain trauma, perinatal brain damage, cerebral malformations, and stroke. These observations indicate that TCDs could improve health care outcomes through early detection of conditions in a safe, repeatable, and reproducible fashion. Our own preliminary data collected by our Pediatric stroke program has indicated that TCD measured cerebral blood flow values vary with increasing age, from birth to late adolescence. As such, normative data is required along the age spectrum for screening and diagnostic purposes in children with presumed abnormalities. However, normative data in the pediatric population has not yet been established; instead, adult values are currently used. Here, we hypothesize that TCD values of cerebral blood flow will increase with age in healthy children, and there will be differences in normative values between same aged males and females. PubMed was searched using the terms "transcranial doppler", "transcranial ultrasound", "infants", "children", "pediatrics", "healthy", "control", "normative", "control subjects" and "reference values" to identify human randomized control trials, meta-analyses and reviews. Two studies found that girls had higher flow velocities in both middle cerebral and basilar artery than age matched boys, but no gender difference was observed in autoregulation in the middle cerebral artery. Six studies found a statistically significant increase in TCD values with child age, but the population size varied, and age cohorts ranged anywhere from neonatal to adult. In contrast, another study focussing on children aged 10 to adulthood found a rapid decrease in TCD values from childhood to adolescence. These differences are explained with a large study that included multiple age cohorts from neonatal to adult. This study found increased TCD values with age in the anterior cerebral artery and in the right and left middle cerebral arteries, but found these values to peak at 5 to 6 years. After this age, the velocities decreased linearly and approached normative adult values. Hence, TCD values in healthy infants and children of both sexes are different from adult controls, highlighting the need to establish and implement a specific normative pediatric baseline of TCD standards. This pediatric TCD baseline is essential for comparison with children experiencing a disease involving intracranial blood vessels for both screening and diagnostic purposes. As cerebral arteries are affected as a result of various clinical conditions, the role of TCDs in screening, diagnosing, and treating a wide array of diseases can also be determined using an established pediatric baseline.

Funded By: Alberta Innovates Summer Research Studentship

women & children's health research institute

Abstract #:	101
Presenter:	Rajesh Alphonse
Supervisor:	Rosychuk, Rhonda
Title:	Emergency Department Use in Children and Youth Facing Death Secondary to Self-Harm: A Population-Based Cohort Study in Alberta, Canada
Authors:	Rajesh Alphonse, MBBS, MTech, PhD, Pediatrics PGY4
	Rhonda J. Rosychuk, Ph.D., P.Stat., PStat®(ASA)
Theme:	Children's health and well-being

Background

In Canada, death by self harm (SH) is the second highest cause of mortality in people aged 15-24 years and the emergency department (ED) is one primary portal of entry into the healthcare system for individuals with SH behaviour. Studying the demographic/clinical characteristics of this high-risk population in the context of SH-associated ED presentations is critical to developing efficient and evidence-based SH prevention/treatment services. Using linked population based databases, we examine visits made by children and youth aged 10-24 yrs for SH reasons to EDs in Alberta.

Methods

This retrospective cohort study uses data from the National Ambulatory Care Reporting System (NACRS). The study population consists of Albertan youth (aged 10 to 24 yrs) during the study period from 2010/11 to 2014/15. The case definition (n = 118) is any youth in this population who presented to an Alberta ED for injury secondary to intentional SH and who either died in the ED or died within 30 days of an ED visit (due to SH or otherwise). Summary statistics described the patients and multivariable logistic regression modeling was performed.

Results

Among 118 individuals in the death cohort, 64.4% (n = 76) died due to SH. SH and non-self harm (non-SH) groups were similar in gender distribution (males, 67.1 % vs 64.3%) with the former group having a lower mean age (median 18 vs 21.5, p = 0.001). No major difference noted in the proportion of SH vs non-SH deaths in fiscal years studied (2010/11 to 2014/15). Four times as many individuals in the SH group were admitted in level-1 triage code ("resuscitation", n = 51) compared to non-SH group (n = 12). The Edmonton zone recorded the highest number of SH deaths in the study cohort (n = 32), four times as many non-SH deaths (n = 8) in the zone. The most frequent method of fatal self harm was by hanging, strangulation or suffocation (n=59; 50%). After adjusting for covariates, being in the 15-19 year age group was independently associated with increased likelihood of death due to self harm (Odds ratio [OR]2.75, 95% confidence interval [CI] 1.05 to 7.61, p = 0.043). Occurrence of death in the emergency department (ED), in contrast to death happening in the community after discharge, was also independently associated with self harm being the reason for death (OR=3.03, 95%CI 1.11 to 9.0, p = 0.0356). Sex, number of ED visits prior to death or the number of hours spent in the ED during a given admission showed no significant association with self harm death.

Conclusion

Our observation indicates that the 15-19 year age group is at an increased risk for self harm death and these deaths are more likely to happen in the ED during presentation for self harm. Future steps include: (i) comparing the study population with other youth presenting to the ED for mental health reasons and/or non-fatal self-harm behaviour, (ii) widening scope of study to include deaths by self-harm that did not have an ED component, (iii) analysing contributors for fatal self-harm behaviour such as social/family reasons and (iv) examining utilization of allied mental health professionals (eg. psychologists) by the youth presenting for SH.

Funded By: WCHRI Resident/Clinical Fellow Trainee Research Grant (1st January 2018 - 31st December 2020)

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Alberta Health Services

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Abstract #: 99
Presenter: Bushra Anjum
Supervisor: West, Lori
Title: The role of sex and the microbiome in production of 'natural' antibodies: impact on ABO antibodies in a mouse model
Authors: Bushra Anjum, Ibrahim Adam, Jean Pearcey, Kesheng Tao, Bruce Motyka and Lori J. West

Dept. Pediatrics, Alberta Transplant Institute, Canadian Donation and Transplantation Research Program, University of Alberta
Theme: Children's health and well-being

Background: ABO histo-blood group incompatibility is a barrier in solid organ transplant due to 'natural' preformed ABO antibodies. The ABH glycan microarray, a novel technique developed in the West lab, was used to determine the isotype (IgM/IgG) and ABH subtype specificity (subtypes I-VI) of natural ABO antibodies in a mouse model. We previously found that BALB/c (BALB) mice produce anti-A antibodies that are specific to subtypes III/IV A-antigens whereas antibodies specific to subtype II A-antigens were low/absent. Females had significantly higher levels of anti-A antibodies compared to males; moreover, females, but not males, showed a distinct shift in anti-A antibody production from IgM to IgG isotype at about the age of sexual maturity (6-9 weeks). It has been hypothesized that natural ABO antibodies develop due to cross-reactivity with components of the gut microbiome. To test this hypothesis, we examined serum ABO antibody levels in germ-free and conventionally-housed male and female mice of different ages.

Methods: Germ-free mice and conventionally-housed mice included the inbred strains C57BL/6 (B6) (females/males, n=10 /10) and BALB (female/males, n=10/10), and the outbred strain Swiss Webster (SW) (females/males, n=4/6). Plasma obtained from tail bleeds at different ages was assessed by ABH glycan microarray for ABO antibodies, including subtype specificity and antibody isotype.

Results: Anti-A and anti-B antibodies were present in germ-free B6, BALB and SW mice at levels similar to that of conventional mice. At 4-weeks of age, IgG (but not IgM) anti-A antibodies were detected in male and female mice at levels similar to that of older (12 weeks) female mice. Anti-A antibodies were present in male mice >8-weeks of age, however these were at low levels vs female mice and remained mostly IgM. In female mice, anti-A antibodies were mostly IgG isotype at 4-weeks of age, predominately IgM isotype at 8-weeks of age, and then shifted to mostly IgG isotype by 12-weeks of age. Anti-B antibodies were detected in both sexes by 8-weeks of age, remained mostly IgM, and were present at lower levels vs anti-A antibodies. Most natural anti-A antibodies, in germ-free or conventionally-housed mice, were specific to subtypes III/IV whereas antibodies specific to subtype II antigens were low/absent.

Conclusion: The distinct IgM to IgG anti-A antibody class-switching in female mice at about the time of sexual maturity (8 weeks) may provide early immunity to pups through passive transfer of IgG anti-A antibody during pregnancy. Detection of natural anti-A antibodies in germ-free mice combined with higher levels of natural anti-A antibody in females vs males suggests a unique sex-dependent, alternative mechanism of natural ABO antibody production than cross-reactivity with gut microbiome antigens.

Funded By: We kindly acknowledge germ-free mouse serum samples from Drs. Ben Willing (UofA) and Kathy McCoy (UofC). This research was funded by the Alberta Innovates Summer Studentship Award and WCHRI Summer Student Award through generous support of the Stollery Children's Hospital Foundation.

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Abstract #:	21
Presenter:	Nayara Antunes Lopes
Supervisor:	Olson, David
Title:	Appropriate collection of placental tissues maintains mRNA and protein consistency across time, villi biopsies, and subjects
Authors:	Lopes NA, Fang X, Penaherrera M, Oberlander T, Schuetz J, King S, Kildea S, Vaillancourt C, Robinson W, Olson DM
Theme:	Pregnancy and developmental trajectories

Introduction: Proper functioning of the placenta is essential for healthy fetal growth and development. Pregnancy-related complications such as preeclampsia can occur as a result of dysfunctional placentas, which can lead to poor pregnancy and newborn outcomes. Therefore, the collection of appropriate placental tissue specimens is vital for molecular studies. The identification of candidate biomarkers of stress, inflammation, and placental dysfunction requires high quality placental samples collected within a consistent timeframe. This study investigates the stability of target biochemical analytes from samples collected from six placentas across nine time points and three placental regions, as part of the NIH Human Placenta Project. We also evaluated interplacental variation due to villi and collection over 48h.

Methods: Human placentas were collected from six heathy women undergoing elective caesarean sections at term in Vancouver, BC. Biopsies were extracted from three different placental regions: villi 1, near the umbilical cord; villi 2, peripheral region; villi 3, intermediate region. To evaluate the stability of biochemical analytes across a timeframe of 48 hours (T0-T48) following placenta delivery, nine collection times points were predetermined. Immediately upon processing, samples were snap-frozen and stored at -80°C until RNA and protein extraction. All nine time points and three villi from one patient and T1 and T2 hours as well as three villi from two additional patients were selected randomly to determine mRNA and protein abundance of target analytes. RT-qPCR was performed to assess placental inflammatory and stress markers such as cytokine receptors IL6R, IL1R, IL1RAcP, cyclooxygenase-2 (COX2) and prostaglandin F2α (PGF2α) expression. Protein concentration of cytokines TNF-α and IL-6 were measured by multiplex. Western blotting was conducted to compare protein abundance of two housekeeping proteins (Succinate dehydrogenase - SDHA and β-Actin) between patients, across time points, and region of collection for all patients. Data were analyzed using one-way ANOVA, $p<0.05$.

Results: Gene expression of all cytokine receptors, COX2, and PGF2α did not vary between patients, across time points, or by region of collection. When outputs from all 3 villi per placenta were combined, mean TNF-α and IL-6 protein abundance displayed a non-significant trend to decrease over 48 hours ($p=0.20$ and 0.22). The abundance of SDHA and β-Actin did not change between villi locations ($p>0.05$). Similarly, for all patients, no changes in reference proteins were observed between the nine time points ($p>0.05$).

Conclusion: Our study demonstrates that our collection and preservation method of placental tissues preserved gene expression of placental inflammatory markers over 48h following delivery of the placenta. Our data suggest that placental collection immediately after delivery using snap-freeze protocol is advised, but later processing of and regional differences in collected samples do not lead to differences in inflammatory markers and reference targets.

Funded By: National Institutes of Health (NIH)

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Abstract #:	92
Presenter:	Saeed Anwar
Supervisor:	Yokota, Toshifumi
Title:	A genotype-phenotype correlation study of exon skip-equivalent in-frame deletions across dystrophin to identify targets for exon-skipping therapies for Duchenne muscular dystrophy
Authors:	Saeed Anwar, Merry He, Kenji Rowel Q. Lim, Rika Maruyama, and Toshifumi Yokota
Theme:	Children's health and well-being

Introduction: Dystrophinopathies, a spectrum of X-linked muscular dystrophies that primarily affects boys, is caused by mutations in the dystrophin gene. Out-of-frame deletions represent most mutational events in Duchenne muscular dystrophy (DMD), the most lethal end of the spectrum. In contrast, in-frame deletions typically lead to a milder phenotype, Becker muscular dystrophy (BMD). Antisense oligonucleotide-mediated exon skipping, an emerging therapy that aims to convert out-of-frame transcript to in-frame, can induce truncated but partially functional dystrophin. The reading frame rule, however, does not always depict the predicted phenotype. We hypothesized that, through analysis of clinical and mutational data available in published literature and patient registries, we can determine promising targets of exon skipping therapy in dystrophin. We, therefore, sought evidence from patient databases and existing literature to obtain clinical data from exon skip-equivalent in-frame deletions and determine the best estimate of clinical outcomes of exon skipping therapy for each exon.

Methods: We collected clinical and mutation data from two patient registries, namely the UMD TREAT-NMD DMD database and eDystrophin. Also, we systematically conducted a detailed review of published literature available on PubMed and Google Scholar to compile phenotypic features of patients with large deletions. A total of 2,508 unique patients were identified to have in-frame deletions. We classified them into exon skip-equivalent mutations, i.e., in-frame deletions starting or ending at each exon, and compared the ratio of BMD patients across the gene using the Fisher's exact test.

Results: Theoretically, there are 1,408 potential in-frame large deletion patterns possible across the dystrophin gene. Our patient pool represented 191 (13.57%) of these potential in-frame deletions. Our analysis identified 26 exons, in which in-frame deletions starting or ending at, to manifest a significantly more severe phenotype. In contrast, we identified 7 exons, including exon 4, 45, 47, 48, 49, 53, and 55, to have a significantly milder phenotype, which are deemed promising therapeutic targets of exon skipping.

Conclusions: We identified promising therapeutic targets of exon skipping therapy based on clinical data from exon skip-equivalent in-frame deletions. However, caution should be taken in interpreting these data as other factors, such as differences of precise mutation patterns among patients and the variability of exon skipping efficacy among different exons, also need to be taken into account. This study suggests that patient data on genotype-phenotype correlation can help the rational design of exon skipping therapy.

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Abstract #: 52
Presenter: Tejal Aslesh
Supervisor: Yokota, Toshifumi
Title: Systemic delivery of a novel peptide-conjugated morpholino oligomer DG9-PMO improves symptoms in a mouse model of spinal muscular atrophy
Authors: Tejal Aslesh, Rika Maruyama, Toshifumi Yokota
Theme: Children's health and well-being

Introduction: Spinal muscular atrophy (SMA), an autosomal recessive disorder, is the most frequent genetic cause of infant mortality worldwide. It is caused by a mutation in the survival of motor neuron 1 (SMN1) gene. SMN2, an SMN1 paralogue, cannot produce enough SMN protein to compensate for loss of SMN1 in SMA. Antisense therapy is a promising strategy to treat SMA. Splice-switching oligonucleotides (SSOs) that bind to SMN2 intron 7 splicing silencer number 1 (ISS-N1) induce exon 7 inclusion and restore the production of proper full-length SMN2 (FL-SMN2) mRNA. Nusinersen (brand name Spinraza), the first approved drug for the treatment of SMA, is an 18-mer SSO. Despite its approval, significant problems persist including injection site adverse effects, treatment costs, and a requirement for highly invasive intrathecal injections. More importantly, recent studies revealed that SMA is a multi-organ disorder affecting the heart, liver, thymus, and spleen; however, nusinersen needs to be injected intrathecally due to renal toxicity and therefore can treat only motor neurons. As such, a compound providing effective yet safe delivery of SSO to the central nervous system (CNS) and body-wide organs is urgently needed to prevent SMA-related morbidity and death.

Methods: To improve the in vivo efficacy of SSOs through better cellular uptake, we developed a novel cell-penetrating peptide called DG9, identified through the in vivo screening in zebrafish. DG9 was derived and modified from a T-cell peptide that is at least 10-to-100-fold more efficient for cellular uptake than previously used peptides. We used DG9 conjugated to an SSO called phosphorodiamidate morpholino oligomer (PMO) targeting SMN2. DG9-PMO was subcutaneously injected into SMA mice to determine the in vivo efficacy. SMN2 expression was evaluated using quantitative PCR and Western blots. We also assessed the functional improvement with tests such as forelimb grip strength, their righting reflex ability, rotarod test, and hindlimb suspension assay.

Results: A single administration of DG9-PMO led to mean survival of 133 days compared to 8 days for non-treated (NT) mice. DG9-PMO-treated mice exhibited up to 10-fold higher expression of the full-length-SMN2 gene compared to NT control and a 5-fold higher expression than the unmodified PMO-treated mice in the CNS and body-wide tissues. These mice also showed significantly increased body weight and improved motor function. No apparent toxicity was observed.

Conclusion: DG9-PMO is a promising therapeutic option to treat SMA, which can overcome the necessity for invasive injections with a single peripheral administration and treat body-wide tissues without apparent toxicity.

Funded By: WCHRI Innovation Grant, Slipchuk SMA Research Foundation Research Grant, the Canadian Institutes of Health Research and the Canada Foundation for Innovation

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Abstract #:	129
Presenter:	Tara Azimi
Supervisor:	Montesanti, Stephanie
Title:	Exploring the experiences and support needs of mothers of children with type 1 diabetes: A qualitative descriptive analysis
Authors:	Tara Azimi
Theme:	Lifelong women's health

Type 1 diabetes (T1D) is increasing among children globally and is presently incurable. A recent worldwide study placed Canada sixth among the top ten countries with the highest rates of T1D in children and adolescents under the age of 15. Studies have reported that under the age of 13 years is a vulnerable developmental period when T1D can be most difficult to control, requiring constant vigilance and caretaking. T1D in children involves sudden and acute complications that lead to practical and emotional problems for patients and their families. Caring for a child with T1D is highly distressing and may lead to depression, anxiety, and caregiver burnout, which is the result of an individual's inability to cope with high levels of emotional, physical and financial stress. Although studies have reported on several psychological consequences of caring for children with T1D, no qualitative study has focused on the experience of mothers in Canada. Furthermore, there is little recent evidence on the supports that are most important to mothers. Understanding the experiences of mothers is critical given that they are often the primary caregivers and decision makers when raising children with a chronic condition. Research also finds that emotional, mental and physical consequences are greater for mothers as carers. Research Question: What are the experiences and support needs of mothers caregiving for a T1 diabetic child under the age of 13? Objective(s): (1) To advance academic knowledge on the experiences of caregiving among mothers of diabetic children, and (2) to identify the support needs of mothers caring for children with T1D to improve their health and mental well-being. Methods: I will use a qualitative design to examine the experience of caring for a child with T1D. Study 1: I will conduct a meta-synthesis, an approach combining findings from qualitative studies to identify common themes on caregiving experiences of primary caregivers of children with T1D. Study 2: Semi-structured interviews will be conducted with mothers in Edmonton caring for T1D children under the age of 13. A maximum variation sampling strategy will be used to guide the selection and recruitment of caregivers. Participants will be recruited from the Pediatric Diabetes Education Centre in Edmonton. I will use a qualitative description approach to provide a rich interpretation of the personal experience of caring for a child with T1D as depicted by participants, and the specific meaning they place on providing this care. Study 3: I will conduct focus groups to identify and prioritize support needs for mothers of T1D children. Strategies prioritised during the focus groups will be validated in a follow-up debriefing meeting where participants will rank the most important strategies to be implemented by health planning stakeholders. Semi-structured interviews and focus groups will be analyzed using content analysis. Significance of Research: Maintaining the health and well-being of mothers as caregivers is critical given that our health system relies on family caregivers as the backbone of care. Understanding the unique experiences and support needs of mothers caring for T1D children is necessary for planning, improving and advocating for services for this population.

Funded By: 1) This research has been funded by the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute.

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3) Public Health Doctoral Scholarship

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Abstract #:	130
Presenter:	Katherine Babyn
Supervisor:	Yuksel, Nese
Title:	Development of a survey to characterize cannabis use and perspectives in women for menopause symptoms
Authors:	Katherine Babyn, Maureen Chan, Amy McMurdo, Sue Ross, Nese Yuksel
Theme:	Lifelong women's health

Introduction

Menopause is a significant transition in a woman's life from a biological and psychosocial standpoint. Many women will experience at least one physical or mood symptom related to hormonal changes occurring with menopause. The use of cannabis for medical purposes has grown in Canada since legalization. Women may be choosing cannabis to help with symptoms commonly associated with menopause. Unfortunately, there is limited evidence regarding cannabis use in menopause. Our goal is to address this gap by developing a novel survey that will characterize medical and recreational cannabis use patterns and perceptions in women who self-report menopause signs and symptoms. A pilot study was conducted with the purpose to refine the survey tool for future research conducted in Alberta, Canada.

Methods

Survey questions were investigator-generated, with reference to literature and grounded in clinical experience. A survey draft was distributed to health professionals for expert review of content. A pilot study using one-on-one, cognitive interviews was completed to assess face validity, feasibility and appropriateness of the survey. Pilot participants were part of the survey's intended target population and recruited through word-of-mouth from known contacts (n=10; women, age ≥35, residing in Alberta). Results were presented as a qualitative summary of general understanding, assessment of content, and overall survey design. Participant comments were subjectively interpreted by the research team to identify survey items requiring revision. Survey responses from the pilot were displayed as frequencies to show patterns in initial data captured.

Results

The cross-sectional survey instrument was developed as a self-administered, online questionnaire with quantitative components (closed-ended, scale questions), taking approximately 10-15 minutes to complete. Sections included: demographics, self-report of health and menopausal status, and cannabis use habits and perceptions. The expert review (n=4) provided clinician-based comments on appropriately self-reporting and defining menopause status. Ten volunteers were interviewed for the pilot study. Feedback indicated the survey was appropriate in length for the topic, contained suitable response categories (including default options for sensitive survey items), and design was inviting and professional. Revisions were done to adjust misinterpreted wording and simplify medical jargon.

Conclusions

We developed a survey tool that was positively received by experts and target participants, with revisions completed prior to usage in a mixed methods study. By going directly to women to ask about their experiences, we will gain insights on if and how cannabis is used during menopause, identify future research needs, and establish a platform for the development of clinical resources for safe and appropriate use of cannabis.

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Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

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Abstract #:	53
Presenter:	Pranidhi Baddam
Supervisor:	Graf, Daniel
Title:	Osteoarthritis in the nasal septum?
Authors:	Pranidhi Baddam(1), Mark Nie(1), Daniel Young(2), Antoine Dufour(2), Daniel Graf(1)
	(1)School of Dentistry, University of Alberta
	(2)Department of Physiology & Pharmacology, University of Calgary
Theme:	Children's health and well-being

Introduction: Nasal septum is a cartilaginous structure that provides critical structural and growth support for the midface. Nasal septum deviation (NSD) is a relatively frequent abnormality, which can be associated with nasal airway obstruction and disordered breathing in children. The etiology of NSD is poorly understood, but its incidence increases during the midfacial growth spurt. Because the nasal septum cartilage is a hyaline cartilage similar to the knee cartilage and since the nasal cartilage contributes to the growth of the midface, we hypothesize that nasal septum deviation is a consequence of underlying cartilage differentiation and growth defects. Here we test this hypothesis in a mouse model for midfacial hypoplasia.

Methods: Mice with a neural crest-specific deletion of Bone Morphogenetic Protein 7(Bmp7) (Bmp7ncko) present with midfacial hypoplasia and nasal septum deviation. We investigated two time-points: 2 weeks, before NSD and 4 weeks, established NSD. Skeletal structures were assessed using micro-computed tomography (µCT). Molecular and cellular differences were established using histology, immunofluorescence and gene expression analysis. RNA sequencing and quantitative shot-gun proteomics was conducted on isolated nasal cartilage and the STRING database was used to identify differentially regulated cellular pathways in the nasal septum.

Results: µCT analysis confirmed the presence of NSD at 4 weeks but not at 2 weeks. At 2 weeks, a reduction in proliferation and an increase in apoptosis in the nasal septum was detected. The nasal cartilage was histologically inconspicuous at 2 weeks, however, structural changes were evident at 4 weeks. The normally hyaline cartilage showed signs of chondrocyte hypertrophy (expression of IHH) at the site of NSD. Molecular changes such as the down-regulation of HIF1 alpha in the nasal cartilage were evident at 4 weeks. Similarly, STRING analysis established that extracellular matrix organization and nitrogen metabolism were already de-regulated at 2 weeks preceding NSD.

Conclusion: Loss of BMP7 resulted in cellular changes in chondrocytes which altered nasal cartilage properties and compromised its growth, placing BMP7 as a critical factor regulating chondrocyte differentiation. Our findings are analogous to those observed in knee osteoarthritis, suggesting that NSD can occur as a consequence of underlying nasal septum cartilage growth and differentiation defects. Overall, NSD, in particular in connection with midfacial growth reduction might indicate altered chondrocyte biology in affected children.

Funded By: WCHRI Innovation Grant

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Abstract #:	61
Presenter:	Jessica Bennett
Supervisor:	Godbout, Roseline
Title:	Understanding the Role of DDX1 Expression in Neuroblastoma Response to Treatment
Authors:	Jessica Bennett, Lei Li, Jack Wang, and Roseline Godbout
Theme:	Children's health and well-being

Introduction:

Neuroblastoma is a paediatric cancer originating from neural crest cells and is the most lethal extracranial solid tumour in children. Over 60% of children diagnosed with high-risk neuroblastoma do not survive past age five. High-risk neuroblastoma is often associated with amplification (increased copies) of the MYCN oncogene. DEAD box proteins are involved in modification of RNA secondary structure and are involved in cellular stress response. Previous research undertaken by the Godbout lab indicates that the DEAD Box 1 (DDX1) gene is co-amplified with the MYCN gene in about 50% of high-risk neuroblastomas, and it may be possible that amplification or knockdown of the DDX1 gene in neuroblastoma cell lines could improve their survival following treatment with DNA damaging agents (ionizing radiation and chemotherapy drugs).

Hypothesis:

Based on the lab's prior knowledge of the role of DDX1, my hypothesis is that DDX1 knockdown will result in an improved cellular response to treatment, as DDX1 is known to play roles in cellular survival as well as in DNA double-strand break repair.

Methods:

Neuroblastoma resistance to treatment was measured indirectly using the soft agar colony formation assay. This assay selects for cancer cells and colony counts can be performed to determine the efficacy of treatment. The soft agar colony formation assay can be interpreted as one colony having originated from a single cancer cell. I am examining the effect of DDX1 knockdown on rate of colony formation in DDX1-amplified and non-amplified cell lines, both prior to and one hour post-treatment with ionizing radiation, and the chemotherapy drugs doxorubicin, vincristine, etoposide, bleomycin, and sodium arsenite.

Results:

Knockdown of DDX1 has opposite effects in DDX1-amplified and non-amplified cells. While knockdown of DDX1 decreases colony formation in DDX1-amplified cell lines, it results in increased colony formation in non-amplified cell lines. While knockdown of DDX1 had no effect on colony formation in cell lines treated with the microtubule-inhibiting chemotherapy drug vincristine, DDX1 knockdown resulted in an improved response to DNA-damaging chemotherapy drugs doxorubicin and etoposide in non-amplified cell lines. The opposite effect was observed in DDX1-amplified cell lines. There is not yet sufficient data to determine the effect of DDX1 expression on neuroblastoma resistance to ionizing radiation, bleomycin, or sodium arsenite.

Conclusion:

Based on my results, DDX1 likely plays a role in the DNA damage response. At basal levels, DDX1 may repair DNA damage induced by ionizing radiation and chemotherapy agents, whereas when DDX1 is overexpressed or knocked down, it is no longer able to perform this function to the same level, thus decreasing neuroblastoma resistance to treatment. Altering the levels of DDX1 could potentially increase the efficacy of radiation and certain chemotherapy drugs in neuroblastoma treatment, leading to a reduction in the mortality of infants and children diagnosed with high-risk neuroblastoma.

Funded By: WCHRI Summer Studentship - Stollery Youth Foundation

Abstract #:	43
Presenter:	James Benoit
Supervisor:	Scott, Shannon
Title:	Acute childhood illness knowledge tools for parents: an environmental scan of mHealth apps.
Authors:	Benoit JRA, Scott SD, Hartling L
	*Scott and Hartling are co-supervisors
Theme:	Children's health and well-being

Intro

Knowing when to take their sick child for healthcare is not easy for parents and not easy for our healthcare system, both in terms of resource utilization and healthcare personnel. Communicating complex health information to parents in a conventional manner has been ineffective due to overuse of jargon and information complexity: roughly 1 in 3 parents of children presenting to the emergency department have low health literacy. Further, pediatric emergency room visits have increased 30% in the last decade without a corresponding increase in hospitalization or case severity. Health decision resources for families with acutely ill children include telehealth (e.g., HealthLink), but utilization rates have been decreasing since 2014, suggesting it may not be meeting user needs.

Mobile health (mHealth) apps such as Pediatric SymptomMD and HANDi Paediatric may address parent/caregiver health literacy and improve parental confidence by providing health education and decision support. The purpose of this environmental scan is to examine available mHealth apps related to acute childhood illnesses on the Google Play and Apple App stores, and describe clinical topics covered, end-user focus, and functionality.

Methods

The Google Play and Apple App stores will be queried using 17 terms, developed in consultation with a research librarian. We will include apps containing information applicable to acute childhood (ages 0-18) conditions, available in Canada or US app stores, and intended for use as knowledge tools by parents (e.g. education or decision support, and not health tracking or interventional treatment). Two reviewers will independently assess each app for inclusion/exclusion, compare results and engage a third reviewer if ambiguity still exists. Relevant apps will be described and assessed independently by two reviewers using questions from the Mobile App Rating Scale (MARS), a validated app assessment framework, in addition to the American Psychiatric Association's app evaluation screening questions. Finally, apps will be assessed for accessibility and usability by parents with low health literacy.

Results

This work is ongoing. Apps will be compared on dimensions of engagement, functionality, aesthetics, and information quality. Results will be presented at WCHRI Research Day 2020.

Conclusion

Gaps in app coverage will be used to guide the development of an innovative mHealth app that focuses on accessible communication with parents (e.g. via voice input of acute childhood illness symptoms), and matches parents with an appropriate knowledge translation (KT) tool for health decision support. The app will passively trace subsequent health decisions to assess KT tool impact.

Funded By: Stollery Science Lab Distinguished Researcher funding - awarded to Hartling & Scott.

women & children's health research institute

Abstract #: 86
Presenter: Gurreet Bhandal
Supervisor: Alexander, R Todd
Title: Mutations in SVEP1 may cause hypophosphatemic rickets via inappropriately increasing FGF23 expression in osteoblasts

Authors: Gurreet Bhandal, Wanling Pan, Todd Alexander

Theme: Children's health and well-being

We identified a 9-year-old girl with hypophosphatemic rickets, who was negative for the known causes of this disorder, including PHEX mutations. However, like patients with PHEX mutations, she had increased circulating fibroblast growth factor 23 (FGF23) levels, a hormone that reduces the expression of renal sodium-phosphate cotransporters, thus increasing urinary phosphate excretion. A trio analysis after whole exome sequencing on the patient and her parents identified 9 de novo mutations, including a mutation in the SVEP1 gene, which has never been reported previously. The purpose of this study was to explore how a mutation in the SVEP1 gene in this patient could be causing hypophosphatemic rickets. I hypothesized that FGF23 production and release from osteoblasts is attenuated by SVEP1. Due to COVID-19, most of the work was in-silico studies and literature review. However, we completed some cell culture and qPCR work to test the effects of active vitamin D or calcitriol (implicated in bone mineralization) on SVEP1, FGF23, and FGF23 receptor expression in MC3T3 cells, an immortalized murine osteoblast cell line. In silico studies, specifically the BioGPS database, revealed the greatest SVEP1 expression in mouse osteoblasts. Literature review and NCBI and GeneCards databases revealed that SVEP1 is a cell adhesion molecule that triggers intracellular signaling pathways modulating cell proliferation and differentiation; it displays 99.24% gene homology to chimpanzees and 81.69% gene homology to mice. Molecular modelling through PROTTER and UniProt databases predicted SVEP1 to be a mostly extracellular 3571 amino acid protein with 4 extracellular domains (von Willebrand factor type A, Sushi, epidermal growth factor like, hyalin repeat domains), 1 transmembrane domain (pentraxin domain), over 80 cysteine residues that have the potential to form disulfide bonds, a signal peptide at the N terminus, and 5 N-glycosylation sites. Using Array Express, we obtained microarray data in which the Phex gene was knocked down in mouse cortical bone; after interrogating the data set, we found that mice with Phex deletions have significantly more SVEP1 expression than wild type mice. Data obtained from JASPAR revealed 26 Vitamin D receptor binding sites upstream of the SVEP1 promoter. Our experimental studies suggest that compared to untreated pre-osteoblasts, Vitamin D treated differentiated osteoblasts have relatively lower FGF23 receptor and SVEP1 expression while Vitamin D treated pre-osteoblasts have relatively higher FGF23 and SVEP1 expression. The findings imply that a mutation in the SVEP1 gene in our patient could be causing excessive FGF23 production and secretion, perhaps leading to problems in osteoblast differentiation. Future directions include validating a SVEP1 antibody to experimentally confirm its localization through immunofluorescence studies, using SVEP1 siRNA to knock SVEP1 down in cell lines and to study FGF23 production and release, and replicating qPCR experiments for greater clarity of results. These findings could explain why this young woman has hypophosphatemic rickets and help improve diagnosis and care for future patients while also providing medical staff with a better idea on potential treatments for hypophosphatemic rickets.

Funded By: Alberta Innovates Summer Research Studentship

Abstract #:	31
Presenter:	Vivian Biancardi
Supervisor:	Pagliardini, Silvia
Title:	Neural crest-specific deletion of Bmp7 leads to midfacial hypoplasia, nasal airway obstruction, and disordered breathing
Authors:	Pranidhi Baddam, Vivian Biancardi, Daniela M Roth, Farah Eaton, Claudine Thereza-Bussolaro, Rupasri Mandal, David S Wishart, Amy Barr, Joanna MacLean, Carlos Flores-Mir, Silvia Pagliardini, Daniel Graf
Theme:	Children's health and well-being

Introduction

Pediatric obstructive sleep apnea (OSA), a relatively common sleep respiratory breathing disorder (SRBD) affecting approximately 1-5% of children, is often caused by anatomical obstruction or collapse of the nasal and/or pharyngeal airways. The resulting sleep disruption and intermittent hypoxia lead to various systemic morbidities including cardiovascular, metabolic, neurocognitive, and behavioral dysfunctions. The multifactorial etiology of OSA reflects the challenges clinicians face for treatment options. Predicting the development of OSA from craniofacial features alone is currently not possible and a controversy remains if upper airway obstruction facilitates reduced midfacial growth or vice-versa. Currently, there is no rodent model that summarizes both the development of craniofacial abnormalities and upper airway obstruction. Mice with neural crest-specific deletion of Bmp7 (Bmp7ncko) present with micrognathia and midfacial hypoplasia. We hypothesize that this mouse model recapitulates many features observed in OSA. Our objectives are to (1) delineate the sequence of craniofacial changes during postnatal (P) development (P days 14, 21 and 30) in Bmp7ncko mice, and (2) evaluate the physiological implications on breathing pattern during normoxic (21% O2), hypoxic (10% O2) and hyperoxic (40% O2) conditions, metabolism and exercise performance at P30 and 45.

Methods

To test the objective 1, we used micro-computed tomography (µCT) and morphometrics analysis. To test the objective 2, we used whole-body plethysmography for breathing recordings, Comprehensive Lab Monitoring System for oxygen consumption and Treadmill Exhaustion Test for exercise performance.

Results

Bmp7ncko mice presented with midfacial hypoplasia and turbinate hypertrophy at P14 that persisted at P30, when nasal septum deviation emerged along with shorter, more acute angled cranial base. All these craniofacial abnormalities contribute to nasal airway obstruction and were associated with respiratory irregularities in 50% of the Bmp7ncko mice, such as greater number of spontaneous apnea (SA) events, an increase in the prolonged post sigh apnea events, lower breathing frequency and longer breath cycles in normoxic conditions. The hypoxic ventilatory response was similar in Bmp7ctrl and Bmp7ncko mice, despite the greater drop in body temperature in Bmp7ncko mice; and hyperoxia exposure did not affect the number of SA events. We also observed an overall reduced oxygen consumption and exercise capacity in the Bmp7ncko mice.

Conclusions

This study demonstrates that craniofacial abnormalities predispose mice to nasal airway obstruction postnatally that could lead to respiratory disturbances and inability to sustain physical exercise. Therefore, the Bmp7ncko mouse can be used as a foundation to identify molecular mechanisms underlying craniofacial abnormalities resulting in airway obstruction to better understand the genetic component contributing to obstruction in children with SRBD.

Funded By: WCHRI Innovation Grant (DG), the American Association of Orthodontists Foundation

(CFM and DG), Canadian Institutes of Health Research (CIHR) (SP) and WCHRI Postdoctoral Fellowship Program (VB).

Abstract #:	131
Presenter:	Kristin Black
Supervisor:	Pin, Sophia
Title:	Venous thromboembolism in patients receiving neoadjuvant chemotherapy for ovarian cancer
Authors:	Kristin A. Black, Sunita Ghosh, Nilanchali Singh, Pamela Chu, Sophia Pin
Theme:	Lifelong women's health

Objectives

The purpose of this study is to determine the incidence of venous thromboembolism (VTE) in patients with ovarian cancer receiving neoadjuvant chemotherapy (NACT). Furthermore, to assess the effect of VTE on treatment trajectory and overall survival, and identify risk factors for VTE in patients undergoing NACT.

Methods

This is a retrospective cohort study of patients diagnosed with ovarian, fallopian tube, or primary peritoneal cancer treated with NACT between 2013 to 2016 in Alberta, Canada. The primary outcome was incidence of VTE during NACT. The secondary outcomes were risk factors for VTE and overall survival. Demographic data, chemotherapy treatment, and incidence of VTE were collected. Statistical analysis included Kaplan-Meier estimates, and univariate and multivariate Cox regression analysis.

Results

284 patients were included in the study. The average age at diagnosis was 63.8 years old. The incidence of VTE during NACT was 13.3%. The median overall survival for the study population was 25.23 months. Kaplan-Meier estimates demonstrate a decrease in overall survival in patients who had a VTE during NACT (15.0 months, 95% CI 14.5 - 16.5) compared to patients who did not (26.8 months, 95% CI 22.8 - 30.9) ($p < 0.0001$). Patients who had a VTE during NACT were less likely to undergo interval debulking surgery, and were more likely to be treated with chemotherapy alone. Multivariate analysis identified albumin < 35 g/L, BMI > 30 kg/m2, and serous histology as risk factors for VTE.

Conclusions

Patients with ovarian cancer receiving NACT are at an increased risk of VTE, which is associated with a decreased overall survival. These findings suggest that thromboprophylaxis may have a role in this patient population.

Funded By: This project did not receive funding.

Abstract #:	22
Presenter:	Cleighton Boehme
Supervisor:	Hornberger, Lisa K
Title:	The Diagnostic Yield of Current Indications for Fetal Echocardiography
Authors:	Cleighton Boehme, Deborah Fruitman, Luke Eckersley, Robert Low, Jeffrey Bennett, Angela McBrien, and Lisa k Hornberger
Theme:	Pregnancy and developmental trajectories

Introduction: Fetal echocardiography (FE) has permitted the prenatal diagnosis of a large spectrum of structural, functional, and rhythm related cardiac disease before birth. There are many indications for fetal echocardiography, all for pregnancies at increased risk of fetal heart disease (FHD). Knowledge of the diagnostic yield of such indications would lead to optimized triaging of those at highest risk of FHD and perhaps a reduction in referrals for lower risk indications to reduce unnecessary resource use. In the current study, we sought to examine the diagnostic yield of FE indications. We hypothesized a referral for suspected fetal cardiac pathology provides the highest yield, whereas other common indications for referral (e.g. maternal diabetes) are associated with much lower yields of FHD.

Methods: We examined the reports of all pregnancies referred to our program for FE between January 2009 and December 2018 to define indication for referral, gestational age at referral, and findings, specifically whether there was no FHD, mild or possible FHD, or moderate to severe FHD. Indications for referral were organized into 13 categories.

Results: Over the study period, 10,327 unique pregnancies were encountered, of whom 462 had mild or possible FHD and 1183 had moderate to severe FHD. Of all indications, extracardiac pathology (20.3% of all pregnancies), suspected FHD (16.8%), and maternal diabetes (16.1%) were among the most common. Of the 13 categories, the indication with the highest yield was a suspected FHD on outside ultrasound (54.6% any FHD, 44.5% moderate/severe FHD). Three categories had more moderate yield of moderate/severe FHD (10-20%) including: arrhythmia (41.5% any FHD, 15.6% moderate/severe FHD), suspected genetic disorder (14.1%, 10.7%), and twins/multiples (12.1%, 10.2%). Three categories had low to moderate yield (3-10% moderate/severe FHD): extracardiac pathology (9.0%, 6.3%), family history of genetic abnormality (4.4%, 3.8%), and heart not well seen (4.9%, 3.1%). The lowest yield categories (1-2% moderate/severe FHD) were assisted reproduction (2.9%, 1.9%), prior fetus/child with structural heart disease (3.6%, 1.8%), other maternal exposure (3.6%, 1.6%), maternal diabetes (2.7%, 1.3%), other family history of structural/functional heart disease (3.2%, 1.1%), and maternal structural heart disease (3.2%, 1.0%).

Conclusions: Suspected FHD, the second most common indication for referral, provided the highest diagnostic yield for any and moderate/severe FHD. Maternal diabetes, on the other hand, represented a large proportion of total referrals, but had a much lower diagnostic yield. This data could lead to improvements in guidelines for fetal echo referral and contribute to optimize triaging of affected pregnancies.

Funded By: WCHRI/RAH Foundation Innovation Grant (Hornberger), DoP Graduate Student Recruitment Scholarship

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Abstract #:	152
Presenter:	Amy Boucher
Supervisor:	Charlton, Carmen L
Title:	Determining the cell-mediated immune response for women with low antibody titers to rubella virus in the Alberta population.
Authors:	Amy M. Boucher, Carmen L. Charlton
Theme:	Pregnancy and developmental trajectories

Introduction: Rubella is generally regarded as a mild, self-limiting illness, however, if acquired within the first 10 weeks of pregnancy the fetus can develop congenital rubella syndrome, which can cause deafness, cognitive impairments, or fetal death. Rubella vaccination has been highly successful, resulting in no indigenous infections in Canada since 2005.

Antibody levels are used to determine whether an individual is immune to infection. However, cutoffs for antibody testing (i.e. susceptible vs. immune to infection) were determined when rubella virus was still circulating and antibody titers were generally higher. Because the level of antibody is decreasing in our population, we no longer know if the cutoff accurately differentiates between susceptible and immune.

Methods: Cell mediated immune response (CMIR) against rubella was assessed by measuring IL-6 and IFN-γ cytokine production from isolated peripheral blood mononuclear cells upon exposure to rubella antigen in a study population of 20 university-aged students. CMIR was then compared to measured antibody levels to assess the correlation between cytokine release and antibody level. Correlates of antibody levels were assessed using Chi-square or Fisher's exact tests for categorical data and Mann-Whitney tests for continuous variables. Multivariable logistic regression was used to identify independent correlates of low antibody levels.

Results: CMIR from the university-aged population (all with antibody levels >10 IU/mL) showed an increase in IL-6 and IFN-γ production upon exposure to rubella antigen. Compared to control samples (not exposed to antigen), samples treated with rubella antigen had average IL-6 concentrations increase from 2680 (±3653) pg/mL to 6989 (±1166) pg/mL and IFN-γ concentrations increase from 44 (±7) pg/mL to 72 (±9) pg/mL after 3 days. These data show the CMIR in individuals with high antibody levels is detectable and robust, however, further testing is needed in our target prenatal population.

To do this, we will test 100 pregnant women with antibody levels below protective cutoffs (<10 IU/mL) and 100 pregnant women with antibody levels above protective cutoffs (≥10 IU/mL) for IL-6 and IFN-γ cytokine production. CMIR and antibody levels will be correlated to examine whether women with antibody levels <10 IU/mL could mount an appropriate immune response upon viral challenge.

Finally, we will examine the effect of a third dose of vaccination for women with antibody levels <10 IU/mL and who have received a full 2 doses of vaccination. Women will be asked to donate blood prior to the third dose and 4-months after. The change in their CMIR will be measured using the same methods described above. CMIR will be stratified by pre- and post-third vaccine dose, antibody levels, age, and time between doses, to assess the effectiveness of a third dose of MMRV vaccine in our population.

Conclusion: Results from our pilot study show CMIR can be measured and are robust in individuals with antibody levels above the cutoff. Our study will help address the public health question of whether to add an additional dose of vaccine to women who are found to be below the antibody cutoff, and whether our population is protected from rubella infection despite waning antibody levels.

Funded By: Merck

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Abstract #: 132
Presenter: Jenneffer Rayane Braga Tibaes
Supervisor: Richard, Caroline
Title: Effect of a North American Diet on Cardiometabolic Risk Factors in Women with Obesity and with or without Insulin Resistance: Preliminary Analysis of the NutrIMM Study
Authors: Jenneffer Rayane Braga Tibaes, Maria Ines Barreto Silva, Alexander Makarowski, Bethany Wollin, Paulina Blanco, Donna Vine, Sue Tsai, Caroline Richard
Theme: Lifelong women's health

Introduction: Heart disease is the primary cause of mortality in women in North America. Diet quality plays an important role in cardiovascular diseases. High-fat diets, usually low in fruits and vegetables, are associated with the development of obesity and insulin resistance (IR). No studies to date have evaluated the effects of a North American diet, under controlled feeding conditions, on cardiometabolic risk factors in women. This study aimed to investigate the effect of consuming an isocaloric North American high-fat diet on cardiometabolic risk factors in women.

Methods: This is a 3 parallel-arm trial in controlled feeding conditions being conducted at the Human Nutrition Research Unit, at the University of Alberta. Three groups of women (Lean-normoglycemic (lean-NG; n=2), Obese-NG (n=6) and Obese-IR; n=3) consumed a diet containing 35% fat (12.5% saturated fat), 48% carbohydrates (mainly refined), and 17% protein for 4 weeks. All food/meals were provided to participants for the duration of the study. Blood samples were collected in the fasting state before and after the dietary intervention and cardiometabolic risk factors were measured. Paired t-test was used to assess differences in variables before and after the intervention and one-way ANOVA was used to compare changes among the three groups.

Results: After the intervention, reductions in IR parameters were observed for HbA1c (-0.10±0.14), insulin (-2.81±3.21), and homeostatic model assessment (HOMA) (-0.65±0.73) (all $p<0.05$). The magnitude of the change within each group (i.e. delta pre-post) for HOMA index tended to be higher in Obese-IR (-1.37±0.61) compared with Obese-NG (-0.48±0.63) and lean-NG (-0.01±0.06) groups ($p=0.07$). Except for a reduction in high-density lipoprotein cholesterol levels (-0.14±0.09; $p<0.01$), no other effect was observed on the lipid profile of women consuming a North American diet.

Conclusion: In conclusion, our preliminary data show that a North American diet, under isocaloric controlled feeding conditions, improved IR parameters in women with obesity and IR while having a minor effect on the lipid profile. Our findings should be interpreted cautiously due to the small sample size.

Keywords: cardiovascular risk; insulin resistance; women; North American diet.

Funded By: Canadian Institutes of Health Research

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Abstract #:	44
Presenter:	An Bui
Supervisor:	Bolduc, Francois
Title:	The application of machine learning technology in addressing the "conundrum" of medical information literacy in media
Authors:	An Bui, Abhishek Dhankar, Osmar Zaiane, Francois Bolduc
Theme:	Children's health and well-being

The spread of fake news has been one of the main causes for the rise of controversial and adverse child medical treatments, such as the use of bleach and chelation therapy as "cures" for autism. Such news can be found virtually anywhere, including personal blogs, online articles, podcasts, chat rooms, games, forums, and social media. Most of these claims are written very persuasively and are 70% more likely to be shared. As we increasingly rely on the Internet for information and communication, there is a constant need to fact-check our sources. This creates a demand for a screening tool to verify if the information is supported by scientific evidence and medical research.

Our research project aims to design a digital filter for false medical contents called MedFact. Harnessing the power of artificial intelligence, MedFact could determine if a controversial online source contains fabricated medical claims in hopes of improving public health literacy. MedFact also ensures that only valuable and reliable medical information is presented to viewers, especially patients who are in need living in rural areas with limited access to professional assistance.

Based on machine learning principles, we generated a database comprised of verified false claims and search queries for MedFact's training. The second step involved collecting verified false medical claims from the literature (e.g. PubMed). We formulated various searchable queries from these claims such as "cure", "miracle", "complete treatment", and "controversies". The queries were used to collect multiple websites and articles that potentially contained false information from Google. These websites were manually compiled and annotated for the type of false statements they contained as well as the medical conditions being referred to. Lastly, we sorted the websites into one of the following: "false", "exaggerated", "unproven", "misleading", and "true" claims. This completed the training database needed for MedFact to identify true and false information from any given website.

With a focus on neurodevelopmental disorders (for example: dyslexia, attention deficit hyperactivity disorder, and autism spectrum disorder) we now have constructed a large database of more than 60 false websites for MedFact's training. We also have accumulated 13 false medical claims of 200 different clinical disorders. Using these data, our trial runs have shown positive results with high accuracy of detecting false information from novel websites. We aim to continue improving MedFact by adding more annotated websites to our database and expand the type of medical conditions MedFact can detect.

Funded By: CIHR and NSERC in partnership with WCHRI, KBHN and CASDA

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Abstract #:	78
Presenter:	Alyson Campbell
Supervisor:	Scott, Shannon
Title:	An environmental scan of Canadian Internet resources and Apps about paediatric concussion.
Authors:	Alyson Campbell, RN, BScN, PhD Candidate; Dr. Vickie Plourde, PhD; Dr. Lisa Hartling, PhD; Arjun Bains, BScN Student; Dr. Shannon D. Scott, RN, PhD
Theme:	Children's health and well-being

Background: Concussions are complex injuries affecting millions of children worldwide. Various organizations have developed educational supports about childhood concussions in a variety of formats including handouts, training tools and videos. Despite the plethora of resources available, uncertainty in how to manage childhood concussions prevails, and knowing which resources are relevant and accurate can be confusing. For many Canadians the Internet and smartphone applications are easily accessible and offer information pertinent to one's health and well-being, including those suffering from concussion. However, research is needed to discover information gaps in relation to these Internet resources and Apps to reduce future resource redundancies and improve knowledge translation, ultimately improving concussion care and outcomes for children and families.

Objectives: To identify Canadian-based Internet resources and Apps for paediatric concussion and extract information about each resource to identify gaps.

Methods: We conducted an environmental scan (ES) of Canadian-based Internet resources and Apps on paediatric concussion. Three main sources were sequentially searched: The Internet (Google) and two App stores (Apple, Google Play). Interviews with key informants from Canadian concussion organizations were conducted to further inquire about resources. Resources meeting the inclusion criteria were evaluated using the Suitability Assessment of Materials (SAM).

Results: 300 Internet websites and 200 apps were searched. A total of 53 resources (51 web-based resources and 2 Apps) met the inclusion criteria. Target audiences included parents (n=11), health care professionals (n=6), teachers (n=5), coaches (n=3), and youth (n=2). Twenty-six resources did not have a specified target audience. Symptoms (n=35), treatment (n=28) and return-to-play (n=24) information was the most common. Portable document format (PDF) (n=20) and infographics (n=8) were the most common formats. SAM scores ranged from 36.8% to 97.2%.

Conclusions: A limited number of resources were developed specifically for children or youth who have sustained concussions, and those that did were sport specific. Only one resource shared a patient or family experience with concussion. Future resources aiming to improve the knowledge and awareness of pediatric concussions requires more inclusivity beyond the athletic community. Additionally, the knowledge and perspectives of those using these resources should be incorporated into their development to enhance relevance, cultural appropriateness and sense-making. More creative and innovative formats may also enhance the overall usefulness and effectiveness of these resources.

Funded By: AC has been funded for this research through the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

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Abstract #:	45
Presenter:	Alyson Campbell
Supervisor:	Scott, Shannon
Title:	An environmental scan of research and health-related youth advisory groups in Canada
Authors:	Alyson Campbell, RN, BScN, PhD Candidate, Lisa Hartling, PhD, Michelle Chan, PhD, Sarah Elliott, PhD, Hannah Brooks, Msc, Shannon. D. Scott, RN, PhD
Theme:	Children's health and well-being

Background: Engaging youth throughout the research process improves the quality and relevance of outcomes and ensures that research projects and knowledge translation tools align with the needs and perspectives of youth. Youth advisory groups provide one way for youth to express their thoughts and opinions on issues that affect them.

Objective: To conduct an environmental scan to better understand what is currently known about research and health-related youth advisory groups (referred to herein as groups) in Canada and identify best practices of these groups. This information will help inform on whether there are any groups that our research programs could work with to support our activities in knowledge translation, as well as inform the potential development of our own group.

Methods: Google and supplementary search methods (e.g., contacting organizations) were used to search for research or health-related groups in Canada. Information about the groups was extracted from websites and key group informants. Twelve interviews were conducted with 13 group representatives and two youth members. Interviews were recorded and transcribed verbatim. Transcripts were analyzed using thematic analysis.

Results: We identified 37 research or health-related groups in Canada. Groups were part of a hospital or healthcare facility (n=15), non-profit or health organization (n=9), or research group or network (n=7). The majority focused on a specific content area (n=23), of which mental health was most common (n=15). Over half the groups advised on health services for children and youth (n=24). Age and number of members across groups varied. Members' ages ranged from 9-35 years. Number of members ranged from five to 60 members.

Interviews identified nine themes relating to group practices: a) group purpose, b) group development process, c) group operations, d) group organizational structure, e) level of adult and youth involvement, f) membership and recruitment practices, g) meeting practices, h) access to the group, and i) advice/recommendations. Challenges and facilitators to the success of groups were described within these themes: a) retaining engagement, b) creating a safe environment, and c) putting youth in positions of influence.

Conclusion: This study provides a comprehensive overview of research and health-related youth advisory groups in Canada. Our findings provide insight into what research and health-related groups currently exist, including their purpose, structure, operations, and best practices. This information can be used to identify groups that researchers and other relevant stakeholders could access, as well as inform the development of a new group.

Funded By: Stollery Distinguished Researchers & WCHRI

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Abstract #:	1
Presenter:	Huachen Chen
Supervisor:	Fu, Yangxin
Title:	Transcription factor ZIC2 regulates multiple biological processes and promotes tumorigenic phenotypes in ovarian cancer
Authors:	Huachen Chen*, Krista Vincent, Luara Lee, Zhihua Xu, Olena Bilyk, Jiahui Liu, Guihua Zhang, Lynne-Marie Postovit, YangXin Fu
	Department of Oncology, Faculty of Medicine and Dentistry, University of Alberta
Theme:	Lifelong women's health

Objectives

Epithelial ovarian cancer (EOC) is the leading cause of gynecological cancer death in women. Ovarian cancer stem cells (CSCs) are resistant to conventional therapies and responsible for cancer recurrence. Combined therapy that targets both bulk cells and CSCs would be a more effective therapeutic strategy to manage this lethal disease. Transcription factor ZIC2 has emerged as an oncogenic factor in various types of cancer. This project aims to investigate the pro-tumorigenic role of ZIC2 in EOC and the underlying mechanisms.

Methods

ZIC2 expression in immortalized human ovarian and fallopian tube epithelial cells, human EOC cell lines, as well as patient-derived xenografts (PDXs) was measured by Western blotting and immunohistochemistry (IHC). ZIC2 knockout (KO) or overexpression models were generated in EOC cell lines. The effect of ZIC2 KO or overexpression on gene expression (real-time RT-PCR, RNA-sequencing, Western blotting and IHC), the percentage of CSCs (ALDEFLUORTM assay), proliferation and survival (neutral red uptake assay and clonogenic assay), migration (Transwell migration assay), anchorage-independent growth (soft agar assay), self-renewal (limiting dilution sphere formation assay), and tumor formation (subcutaneous xenograft model) was examined in EOC cells.

Results

The TCGA (The Cancer Genome Atlas) database analysis indicated that higher ZIC2 mRNA expression is associated with shorter survival of EOC patients. ZIC2 KO resulted in decreased cell growth, migration, anchorage-independent growth, CSC population and sphere-forming ability, as well as tumor formation in the mouse subcutaneous xenograft model. Overexpression of ZIC2 increased CSC population and sphere-forming ability. In the in vitro differentiation assay CSC population decreased in ZIC2 wild-type (WT) and ZIC2 overexpression cells at a much slower rate than in ZIC2 KO and empty vector cells, respectively, indicating that ZIC2 plays a critical role in maintaining the CSC population in EOC. Mechanistically, ZIC2 KO dramatically down-regulates the expression of genes critical for multiple biological processes, including CSC, cell cycle, EMT, signaling kinases, invasion and metastasis, and mRNA binding, which was confirmed by Go Ontology (GO) and Gene Set Enrichment analyses (GSEA). Western blotting and IHC confirmed that CSC-associated gene ALDH1A1 and proliferation-promoting gene cyclin D2 (CCND2) were expressed in the ZIC2 WT, but not in ZIC2 KO, EOC cells-derived xenografted tumors.

Conclusion

Our in vitro and in vivo work indicates that ZIC2 is a pivotal gene regulator and promotes tumorigenic phenotypes through regulating the biology of the bulk cells and CSCs in EOC, suggesting that ZIC2 is a promising therapeutic target for EOC.

Funded By: WCHRI innovation grant and bridge fund

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Abstract #: 153
Presenter: Jenelle Chen
Supervisor: Davidge, Sandra
Title: The role of endoplasmic reticulum and oxidative stress in pregnancy at an advanced maternal age

Authors: Jenelle Chen 1,2,3, Mazhar Pasha 1, 2,3, Raven Kirschenman 2,3, Amy Wooldridge 2,3, Floor Spaans 2,3, Sandra T. Davidge 1, 2,3 Christy-Lynn Cooke 2,3

1Department of Physiology, 2Department of Obstetrics and Gynecology, 3Women and Children's Health Research Institute, University of Alberta, Canada

Theme: Pregnancy and developmental trajectories

Introduction: Pregnancy at an advanced maternal age (AMA) (≥ 35 years) has been associated with impaired vascular function and abnormal adaptations to pregnancy. Vascular endoplasmic reticulum (ER) stress increases with age, but it is unknown if ER stress contributes to abnormal vascular adaptions observed in AMA pregnancies. ER stress is associated with oxidative stress through the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which may also be increased in AMA. We hypothesize that vascular ER and oxidative stress will be higher in aged compared to young rats, and that pregnancy will exacerbate this.

Methods: We used four rat groups in our study: young (4 months of age) non-pregnant rats, young pregnant rats, aged (9 months of age, equivalent to ~35 years of human age) non-pregnant rats and aged pregnant rats (n=3/group). Rats were euthanized on gestational day 20 (term=22 days), or at matched age for the non-pregnant groups. Thoracic aortas were isolated and snap frozen for molecular characterization. Expression of ROS-producing enzyme NOX4 and ER stress markers GRP78 & XBP1 was quantified by Western blotting and normalized to total protein staining. The levels of markers of oxidative stress (superoxide production [ROS[and peroxynitrite levels [RNS]) were measured using dihydroethidium (DHE) and nitrotyrosine staining, respectively. Data were analyzed by two-way ANOVA with Sidak's post-test, $p<0.05$ was considered statistically significant.

Results: Our preliminary data showed that compared to young pregnant rats, aged pregnant rats had increased NOX4 expression ($p=0.038$). There were no apparent differences in NOX4 expression between non-pregnant and pregnant rats in either the young or aged groups. GRP78 levels tended to be higher in aortas from aged compared to young rats (overall aging effect; $p=0.07$), but there was no difference in GRP78 levels between non-pregnant and pregnant animals within each group. XBP1 levels were not different between any of the groups. Additional pilot data revealed that aortas from aged rats may have higher peroxynitrite levels compared to young rats, while pregnancy in aged animals appeared to decrease peroxynitrite levels compared to the non-pregnant aged group. Pilot DHE data showed that there appear to be no changes in superoxide levels between all groups.

Conclusion: Aged rats tended to have increased aortic NOX4 expression and higher GRP78 and RNS levels compared to their young counterparts. Furthermore, pregnancy in aged rats did not alter our markers of ER stress, NOX4 expression or ROS levels. However, pregnancy seemed to be beneficial as our pilot data suggested that aortic RNS were reduced in aged pregnant rats compared to non-pregnant rats. These preliminary data are intriguing and additional experiments to increase n-numbers will allow us to further assess the complex interaction between pregnancy and aging.

Funded By: Acknowledgements: JC is supported by summer studentships from WCHRI and from Alberta Innovates. This study was funded by a CIHR Foundation grant and by the generosity of the Stollery Children's Hospital Foundation and the Lois Hole Hospital for Women through WCHRI.

women & children's health research institute

Abstract #:	36
Presenter:	Linda Chen
Supervisor:	Cheung, Po-Yin
Title:	Use of Step-wise Lung Recruitment Maneuvers in Preterm Infants using High Frequency Oscillation with Volume Guarantee: An Retrospective Observational Study
Authors:	Linda Gai Rui Chen, Po-Yin Cheung MBBS, PhD, Brenda Hiu Yan Law, MD, MSc

Theme: Children's health and well-being

Background: Preterm infants with respiratory distress syndrome or chronic lung disease may be mechanically ventilated using high frequency oscillation with volume guarantee (HFO-VG) mode. Compared to traditional oscillation with fixed ventilation pressures, VG may result in more stable CO2 removal. In some infants, worsening oxygenation failure may prompt the use of step-wise lung recruitment maneuvers (LRM), using progressively increasing mean airway pressures (MAP) to recruit atelectatic lung and to determine lung characteristics such as opening and closing pressures. However, use of LRM in HFO-VG has not been studied.

Methods: A cohort of preterm infants admitted to the Royal Alexandra Hospital NICU who had LRMs while on HFO-VG ventilation during a six month period (July to December 2019) was identified from a prospective quality improvement audit. Hospital charts were then retrospectively reviewed to identify patient characteristics, clinical respiratory and ventilator parameters 24 hours before, during, and 24 hours after each recorded LRM, as well as hospital outcomes up to initial discharge or transfer from the NICU.

Results: Ten infants and 21 LRMs were identified. Infants had a median GA of 25+6 weeks (IQR 24+2 to 27+0), with a median birth weight of 845 g (744-962). Two infants died prior to discharge or transfer. All survivors had severe chronic lung disease as evidenced by the need for invasive or non-invasive positive pressure ventilation at 36 weeks. LRMs were performed at a median post-natal age of 26 days (12-44). Median starting mean airway pressure (MAP) was 16 cmH2O (14-17), median highest MAP was 23.5 cmH2O (22-24.8). Most (67%) LRMs resulted in higher MAP, two (9.5%) resulted in hypotension, and no infants had pneumothorax during or within 24 hours of a LRM. There were no differences in median oxygen saturation index (OSI) before and after each LRM (8.4 vs. 9, p=0.09), or SpO2/FiO2 (1.8 before vs 1.8 after, p = 0.8).

Conclusions: In a tertiary care NICU, LRMs on HFO-VG were performed on extreme preterm infants with severe lung disease. Despite high ventilation pressures only a minority of infants had hypotension during the study, and none developed a pneumothorax. LRMs achieved only transient improvement or stabilization in oxygenation. Further study is needed to determine optimal ways to achieve lung recruitment in this population.

Funded By: Northern Alberta Neonatal Program and the Stollery Children's Hospital Foundation

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Abstract #:	107
Presenter:	Yuan Yao Chen
Supervisor:	Kozyrskyj, Anita
Title:	Maternal prenatal milk consumption reduces infant gut microbiota dysbiosis
Authors:	Chen YY, Winsor GL, Azad MB, Becker AB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Brinkman FSL, Kozyrskyj AL
Theme:	Children's health and well-being

Background: Several benefits of prenatal maternal milk consumption has been demonstrated, including but not limited to reducing Clostridium difficile colonization and preventing cow's milk allergy in offspring. We previously found a higher fecal abundance of Enterobacteriaceae but lower abundance of Bacteroidaceae at age 3 months to be associated with food sensitization in 1-year old infants. Whether maternal milk intake during pregnancy influences the offspring gut microbiota profile, particularly the abundance of Enterobacteriaceae and Bacteroidaceae, remains unknown. Therefore, the present study aims to evaluate the impact of prenatal milk intake on this infant gut microbiota biomarker of food sensitization.

Methods: This study included 1,618 families representing a subset of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. A food frequency questionnaire (developed by the Fred Hutchinson Cancer Research Center) administered at 18 weeks of pregnancy was the source of information on maternal prenatal milk, vegetable and other food consumption. Personal use of cleaning products (purell-type hand cleaner and eco-friendly products) was also self-reported by mothers on prenatal questionnaires. Infant fecal samples were collected at 3-4 months of age and analyzed by 16S rRNA gene sequencing. The Enterobacteriaceae to Bacteroidaceae (E/B) ratio was calculated to indicate the gut dysbiosis status. Correlations between prenatal early exposures and the E/B ratio were calculated using the Spearman's rank correlation and multiple testing correction was performed using the Benjamini Hochberg method; the effect of milk intake level on the E/B ratio was estimated using one-way ANOVA.

Results: Higher maternal milk consumption during pregnancy tended to be associated with a reduced E/B ratio in infants ($P=0.057$). Specifically, infants of mothers who consumed greater than or equal to 3 cups of milk per day had an E/B ratio of 381.12 ± 927.17 (mean ± SD) versus 711.83 ± 1627.92 for those of mothers that did not drink milk during pregnancy. Meanwhile, maternal prenatal milk consumption was positively correlated with vegetable intake and eco-friendly product usage ($r = 0.021$, $q < 0.001$; $r = 0.197$, $q < 0.001$, respectively).

Conclusions: Our findings indicate that prenatal milk consumption may have a protective role in food allergy by preventing gut dysbiosis. Since these mothers also lead a healthy lifestyle (e.g, higher vegetable intake and eco-friendly product usage), further research is required to determine the most influential factors on the microbiota of pregnant women and their offspring.

Funded By: Canadian Institutes of Health Research (CIHR) and Genome Canada

women & children's health research institute

Abstract #: 102
Presenter: Minyeong Cho
Supervisor: Jiang, Yuanyuan
Title: Child self-perceptions of competence in five life domains as related to helpless attributions and depressive symptoms
Authors: Cho, Minyeong & Jiang, Yuanyuan
Theme: Children's health and well-being

Introduction.

Helpless attributions involve explanations for negative events as internal, stable, and global, and positive events as external, unstable, and specific (Thompson, 1998). Past research has been conducted regarding helpless attributions in children, suggesting that more helpless attributions are associated with higher depressive symptoms in children (Gladstone & Kaslow, 1995). The literature also suggests that lower child self-perceptions of competence may be associated with higher child depressive symptoms (McQuade, Hoza, Murray-Close, Waschbusch, & Owens, 2011). More research is needed to understand the different domains of self-perceptions as related to helpless attributions and depressive symptoms. In this study, child self-perceptions of competence in five areas are examined: academic, social, physical, behavioural, and general self-worth. Lower child self-perceptions are predicted to be related to more helpless child attributions and greater child depressive symptoms.

Methods.

Forty-eight children six to eleven-year-old children with and without ADHD and their parents completed questionnaires. Children completed the following self-report questionnaires: (1) the Children's Attributional Style Questionnaire-Revised (CASQ-R; Kaslow & Nolen-Hoeksema, 1991), which measured child attributions in relation to positive and negative events, and (2) the Self-Perception Profile for Children (SPPC; Harter, 1985), which examined children's self-perceptions of competence in various life domains. Parents completed the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), which assessed depressive symptoms of their child.

Results.

Bivariate correlations examined the associations between child self-perceptions, helpless attributions, and depressive symptoms. Higher child self-perceptions in the academic, social, physical, behavioural, and self-worth domains were significantly related to lower helpless attributions, $r = -.58$, $p < .001$, $r = -.35$, $p < .05$, $r = -.63$, $p < .001$, $r = -.36$, $p < .05$, $r = -.30$, $p < .05$, respectively. Interestingly, higher child self-perceptions in all domains were unrelated to depressive symptoms.

Conclusion.

Child self-perceptions of competence in five domains were significantly positively associated with child helpless attributions. However, child self-perceptions were not related to child depressive symptoms, as reported by parents. These findings suggest that children's perceptions of their abilities in a variety of areas of life can be indicative of how they interpret positive and negative events that happen to them and vice versa. Future studies would do well to examine these relationships with a longitudinal methodology to better determine cause and effect. In addition, studies of children meeting diagnostic criteria for depression may yield differing results. Overall, these results suggest consistency in children's reports, and may be useful clinically to better understand how to improve child self-perceptions and attributions.

Funded By: The University of Alberta Faculty of Education Support for the Advancement of Scholarship Grant

women & children's health research institute

Abstract #:	2
Presenter:	Won-Shik Choi
Supervisor:	Godbout, Roseline
Title:	MYC mediates retinoic acid resistance by suppressing cellular retinoic acid-binding protein (CRABP2) transcription in HER2-enriched breast cancers
Authors:	Won-Shik Choi, Rong-Zong Liu, Caitlin Mak, Roseline Godbout
Theme:	Lifelong women's health

Introduction: HER2-positive (HER2+) breast cancers express high levels of the growth-promoting HER2 protein on their cell surface. The development of a targeted drug, trastuzumab, has greatly improved the clinical outcome for HER2+ patients. However, intrinsic and acquired resistance to trastuzumab are common, with cancer stem cells driving resistance to trastuzumab. Retinoic acid (RA) induces cancer stem cell differentiation, suggesting possible synergistic action with trastuzumab for the elimination of HER2+ breast cancer stem cells. A number of genes regulate RA activity, including RA receptors which function as transcription factors (e.g. RARalpha and PPARbeta), and RA binding proteins CRABP2 and FABP5, which deliver RA to RARalpha and PPARbeta, respectively. RARalpha and PPARbeta have opposite functions, with RARalpha promoting differentiation and PPARbeta promoting proliferation in response to RA. The HER2 gene (ERBB2) is frequently co-amplified with the gene encoding RARalpha in HER2+ breast cancer. It is surprising, therefore, that HER2+ breast cancers are refractory to RA treatment.

MYC is an oncogene that inhibits RARalpha activity in leukemia cells. Importantly, MYC is preferentially amplified and overexpressed in HER2+ breast cancers. My research aims to elucidate the mechanism underlying RA resistance in HER2+ breast cancers, with a special focus on the role of MYC. Hypothesis: MYC regulates RA action through inhibition of the CRABP2-RARalpha pathway and activation of the FABP5-PPARbeta pathway.

Methods: Using TCGA gene profiling datasets, correlations between the expression of MYC and that of HER2, RARalpha, and CRABP2 were investigated. MYC levels were manipulated in selected HER2+ breast cancer cells using expression vectors and siRNAs. These cells were then subjected to RA treatment. Cell proliferation was measured using the crystal violet assay. RAR activation was measured using the luciferase reporter assay. MYC binding to the CRABP2 promoter region was investigated using the gel shift assay.

Results: MYC is preferentially amplified in HER2+ breast cancers and its RNA levels were negatively correlated with CRABP2 expression levels. Depletion of MYC in HER2+ breast cancers upregulates CRABP2 at both the RNA and protein levels. Furthermore, we found that MYC binds to the CRABP2 promoter region suggesting that MYC may directly suppress CRABP2 gene transcription activity. Ectopic expression of MYC inhibited, whereas depletion of MYC activated RAR activity. Consistently, ectopic expression of MYC increased RA resistance, whereas depletion of MYC sensitized cells to RA treatment. When CRABP2 was depleted along with MYC-knockdown, cell proliferation was rescued, suggesting that MYC mediates RA resistance at least partially through downregulation of CRABP2. We also found that RA treatment enhances trastuzumab responsiveness in HER2+ breast cancer cells.

Conclusion: MYC attenuates the anti-cancer effects of RA by inhibiting the CRABP2-RARalpha pathway in HER2+ breast cancer cells. This study sheds light on the role and mechanism of MYC in governing RA resistance in HER2+ breast cancer cells. Our results support the use of RA and trastuzumab for the treatment of subsets of patients with HER2+/low MYC breast cancers.

Funded By: Food and Health Innovation Initiative, Canadian Cancer Society Research Institute, and Women & Health Research Institute

Abstract #:	16
Presenter:	Rozalyn Chok
Supervisor:	Bruce, Aisha A
Title:	Screening and Diagnosis of Heparin-Induced Thrombocytopenia in the Pediatric Population - A Single Tertiary Center Experience
Authors:	Rozalyn Chok, Elona Turley, Aisha Bruce
Theme:	Children's health and well-being

Introduction:

Heparin-induced thrombocytopenia (HIT) is a serious immune-mediated side effect of heparin. The incidence of HIT in the pediatric population is reported at up to 3.7%, but the diagnostic approach varies considerably in the literature. Since the treatment of HIT is immediate discontinuation and future avoidance of heparin, overdiagnosis of HIT bears serious consequences. At our center, we employ a stepwise approach to laboratory testing for clinically suspected HIT. This involves an initial immunologic (ELISA) screen which, if positive, is followed by one or more confirmatory functional assays. Serotonin release assay (SRA) is the gold standard for diagnosis but is not universally available. Lumi-aggregometry is a functional assay available at our center which is validated against the SRA. In this study, we aimed to determine the proportion of screening ELISA tests at our center that go on to receive a confirmatory diagnosis of HIT by Lumi-aggregometry or SRA.

Methods:

A retrospective cohort study was performed at the Stollery Children's Hospital, a tertiary pediatric referral center. The study included patients aged 0 to 18 years admitted from 2008 to 2018 who received a HIT screening ELISA test. Data was obtained from the hospital laboratory database. Chart review was performed for patients with a positive HIT screen for the purposes of calculating the 4T score, a clinical scoring system for HIT validated in adults. Data was analyzed descriptively using frequency tables. Logistic regression models were used to assess the relationship between positive HIT screen and demographic variables.

Results:

233 records met inclusion criteria. There were 23 positive or equivocal ELISA results, for a positive screen rate of 9.9%. There was no statistically significant association between positive screen and demographic variables of age (p=0.132), sex (p=0.911), or requesting service (p=0.848). Neonates had the lowest positive screen rate (2.0%) while adolescents had the highest (16.2%). 47.8% of patients with a positive screen had a low clinical risk of HIT based on 4T score, and heparin was never discontinued in these patients. Of the 5 patients (22%) who were switched to alternative anticoagulation, 3 (60%) developed clinically significant bleeding. There was one case of confirmed HIT (0.4%), which was diagnosed based on SRA.

Conclusion:

HIT is rare in the pediatric population at our center, with only one confirmed case over the 10-year study period. HIT should be considered because of its high morbidity and mortality; however, diagnosis should be based on clinical suspicion and both screening and confirmatory testing to minimize false positive diagnoses.

Funded By: generous support of the WCHRI Resident Trainee Research Grant (2019).

Abstract #: 133
Presenter: Braden Chow
Supervisor: Menon, Geetha
Title: Potential clinical implications of uncertainties associated with in vitro determination of radiobiological parameter values used in cervical cancer brachytherapy
Authors: Braden Chow (University of Alberta), Brad Warkentin (University of Alberta), Fleur Huang (University of Alberta), Armin Gamper (University of Alberta), Geetha Menon (University of Alberta)
Theme: Lifelong women's health

Introduction: Cervical cancer brachytherapy (BT), delivered by either high-dose rate (HDR) or pulsed-dose rate (PDR) regimens, is prescribed in units of radiobiological dose and utilizes the parameters α/β and T1/2 (half-time of repair). Our research group has previously reported on the fitting, to the modified Linear Quadratic model, of in vitro experimental cervical cancer cell survival data that yielded smaller α/β ratios (4.20-6.48 Gy) and larger T1/2 (1.5-5.3 hours) values than conventionally assumed (α/β: 10 Gy, T1/2: 1.5 hours). The experiments suggested the potential for PDR BT to deliver more radiobiological dose than clinically equivalent HDR BT. Several uncertainties have since been identified in the experimental procedure. This research refined our previous analysis to verify that previous conclusions are not affected by these uncertainties.

Methods: To determine α/β and T1/2, clonogenic assays were conducted by irradiating four cervical cancer cell lines (C-33A, CaSki, SiHa, and SW756) in single acute fractions and fractionated schedules using clinical afterloaders. Further analysis was conducted to quantify uncertainties associated with the experimental procedure, including delivery uncertainties (afterloader source positioning, calibration, and transit time), calculation accuracy of the treatment planning software, and experimental uncertainties (colony counting, variations in experimental conditions). Least chi-squared fitting of experimental survival data, with incorporation of these uncertainties, was used to update the α/β and T1/2 values.

Results: Uncertainties in the dose delivered and the cell survival fraction were estimated to be <1.5% and <4%, respectively. The largest uncertainties were identified with source strength calibration and variations in cell uniformity across the tissue culture dishes. Factors affecting experimental condition, such as the temperature of the irradiated cells, did not significantly contribute to the overall uncertainty. Introduction of the uncertainty budget widened the range of calculated parameter values (α/β: 3.64-8.03 Gy, T1/2: 1.3-6.1 hours) but did not affect the overall trend. Recalculation of potential impact on clinical treatments yielded trends similar to our previous findings; for multiple cell lines, a PDR BT schedule may deliver significantly more radiobiological dose than a conventionally clinically equivalent HDR BT treatment. Using the parameters identified, PDR BT may deliver >34 Gy additional radiobiological dose (>27 Gy without consideration of uncertainties) compared to the intended 90 Gy treatment schedule. The current recommendations for improving patient outcome, including escalating treatment tumour dose, highlight a potential benefit for PDR BT; compared to HDR BT, it may deliver these higher dose prescriptions.

Conclusion: Reanalysis of previous findings by incorporating experimental uncertainties reinforces our previously reported trends in cervical cancer radiobiological parameter values and suggest PDR BT may deliver more radiobiological dose than conventionally equivalent clinical HDR BT, potentially impacting patient outcome.

Funded By: This research has been funded by generous supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute.

Abstract #: 3
Presenter: Mackenzie Coatham
Supervisor: Postovit, Lynne-Marie
Title: Aggressive Dedifferentiated Endometrial Cancer can be recapitulated in cell lines with absent chromatin remodeling protein SMARCA4 and treated with synthetic lethality approaches
Authors: Mackenzie Coatham, Zhihua Xu, Guihua Zhang, Jiahui Liu, Edmund Su, Dylan Dieters-Castator, Gilles Lajoie, Franco Vizeacoumar, Martin Hirst, Cheng-Han Lee, Lynne Marie Postovit
Theme: Lifelong women's health

One of the most lethal yet rare subsets of uterine cancer is dedifferentiated endometrial carcinoma (DDEC). Less than 20% of patients diagnosed with DDEC survive compared to the over 80% of uterine cancer patients with high-grade endometrial cancer diagnoses. DDEC tumors possess both well-differentiated and undifferentiated regions. Previously, we demonstrated that 80% of the undifferentiated regions in DDEC lesions lack the expression of core chromatin remodeling proteins, SMARCA4 or ARID1A and ARID1B. We hypothesize that loss of these proteins, which are known regulators of transcription may lead to the induction and/or maintenance of gene expression programs that drive dedifferentiation, metastasis and therapy resistance.

SMARCA4-deficient endometrial cancer (EC) cell line models were generated by CRISPR gene editing and were found to be less capable of self-renewal and anchorage-independent growth. SMARCA4 knockout cells were found to be more senescent than their wild-type counterparts, possessing more positive beta-galactosidase stained cells and expressing higher levels of p21 and H3K9me3. Existence of a senescent associated secretory phenotype (SASP) together with upregulation of interferon and IL2/STAT5 signaling in the absence of SMARCA4 were determined by mass spectrometry of conditioned media and RNA sequencing, respectively. Tumors formed from SMARCA4-deficient EC cell line models in immune-compromised mice recapitulated the mixed phenotype observed in patient DDEC lesions. Endometrial cancer cells lacking SMARCA4 expression were also found to be more sensitive to inhibition with clinically available therapeutics targeting CDK4 and EGFR. Synergistic effects upon combining therapies against CDK4 and EGFR were observed in SMARCA4 knockout cells. Response to CDK4 inhibition in the absence of SMARCA4 is likely mediated through dysregulation of the p16/cyclin D1/Rb pathway.

Exome sequencing in addition to single cell RNA-Seq and ATAC-Seq will be carried out in the future to elucidate whether it is the consequence of acquired mutations, changes in gene expression or alterations to nucleosome occupancy that contribute to cellular dedifferentiation in the context of DDEC.

Funded By: Alberta Innovates Health Solutions

Alberta Cancer Foundation

Canadian Institutes of Health Research

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Abstract #:	32
Presenter:	Ellery Cunan
Supervisor:	van Manen, Michael
Title:	Use of a single loading dose of caffeine for the treatment of apnea of prematurity in moderate to late preterm neonates
Authors:	Ellery Cunan, Marc-Antoine Landry, Tara Follett, Jagmeet Bhogal, Sarah Rathwell, Michael van Manen
Theme:	Children's health and well-being

Introduction: Apnea of prematurity is defined as a pause in breathing lasting longer than 20 seconds, or between 10 to 20 seconds when accompanied by bradycardia (heart rate below 80 beats per minute) or oxygen desaturation (SaO2 falling below 80%), in infants born before 37 weeks gestational age. Caffeine has been used to manage apnea of prematurity since the 1970s, utilizing a loading dose of caffeine followed by daily maintenance therapy. Though current research supports caffeine use in extremely premature infants, it is unclear whether caffeine's therapeutic benefits outweigh its potential harms in moderate to late premature infants. Further, there is variation in clinician practice regarding the duration of caffeine therapy and the timing of discontinuation. The aim of this study was to evaluate the feasibility of a treatment approach of a single loading dose of caffeine without routine maintenance caffeine therapy for moderate to late preterm infants.

Methods: We conducted a multi-centre pilot study with enrolment from January 2019 through July 2020. Infants admitted to three NICUs in Edmonton, Alberta, born at a gestational age of 33+0 to 35+6 weeks, and who received a loading dose of caffeine therapy (10 mg/kg of caffeine base) were eligible for enrolment. Following enrolment, health care providers were still able to decide to begin maintenance caffeine therapy at their discretion, in keeping with existing clinical practice. Descriptive data were abstracted from hospital charts. Comparisons were made between patient groups based on whether caffeine was given after the initial loading dose.

Results:

38 patients were enrolled in the study. 15 infants (39%) were born at a gestational age of 33 weeks, 15 infants (39%) at 34 weeks, and 8 infants (21%) at 35 weeks. 23 infants (61%) were female. 25 infants (66%) were singleton births. Following the initial caffeine load, 28 patients (74%) did not receive additional caffeine therapy, while 10 patients (26%) were managed on caffeine. Demographic and clinical variables were explored to identify predictors for reloading with caffeine. Gestational age at birth did not predict whether caffeine was given after the initial loading dose.

Conclusion:

This study has ultimately shown that the provision of a single loading dose of caffeine for the treatment of apnea of prematurity is a feasible treatment approach, with the majority of patients enrolled in our pilot study not having required a resumption of caffeine therapy. Future trials at a larger scale can be considered to further delineate appropriate considerations for defining the patient population most likely to benefit from this approach.

Funded By: WCHRI

Abstract #:	69
Presenter:	Chentel Cunningham
Supervisor:	Scott, Shannon
Title:	Preliminary Results of an Environmental Scan about Web-based Pediatric Heart Failure Parent Tools/Resources for Parents and Caregivers
Authors:	Chentel Cunningham, Hyelin Sung, Shannon Scott
Theme:	Children's health and well-being

Introduction: Successful outpatient convalescence of a child with heart failure involves effective parent education. Parents must become proficient in a new suite of complex medical knowledge about their child's heart failure symptoms and management strategies. Learning, combined with extreme levels of stress about their child's survival, brings rise for gaps in parental knowledge. These gaps can result in numerous unnecessary access to the health care system, less participation in health care decisions, along with heightened familial anxiety. To date, there is little understanding of what educational tools or resources exist for parents in this context to help avoid these troublesome knowledge gaps. Environmental scans (ESs) are a newer methodology used to understand what tools or resources are available for specific contexts. ESs can also include an assessment of the tool's ability to meet the needs of a particular audience (e.g., parents).

Methods: With a comprehensive search guided by currently published ES literature, educational web-based tools/ resources, and organizations about pediatric heart failure that target family audiences were identified. ESs search strategy is broken down into three parts: (1) application (app) search via Apple App™ store and Google Play™, (2) online internet search, and (3) key informant interviews. The search is limited to the first 100 websites and 50 applications retrieved. Inclusion criteria were if the tool/resource was based in Canada and the United States, specifically focused on pediatric heart failure, and written in English language. Key informants for each included tool/resource will be contacted and interviewed using semi-structured interviews. The purpose of key informant interviews are to complement the application and online searches, adding richer detail and understanding of each tool/resources development's process.

Results: Thus far, only the application portion of the study is completed. Preliminary results in the application search of the first 50 apps from Apple and Google Play app stores. There were no applications identified about to pediatric heart failure for parents or caregivers to access. There were a small number of applications that included a portion about pediatric heart failure. The majority of applications were targeted for health care providers audience. It is anticipated that there will be relevant internet resources, as a scan and partial data collection for the retrieved 600 internet search results has identified relevant online tools/resources.

Conclusion: ESs are an appropriate method used to uncover educational application and internet tools/resources for parent audiences. Preliminary results in the application search revealed no available pediatric heart failure tools/resources tailored to parent knowledge needs. Partial completion of the internet search has already identified a small number of relevant tools.

Funded By: Women and Children's Health Research Institute, University of Alberta, Stollery Children's Hospital, Canadian Institutes of Health Research

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Abstract #:	108
Presenter:	Samantha Cyrkot
Supervisor:	Mager, Diana
Title:	The impact of COVID-19 on the food environment, the cost of gluten-free foods, and youth diet quality in households with youth with celiac disease in Alberta
Authors:	Samantha Cyrkot RD MSc (cand), Dominica Gidrewicz MD MSc FRCPC, Justine M. Turner MD PhD FRCPC, and Diana R. Mager PhD MSc RD
Theme:	Children's health and well-being

Introduction: The Coronavirus Disease 2019 (COVID-19) global pandemic has increased the risk for food insecurity in several populations, including youth with chronic diseases. Food insecurity can result in adverse changes to overall diet quality (DQ), particularly in youth on therapeutic diets such as the gluten-free diet (GFD). This pilot study examined the impact of COVID-19 on the food environment (home/grocery), gluten-free (GF) food costs and DQ of youth with celiac disease (CD) in households pre (PreCOV) and during (COV) COVID-19 in the first 60-90 days. We hypothesized that the emergence of COVID-19 would result in significant changes to food shopping habits (i.e. shopping frequency, food purchasing decisions), increased total food costs, and reduced youth DQ.

Methods: We prospectively studied CD youth (12-18 years, CD duration 3.1y±2.3) and their families PreCOV (n=10) and COV (n=5). Food shopping habits, dietary intake, and DQ were assessed using the Perceived Nutrition Environment Measures survey, two 24-hour recalls (weekday, weekend day) and the Canadian Healthy Eating-Index, respectively. Food costs ($CAD) were obtained from household food purchasing receipts collected over two weeks.

Results: No significant differences were noted for child-age (15y±1.1), weight-z (0.3±0.9), height-z (0.1±1), household size (4±0.7), number of children in household (2±0.7), number of household members following the GFD (2±0.9), maternal/paternal education or mean household incomes between PreCOV and COV households (P>0.05). Mothers (n=13) reported being the primary household grocery shopper (≥once/week) with 13 households purchasing a combination of GF and gluten-containing foods (P>0.05). Food purchasing decisions (i.e. making food choices by reviewing food labels) were not significantly different between groups but PreCOV reported having more energy-dense foods (e.g. chips, candy) available within the home than COV (P=0.01). Mean household two-week food expenditure was not different between groups (n=92, $506.26±108.83 [PreCov] vs n=110, $618.57±176.42 [COV]; P=0.15) and >$100 increase in costs was not associated with major increases in the number of food items purchased (P=0.27). Mean food costs for packaged GF grains were not significantly different between groups for bread (n=21, $1.24/100g±0.2), pasta (n=15, $0.87/100g±0.5), or breakfast cereals (n=12, $1.07/100g±0.3) (P>0.05). The cost of staple fresh fruits/vegetables (e.g. apples, potatoes) were also not significantly different from PreCOV to COV (P>0.05). No group differences were noted for youth DQ (total [54.2±13.4], adequacy [30.7±8.3], moderation [19.5±6.2] or variety [4.2±3.4]; P>0.05) but mean scores were classified as 'needs improvement'. Differences in percent macronutrient intake (i.e. protein, fat, carbohydrates) were not significantly different between groups (P>0.05).

Conclusions: The COVID-19 pandemic did not significantly change shopping frequency, food purchasing decisions, GF food costs or youth DQ in households with youth with CD in the short term. Ongoing longitudinal research is needed given the evolving nature of the COVID-19 global pandemic.

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Abstract #: 93
Presenter: Renée Dicipulo
Supervisor: Waskiewicz, Andrew
Title: Evidence for crosstalk between Taz and Wnt in the zebrafish hindbrain ventricle
Authors: R. Dicipulo, L. G. Selland, A. W. Waskiewicz
Theme: Children's health and well-being

Introduction

The brain ventricle system, consisting of several cavities and the cerebral spinal fluid within, is integral for normal everyday function. Improper morphogenesis and the inability to properly regulate cerebrospinal fluid (CSF) are therefore associated with early onset congenital neurodegenerative defects, including hydrocephaly, which is characterized by an abnormal buildup of CSF and cognitive impairment. Though we know genes involved in ventricle development, how these key players are regulated and how this fits into a comprehensive model are still unknown. In this project, our goal was to identify specific signalling pathways involved and the genes required for proper formation of the brain ventricle system. We recently uncovered evidence of brain ventricle-specific activity of the Hippo signalling pathway. Therefore, we hypothesize that Taz, a transcriptional co-regulator canonically involved in the Hippo signalling pathway, is a key regulator of brain ventricle formation.

Methods

To understand the roles of Taz in brain ventricle development, Transcription Activator-Like Effector Nucleases (TALENs) were used to generate zebrafish taz knockouts. We utilized transgenic zebrafish lines and fluorescence microscopy to visualize structures within the brain and signalling pathway outputs. In situ hybridization (ISH), Taz immunohistochemistry, mRNA injection and Western blots were used for gene expression and protein localization and quantification studies. Pharmacologic modulation of WNT and NOTCH pathways was used to examine crosstalk amongst Hippo, WNT, and NOTCH pathways.

Results

Analyses of taz mutants demonstrated decreased hindbrain BVS size due to failure of ventricle midline separation. In addition, in locations of defective midline separation, we observed disorganized apicobasal polarity. Findings by Azzolin et al. 2014 suggested an in-vitro interaction between Wnt and Hippo signaling, in that TAZ interacts with the β-catenin destruction complex, and is degraded in WNT-off cells. We therefore tested whether hindbrain Taz protein levels were regulated by the WNT pathway. In wild-type embryos, Taz protein is localized to hindbrain segment boundaries, the known domain of active Wnt signaling. Our studies have shown that pharmacological inhibition of Wnt signaling results in loss of intersegmental stabilization of Taz, indicating Wnt-dependent recruitment of Taz to segment boundaries. In addition, Western Blots show that co-injection Taz and Axin, a component of the β-catenin destruction complex, results in increased Taz protein detection, suggesting a direct interaction. In addition to Wnt involvement, preliminary studies have suggested interactions between Taz and Notch signaling pathway components. In taz mutants, there is a strong downregulation of the Notch modulator rfng at the segmental boundaries.

Conclusions

Taken together, our research results indicate that Taz lies at the interface of three signalling pathways: Wnt, Hippo, and Notch. By better understanding the genetic regulation of the BVS we are better able to determine genetic causality of neurodegenerative disease that are caused by improper formation of the BVS.

Funded By: WCHRI, NSERC, Alberta Innovates

Abstract #: 87
Presenter: Nicole Dittmann
Supervisor: Voronova, Anastassia
Title: The neurodevelopmental role of cell-to-cell communication between striatal neurons and subventricular zone neural stem cells
Authors: Nicole Dittmann, Pouria Torabi and Anastassia Voronova

Theme: Children's health and well-being

The mammalian brain contains two neural stem cell (NSC) niches: the subventricular (SVZ) and subgranular (SGZ) zones. NSCs located in the SVZ niche produce neurons and glial cells (non-neuronal cells such as astrocytes and oligodendrocytes) throughout life and participate in both embryonic and postnatal brain development and regeneration. The SVZ NSCs are closely located to a brain area termed the striatum, which is responsible for movement, cognition and behaviour. Notably, striatal neurons and/or SVZ NSCs are aberrant in children with neurodevelopmental disorders. Yet, we understand very little about the importance of striatal SVZ niche. Our lab has previously shown embryonic NSC function is regulated by factors secreted by inhibitory neurons (Voronova et al. 2017 Neuron). I hypothesize postnatal SVZ NSCs are regulated by neighbouring striatal neurons.

To address this question, I cultured primary murine postnatal SVZ NSCs in control media or media conditioned by primary striatal neurons as i) secondary neurospheres to allow proliferation; and ii) monolayer to allow simultaneous proliferation and differentiation. My data demonstrate an increase in the number of secondary neurospheres and Ki67-positve cells in monolayer cultures in the presence of media conditioned by striatal neurons, which is indicative of increased proliferation. I am currently investigating whether NSCs and/or their derivatives, such as oligodendrocyte progenitors and astrocytes, display increased proliferation in response to factors secreted by striatal neurons.

My results suggest that striatal neurons may have a role in regulating NSCs in the SVZ niche of the brain. Striatal neurons are known to secrete neurotransmitter GABA, which inhibits NSC proliferation in the developing and adult brain (LoTurco et al., Neuron, 1995; Fernando et al., PNAS, 2011). Thus, we believe that pro-proliferative effect is due to a different repertoire of secreted factors. Future work intends to discover the signalling molecules responsible for the observed changes. It is our hope the results from this project may inspire future therapies aimed at engaging neural stem cells for brain regeneration in patients with neurodevelopmental disorders.

Funded By: This work was supported by CIHR grant (to A.V.), NMHI Graduate Fellowship Award and 75th Anniversary Award (to N.D.), and NSERC USRA (to P.T)

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Abstract #:	46
Presenter:	Andrea Eaton
Supervisor:	Ball, Geoff DC
Title:	Determining stakeholders' priorities for child and family research - progress to date
Authors:	Eaton A, Dyson M, Goikert R, Rajani H, Ladha T, Birken C, Maguire J, Ball GDC
Theme:	Children's health and well-being

Introduction. The Northeast Community Health Centre (NECHC; Edmonton, AB) serves many lower income, refugee and immigrant families. There is a unique opportunity to give a voice in research to the families and their healthcare providers (HCPs) at the NECHC as these families are often marginalized. Community engaged research (CER) includes partnering with stakeholders (parents, HCPs) to identify research priorities and improve health outcomes. Conducting CER that aligns with stakeholders' priorities may enhance the likelihood of active participation in future research. Our study objectives are to (i) identify questions that parents and HCPs (of children aged 0-17 years) at the NECHC have regarding children's and families' health and well-being, and (ii) determine which of these questions are perceived to be of highest importance to inform future research.

Methods. This mixed methods participatory research study, based at the NECHC, involves sequential surveys and focus groups. The study started in July 2019, and will continue until December 2020, including a 5-month interruption due to Covid-19. Partnering with stakeholders, we are soliciting input and rank-ordering priorities regarding child- and family-related health and medical questions considered to be the most important to parents and HCPs. Stakeholders' data and priorities are being collected following an augmented James Lind Alliance (JLA) framework, an eight step, group-based process that includes stakeholder engagement at every step with stakeholders being active, integral partners in the research process. This approach integrates several research stages and methods (online surveys [quantitative], focus groups [qualitative]) tdesigned to generate a list of 'Top Ten' research priorities.

Results. To date, we have completed 3 of 8 steps in the JLA. Step 1 established a steering committee of individual stakeholders joining with researchers to advise on processes through the study. In Step 2, an online REDCap survey was co-created by the steering committee members to gather questions and uncertainties from parents and healthcare providers. Step 3 included gathering questions from approximately 1200 submissions from 125 stakeholders (n=100 parents; n=25 HCPs); data cleaning is underway. Preliminary analyses revealed that research questions related to nutrition, screen time, mental health, and access to resources/supports are common. The next steps (4, 5, 6) include consolidating, refining, and prioritizing (7) questions to produce a 'Top Ten' list of research priorities to be disseminated (8).

Conclusion. Parents and HCPs have a diverse range of unanswered questions with main preliminary themes of nutrition, screen time, mental health, and healthcare access. Submitted questions will next be prioritized by stakeholders through online surveys and focus groups to create the 'Top Ten' research priorities for child and family health research at the NECHC. As the creation of an authentic, open and honest partnership between researchers and stakeholders is crucial in quality and valued CER, this research is a critical first step to develop a long-term plan to conduct practice-based, patient-oriented research to meet the interests and priorities of families and HCPs in northeast Edmonton.

Funded By: WCHRI Community/Clinical Research Integration Support (CRISP) Grant

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Abstract #:	23
Presenter:	Jenna Evanchuk
Supervisor:	Field, Catherine J
Title:	Yogurt intake before pregnancy is associated with improved maternal mental health at 24 weeks postpartum
Authors:	Jenna Evanchuk, Mohammadreza Pakseresht, Rhonda C. Bell, Catherine J. Field and the APrON Study Team
Theme:	Pregnancy and developmental trajectories

Introduction:

Dairy foods are a major source of important nutrients including protein, calcium and various vitamins, which are essential for proper infant and child development. Increasing dairy intake has been a prominent dietary recommendation for most pregnant and lactating Canadian women. However, recommendations for the consumption of dairy is largely absent from the new Canadian Food Guide. The objective of this project was to determine the relationship between dairy product intake by women before, during and after pregnancy and key maternal, infant and child health outcomes.

Methods:

The APrON study, a prospective cohort project which gathered dietary and biological data from nearly 2200 pregnant women, was conducted at local clinics and hospitals in Edmonton and Calgary starting in 2009. Nutritional and developmental data was also collected from the infants and children of women who participated in APrON. Dietary, anthropometric and mental health data from mothers and anthropometric and developmental data from infants and children were analyzed. Maternal total and individual dairy product intakes were quantified with a food frequency questionnaire before pregnancy and 24-hour dietary recalls, which were conducted during each trimester and at 3 months postpartum. A serving of milk, yogurt and cheese was equal to 1 cup, ¾ cup and 50 g, respectively. The presence of pregnancy and non-pregnancy related complications were summed and compiled into a total score for each maternal participant. Child neurodevelopment was estimated using emotional control and attentional problems scores from the Behaviour Rating Inventory of Executive Function Preschool (BRIEF-P) and Child Behaviour Checklist (CBCL) questionnaires, respectively. Multivariate regression models were developed when controlled for potential confounders.

Results:

The average maternal intake of dairy significantly increased across pregnancy (the mean and standard deviation of intake in the first (n= 291) versus third trimester (n= 927) was 2.31 servings/day ± 1.49 and 2.81 servings/day ± 1.70, respectively; $p<0.001$). There were no significant relationships between milk, yogurt, cheese or total dairy intakes and gestational weight gain, maternal complication scores, infant birth weight, length and head circumference, and child neurodevelopment scores at 2 and 3 years of age. However, women who reported consuming more servings of yogurt before they became pregnant ($\bar{x}$= 0.14 servings/day) had a significantly lower Edinburgh Postnatal Depression Scale (EPDS) score at 24 weeks postpartum (p= 0.009), where a lower score indicates that a woman has less symptoms consistent with postpartum depression. There was also a trend towards this relationship at 12 weeks postpartum (p= 0.055).

Conclusion:

The results suggest that an increased yogurt intake before pregnancy is associated with lower EPDS scores at 24 weeks postpartum. Results also suggest that milk and dairy intake throughout gestation and postpartum are not significantly associated with any negative maternal, infant or child health outcomes for the variables measured. Milk and dairy products may provide significant health benefits and their consumption before, during and after pregnancy should not be discouraged.

Funded By: Dairy Farmers of Canada. The APrON cohort was funded by a grant from Alberta Innovates. J. Evanchuk received funding from WCHRI Summer Studentship and NSERC USRA.

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Abstract #:	24
Presenter:	Yuliya Fakhr
Supervisor:	Hemmings, Denise G
Title:	Novel mechanisms of disrupted placental barrier formation: lipid mediators and inflammatory signaling
Authors:	Fakhr Y, Webster K, Hemmings DG
Theme:	Pregnancy and developmental trajectories

Introduction: Preeclampsia (PE) is an inflammatory pregnancy disorder affecting 5-8% of pregnancies. Poor formation of the syncytium (ST), the site of the nutrient and oxygen exchange in the placenta, plays a key role in the development of PE. The ST forms through a regenerative cycle: the stem cytotrophoblast proliferates, differentiates, fuses to form a multinucleated ST, and sheds by cell death into maternal blood. In PE, progenitor cytotrophoblasts display low fusion rates and increased apoptosis. One factor that decreases fusion and increases apoptosis is the inflammatory cytokine, tumor necrosis factor-α (TNF-α). In endothelial cells, TNF-α exerts its apoptotic effects through sphingosine 1-phosphate (S1P), a bioactive lipid. Both factors are elevated in the plasma of mothers with PE. Similar to TNF-α, S1P inhibits ST formation. We investigate the role of S1P in mediating TNF-α-induced inhibition of ST formation to find a mechanism for this occurrence in women with PE. We hypothesize that TNF-α exerts its effects on the ST by modulating S1P regulatory enzymes and receptors (S1PRs).

Methods: Chorionic explants isolated from healthy term human placentas are used as a model. Incubation for 4 days allowed the existing ST to shed. Explants were then treated with or without 1ng/mL TNF-α for 2 days post-incubation to allow ST to reform. This was done with or without 1□M PF-543, an inhibitor of sphingosine kinase 1, the S1P synthesizing enzyme. Cell death and function of ST were measured using colorimetric assays at 24 and 48 hrs post-treatment (n=5) to detect lactate dehydrogenase (LDH) and human chorionic gonadotropin (hCG), respectively. Immunofluorescent staining of nuclei with DAPI and cell membranes to detect E-cadherin was done at 48 hrs (n=4) to assess cell fusion. S1P regulatory enzymes and S1PR1-3 mRNA expression were measured by qRT-PCR from 0-48 hrs post-treatment (n=5-7).

Results: TNF-α and PF-543, separately and in combination, decreased hCG release and formation of ST ($p=0.008$, $p=0.003$). TNF-α increased LDH release whereas PF-543 decreased it. Pre-treating explants with PF-543 prior to adding TNF-α blocked TNF-α-induced LDH release. TNF-α treatment did not change mRNA expressions of any S1P synthesizing, degrading, or dephosphorylating enzymes or S1PR1 receptors. Only S1PR3 mRNA expression increased after 48 hrs of TNF-α treatment ($p=0.03$). In the no treatment control, sphingosine 1-phosphate phosphatase 1 (SGPP1; $p=0.04$) and S1PR1 ($p=0.01$) expression increased after 48 hrs of ST re-formation.

Discussion and Conclusion: TNF-α-induced cell death is mediated by production of S1P. This can be explained by TNF-α also muting the normal surge of the degrading enzyme SGPP1. Similarly, TNF-α blocks the normal increase in S1PR1. S1PR1 signaling is anti-apoptotic, thus TNF-α-induced S1PR1 downregulation can contribute to increased cell death. TNF-α increases S1PR3 expression, implying that S1PR3 signaling could facilitate TNF-α-induced effects in the placenta. Blocking production of S1P inhibits ST fusion, implying that S1P increases ST formation, potentially by signaling through S1PR1. These results indicate that S1P receptors can be targeted to protect against TNF-α-induced dysregulation of placental development as found in PE.

Funded By: Operating funding: CIHR (Canadian Institutes of Health Research), Li Ka Shing Institute of Virology, WCHRI (Women and Children's Health Research Institute)

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Abstract #:	11
Presenter:	Alexa Ferdinands
Supervisor:	Raine, Kim D
Title:	The ruling of weight: A qualitative exploration of youth body weight surveillance work
Authors:	Alexa Ferdinands, Tara-Leigh McHugh, Kate Storey, Kim D. Raine
Theme:	Children's health and well-being

Introduction:

Dominant weight discourses, which frame obesity as an individual responsibility, continue to undermine child and youth health promotion efforts in Canada. By associating obesity with amorality, young people with obesity are stigmatized in all domains of life, leading to health consequences such as anxiety, disordered eating, and depression. However, details are lacking about how these stigmatizing experiences are repeatedly coordinated to happen, particularly from a youth standpoint. Therefore, we aimed to explicate the social organization of higher weight youths' everyday work.

Methods:

This qualitative study used institutional ethnography to examine the everyday work of young people in larger bodies. Work was interpreted in a generous sense to include anything requiring thought and intention. Data generating strategies included individual and group interviews with 16 youth between 15-21 years old in Edmonton, Alberta. We asked participants open-ended questions like, "what did it feel like to grow up in your body," dipping back into their childhood to explore the trajectory of their experiences. Analytic techniques included indexing, mapping, and writing narrative accounts of participants' stories.

Results:

Weight surveillance work was prominent across all participants' accounts. Participants, and those around them, constantly assessed and monitored their own and each other's weights, often using the Body Mass Index tool for comparison. The results of these assessments informed participants of their next steps; that is, whether they needed to lose weight to fit in, literally and figuratively. The answer to this question was nearly always "yes"-there was always body work to be done. Participants learned this work was important through interactions with respected adults in their lives, including parents, healthcare providers, and educators. However, participants also challenged dominant weight discourses, such as by trying to prove others wrong about what larger people are and are not capable of. Study findings are now being used to engage youth in social action to counter obesity stigma.

Conclusion:

In starting our investigation with the everyday happenings of youths' lives, we uncovered how their stigmatizing experiences were organized by dominant weight discourses. Participants learned how and why to do the work expected of them through social relations. As public health researchers, we are ethically obliged to challenge these discourses to better serve the interests of children and youth. We must critically reflect on taken-for-granted approaches to "solving childhood obesity", and advocate for strategies that allow young people to speak for themselves on issues affecting their health and well-being.

Funded By: WCHRI Graduate Studentship, WCHRI PaCET Award, Vanier Canada Graduate Scholarship, Izaak Walton Killam Memorial Graduate Scholarship, Edmonton Community Foundation Grant

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Abstract #: 134
Presenter: Higinio Fernández-Sánchez
Supervisor: Salami, Bukola
Title: An intersectional approach to the health of Mexican women who remain behind during transnational migration: A scoping review
Authors: Higinio Fernández-Sánchez, Jordana Salma, Bukola Salami
Theme: Lifelong women's health

Introduction: The absence of men who migrate transnational may impact the health and wellbeing of women who remain behind in Mexico. As the world continues to interconnect at rapid rates, transnational migration has become the center of attention for many governments worldwide. The International Organization for Migration reported nearly 272,000,000 international migrants in 2019. In Mexico, more than 11,000,000 Mexicans resided in the United States in 2017 and over 400,000 entered Canada in 2018. Even though the number of Mexican women migrating has also increased, the vast majority of migrants are men who have left their families behind.

Objective: To explore the existing literature on the health of Mexican women who remain behind in their communities of origin while their partners migrate abroad.

Methods: A scoping review informed by an intersectionality framework was conducted from January to April 2020. The electronic databases Medline, Global Health, CINAHL, Gender Studies Database, Dissertations & Theses Global, and Latin America and Caribbean Health Sciences Literature were searched. Articles were included if they focused on Mexican women who remain behind across transnational spaces. Two independent reviewers screened and selected articles. Data were analyzed and synthesized using descriptive statistics for numerical data and content analysis for qualitative data. Software aided in data exploration; statistical package for the social sciences and Quirkos.

Results: Nineteen articles were included for analysis; within those, the primary design was qualitative (n=11). Most studies lacked a theoretical framework (n=10); the majority were empirical published studies (n=11), and most used interviews (n=12) to collect data. All of the articles studied cis-heterosexual Mexican women. Several authors discussed mental health concerns, such as feelings of abandonment; symptoms of distress; difficulty sleeping and obsessive thinking; anger; anxiety, stress, and depression; and emotional disorders. Many of these problems are attributed to the women's inability to communicate with their partners, unexpected health emergencies, worries about their partners' wellbeing, fear of their partners' deportation, and the increase in the women's responsibilities. To a lesser extent, Mexican women are also seen to experience heart-related diseases, being overweight or obese, and having higher barriers to healthcare access, like the lack of medications or healthcare practitioners.

Conclusion: These findings provide direction for future research that could examine the experiences of women who have preexisting health conditions, Indigenous women, mothers of children with special needs, and the reunification experiences and health needs of Mexican women and their returning migrant partners.

Keywords: Intersectionality; Gender; Mexico; Scoping review; Transnational migration; Women.

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Abstract #:	54
Presenter:	Sabrina Fox
Supervisor:	Waskiewicz, Andrew
Title:	BMP3 is a novel regulator of ocular fissure closure
Authors:	Sabrina C. Fox, Sonya A. Widen, Lisa B. Prichard, Ordan J. Lehmann and Andrew J. Waskiewicz
Theme:	Children's health and well-being

Introduction

The ocular fissure is a transient structure in the ventral eye that serves as an entry point for the developing ocular vasculature. Failure of ocular fissure closure results in coloboma, which is a congenital disorder characterized by gaps in ocular tissues. Coloboma occurs in approximately 2-14 per 10, 000 live births and is the second leading cause of pediatric blindness. Previous work has identified the Transforming Growth Factor-Beta (TGF-β) and Bone Morphogenetic Protein (BMP) signalling pathways as major regulators of fissure closure, and sequencing of human patients with microphthalmia/coloboma revealed potentially deleterious variants in BMP3 (a known TGF-β ligand). Therefore, we hypothesize that BMP3 is an important regulator of optic fissure closure.

Methods

Whole exome sequencing was performed on DNA from patients in a three-generation pedigree of autosomal dominant coloboma and microphthalmia. Sanger sequencing was performed on DNA from a cohort of patients with microphthalmia, anophthalmia and/or coloboma that are unrelated to the pedigree family. Cos9 cells were transfected with constructs containing wild-type BMP3 or BMP3 containing different genetic variants, and secretion of BMP3 protein was assayed using western blot. CRISPR/Cas9 genome editing was used to create a frameshift mutation in zebrafish bmp3, and the presence of open optic fissure in these mutants was assessed using laminin antibody staining at 65 hours post fertilization (hpf). In-situ hybridization was used to determine the spatial expression of bmp3 and dorsal/ventral gene expression markers in zebrafish embryos. Antibody staining for phosphorylated Smad3 (pSmad3) was used to assess TGF-β signalling in the ventral eye. The pharmacological treatment Specific Inhibitor of Smad3 (SIS3) was used to inhibit TGF-β signalling, and treated embryos were scored for the presence of open fissures at 65hpf and compared to control embryos.

Results

We have shown that BMP3 variants identified in human patients result in misfolding and aberrant secretion of the BMP3 protein. We have also shown that bmp3 mutant zebrafish embryos display delayed ocular fissure closure, suggesting that bmp3 has a critical role in early eye morphogenesis and ocular fissure closure. We have shown that bmp3 is expressed in the zebrafish head mesenchyme and forebrain during early ocular development. Additionally, we have found that TGF-β signalling is active adjacent to the ocular fissure, further suggesting a role for bmp3 in fissure closure. This is consistent with other findings that bmp3 mutant embryos are sensitized to a suboptimal dose of TGF-β inhibitor, resulting in an increased penetrance of fissure closure defects. Interestingly, a population of neural crest cells lie in close proximity to the region of active TGF-β signalling, suggesting that Bmp3 protein may be secreted by these cells to facilitate choroid fissure closure.

Conclusions

These results demonstrate that Bmp3 is a novel regulator of optic fissure closure. Analysis of Smad3 phosphorylation and synergy with SIS3 support a novel mechanism whereby Bmp3 regulates migratory neural crest in the vicinity of the choroid fissure. This highlights the importance of periocular mesenchyme in the causality of coloboma.

Funded By: National Science and Engineering Research Council (NSERC), Canadian Institute for Health Research (CIHR), Women and Children's Health Research Institute (WCHRI), Glaucoma Research Society of Canada.

Abstract #:	79
Presenter:	Felipe Ganz
Supervisor:	Pritchard, Lesley
Title:	Is physical activity-related self-efficacy associated with moderate to vigorous physical activity and sedentary behaviour among children with cerebral palsy?
Authors:	Felipe Ganz, Virginia Wright, Patricia J. Manns, Lesley Pritchard
Theme:	Children's health and well-being

Purpose: To determine how physical activity-related self-efficacy is associated with physical activity and sedentary behaviour time among ambulatory children with cerebral palsy.

Method: Children with cerebral palsy, Gross Motor Function Classification System (GMFCS) Levels I-III,

aged 9-18 years (n=26) completed the task self-efficacy component of the Self-Efficacy Scale and wore

ActigraphGT3X+ accelerometers for five days. Correlations (Pearson and Spearman rank-order; alfa=0.050) were conducted to evaluate the relationships between age, GMFCS level, self-efficacy, and both daily moderate to vigorous physical activity and sedentary time. Linear regression models were used to determine relationships among the independent variables and MVPA and sedentary time.

Results: Self-efficacy was negatively associated with sedentary time (r= -0.332, p=0.049) and positively

correlated with MVPA time (r=0.428, p=0.015). In linear regression models, GMFCS level (β=0.439,

p=0.003) and age (β=0.605, p<0.001) were associated with sedentary time (R2=0.584) and gross

motor function (β=-0.462, p=0.006), age (β=-0.344, p=0.033) and self-efficacy (β=0.281, p=0.080) were

associated with MVPA time (R2=0.508).

Conclusions: This research suggests that self-efficacy, age and gross motor function are associated with moderate to vigorous physical activity in children with cerebral palsy. Additional research is needed to confirm these findings and further explore the influence of self-efficacy on sedentary behaviour.

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Abstract #:	33
Presenter:	Catalina Garcia Hidalgo
Supervisor:	Schmolzer, Georg M
Title:	The RETAIN digital simulator improves healthcare providers' knowledge of the neonatal resuscitation algorithm
Authors:	Simran K Ghoman, Maria Cutumisu, Catalina Garcia Hidalgo, Georg M. Schmölzer
Theme:	Children's health and well-being

Introduction:

Approximately 10% of infants require cardiorespiratory support at birth. These neonatal resuscitation events are infrequent but high risk. One million infants die each year from asphyxia at birth with half of these deaths caused by deficiencies in healthcare providers (HCPs) competencies. As such, HCPs must have and maintain thorough knowledge of the neonatal resuscitation algorithm. Simulation-based education is recommended to maintain HCPs knowledge and understanding of neonatal resuscitation. However, simulation-based education is resource intensive and in light of the current COVID-19 pandemic, accessible and safer alternatives are required. We have developed a computer game digital simulator titled RETAIN (REsuscitation TrAINing) in which HCPs take on the role of a resuscitator and provide care for a simulated newborn requiring cardiorespiratory support. This study examined whether playing the RETAIN digital simulator improves HCPs neonatal resuscitation knowledge.

Methods

Fifty neonatal HCPs were recruited from a tertiary perinatal centre. Participants were composed of 27 nurses, 3 nurse practitioners, 14 respiratory therapists and 6 doctors. HCPs performed a pre-test to determine their baseline knowledge, two digital simulation scenarios using RETAIN and a post-test to determine knowledge acquisition. Two months later the participants repeated the post-test to determine knowledge retention. Descriptive analyses were conducted to determine whether performance changed over time.

Results

Following scenarios using the RETAIN digital simulator correct performance increased. 21/50 (42%) passed the pre-test, 39/50 (78%) passed the post-test and 30/43 (70%) passed the 2-month post test. Generalized linear model analysis determined that performance on all post-tests was significantly improved compared to the pre-test performances.

Conclusions

Training with the RETAIN digital simulator improved and maintained HCPs knowledge of the neonatal resuscitation algorithm. Digital simulation can be a valid simulation-based education alternative.

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Abstract #:	62
Presenter:	Mansi Garg
Supervisor:	Godbout, Roseline
Title:	Role of DDX1 and ATM in Ataxia Telangiectasia Cellular Response to Stress
Authors:	Mansi Garg, Lei Li, Roseline Godbout
Theme:	Children's health and well-being

Ataxia telangiectasia (A-T) is a group of genetic neurodegenerative disorders with onset of symptoms in early childhood, usually in children under 5 years of age. The disease is characterized by progressively impaired coordination of body movements, reddish lesions on eyes and skin (telangiectasia), predisposition to cancer, immunodeficiency resulting in frequent respiratory infections and sensitivity to radiation. The disease is caused by mutation in the ATM gene (A-T mutated). ATM protects our cells from various stress conditions by assisting in DNA damage repair, cytotoxic stress response, gene regulation and cell growth.

Earlier reports from our laboratory have shown that ATM phosphorylates and recruits Dead Box Protein 1 (DDX1) for DNA damage repair. DDX1 is an RNA unwinding protein primarily found in the nucleus of normal and cancer cells. It is essential for embryonic development and stress regulation. When DNA is damaged in irradiated cells, DDX1 and ATM co-localize to damage sites and aid in DNA repair. On the other hand, when the cells are exposed to other types of stress such as oxidative stress, DDX1 localizes to stress granules where it facilitates stress resolution.

Cells are routinely exposed to different types of stress. The role of ATM and DDX1 in DNA double strand break repair has already been documented and may be a contributing factor for increased radiosensitivity in A-T patients. In addition, A-T, along with many other neurodegenerative diseases, is also associated with oxidative stress caused by overproduction of reactive oxygen species (ROS) and impaired mitochondrial function. In this project, we are investigating the role of ATM and DDX1 in cellular response to oxidative stress. Fibroblasts from control (GM38) and A-T patients were used to test our hypothesis. Oxidative stress was induced by treatment with 0.5 mM sodium arsenite for 45 min and cells were used for detection of cellular ROS (using the DCF-DA reagent) and mitochondrial ROS (using the MitoSOX reagent). We observed elevated cellular and mitochondrial ROS levels in A-T fibroblasts as compared to GM38. Moreover, depletion of DDX1 and/or ATM in GM38 also resulted in elevated ROS levels, indicating a role for DDX1 and ATM in cellular response to stress.

We also examined the role of DDX1 and ATM in the formation and resolution of stress granules in response to arsenite-induced oxidative stress. Depletion of either ATM or DDX1 in fibroblasts did not affect the formation of stress granules, although delays in stress recovery were noted.

DDX1's role in stress recovery may be linked to its RNA binding property. We observed enrichment of 12 previously identified target RNAs in DDX1-immunoprecipitated fractions derived from GM38 fibroblasts under stress conditions. However, when A-T fibroblasts or ATM depleted GM38 fibroblasts were exposed to arsenite-induced stress, there was a decrease in these DDX1-bound RNAs. These results suggest that depletion of ATM affects the RNA binding property of DDX1. We will pursue these analyses with the goal of gaining a better understanding of the mechanism(s) underlying the spectrum of phenotypes observed in children with A-T.

Funded By: Canadian Institutes of Health Research (CIHR) and Women and Children's Health Research Institute (WCHRI).

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Abstract #:	70
Presenter:	Michael George
Supervisor:	Noga, Michelle L
Title:	Computer-Aided Pattern Recognition in Medical Imaging: Application in the Catheterization Laboratory.
Authors:	Michael G. George, Dr. Kumaradevan Punithakumar, Dr. Michelle Noga
Theme:	Children's health and well-being

The focus of this research project was to create a system for automated segmentation of three-dimensional imaging data used to inform pediatric interventional cardiology procedures to correct pathologic congenital abnormalities in pulmonary vasculature. Currently, most physicians performing these procedures rely on manual inspection of X-ray images, often without the ability to obtain quantitative measurements on the fly. While the use of three-dimensional imaging modalities in cardiac catheterization is increasingly used for interventional procedures in children, image segmentation required to aid interventions requires expert user time and attention. This also detracts the physician's attention from the task at hand. Automated segmentation was proposed to reduce the reliance on the physician or expert technologist, allowing for faster and more repeatable interpretation of the relevant information, and permitting the operating physician to focus their time and energy on the patient and procedure. An algorithmic approach was developed using a retrospective compilation of anonymized X-ray imaging datasets from procedures performed at the catheterization lab in the Mazankowski Alberta Heart Institute. In part 1 of this work, an initial segmentation algorithm was developed to accurately identify the pulmonary arterial vasculature by calculating the likelihood that each voxel belonged to a vessel-like structure. Identified structures corresponding to the vessels of interest were then isolated based on connectivity, morphology, and greyscale value in the imaging dataset. To improve segmentation quality, datasets were preprocessed with an algorithm developed to remove starburst artifacts from the images caused by intraoperative metallic catheters within the imaging field of view. The resulting approach produced a robust image segmentation strategy which was verified by expert visual inspection to confirm accuracy. However, this initial algorithm is not optimized for speed or minimization of user input. In part 2 of this work, a subset of scan data segmented using the initially developed algorithm will be generated for use in training and iteratively developing a machine-learning algorithm which is capable of automatically identifying the pulmonary arterial vasculature without the need for user input and supervision. The resulting algorithm processing time and accuracy will be assessed by performing automated segmentation on the remaining data sets and calculating corresponding Dice coefficients and Hausdorff distances relative to expert verified segmentations. As this work progresses, additional information about the size, location, and structure of the vascular structures of interest will be provided with the goal of reducing procedure times and improving patient outcomes.

Funded By: The Women and Children's Health Research Institute summer studentship, the Stollery Children's Hospital Foundation, and the University of Alberta Department of Radiology and Diagnostic Imaging.

Abstract #:	94
Presenter:	Kara Goodkey
Supervisor:	Voronova, Anastassia
Title:	Investigating brain defects in a mouse model of neurodevelopmental KBG syndrome
Authors:	Kara Goodkey, Yana Kibalnyk, Tim Footz, Anastassia Voronova
Theme:	Children's health and well-being

Ankrd11 (ankyrin repeat domain 11) functions as a chromatin remodeler. Chromatin is the condensed structure of genomic DNA that impacts global gene expression. In turn, global gene expression regulates cell and organism function. Mutations in the Ankrd11 gene lead to KBG syndrome, a rare neurodevelopmental disorder that has been diagnosed in ~500 children worldwide. KBG syndrome patients display aberrant brain development, global developmental delay, autism, and intellectual disability. Our lab has shown that Ankrd11 regulates formation of nerve cells during embryonic development. However, the role of Ankrd11 in oligodendrocyte (glial [non-neuronal] cell) development is currently not known. This is an important question to address because oligodendrocytes form myelin (major white matter component) in the brain and are required for efficient neural communication. Moreover, oligodendrocytes can be targeted pharmacologically to restore proper cognition and behaviour in mouse models with neurodevelopmental disorders. This project will determine the role of Ankrd11 in oligodendrocyte development from neural stem cells and provide the potential foundation to improve cognition and learning development in children diagnosed with KBG syndrome. To achieve this, I used a KBG syndrome mouse model, where Ankrd11 was removed (knocked out) specifically in neural stem cells, which generate oligodendrocytes through an intermediate progenitor cell termed oligodendrocyte precursor cell (OPC). Brains from these ablated animals were sectioned and stained using antibodies for OPCs (early embryonic development) or oligodendrocytes (late postnatal development). My results show Ankrd11 deficiency in neural stem cells leads to a decrease in OPC numbers in the late embryonic cortex. In postnatal cortex, Ankrd11 deficiency in neural stem cells leads to a potential increase in mature oligodendrocytes within the corpus callosum (white matter tracts) with a concomitant decrease in mature oligodendrocytes within the cortical gray matter. Notably, these cellular changes occurred specifically in the rostral areas of the murine brain. My data suggest that Ankrd11 loss-of-function may lead to aberrant oligodendrocyte differentiation. Further studies will be conducted to determine the impact this shift in differentiation has on myelination, learning, and development. My results may provide an explanation for learning and developmental delay seen in KBG syndrome patients. The results of this project hope to offer better counselling to affected families and may inspire novel therapies or cellular targets for pharmacological intervention for KBG syndrome and other similar neurodevelopmental.

Funded By: Stollery Childrens Hospital Foundation (K.G.), Women and Children Health Research Initiative (K.G.), University of Alberta start-up grants (A.V.)

Abstract #:	47
Presenter:	Mikayla Gray
Supervisor:	Hicks, Elizabeth
Title:	Get the lead out! A review of lead exposure sources and guide to their identification and assessment for public health and environmental health authorities
Authors:	Mikayla Gray, Abbeir Hussein, Anne Hicks, Lesley Brennan, Bernice Schaddelee-Scholten and Joanna Tempowski
Theme:	Children's health and well-being

Introduction: Lead is a naturally occurring heavy metal that is widely used despite known toxic effects at low concentrations[1]. Given the abundance of adverse health effects and lack of known safe threshold for lead exposure, it is imperative to localize, quantify and regulate lead emissions. Of particular concern is that lead exposure is more prevalent in children due to increased inhalation, hand-mouth behaviour and intestinal absorption[2]. Lead primarily acts as a neurotoxin and has been shown to cross the blood brain barrier in utero by mimicking calcium[3]. This exposure leads to significant impairment in cognitive, emotional and behavioural development, the effects of which last a lifetime. Additionally, lead accumulates in cortical bone and can be resorbed back into the bloodstream during normal bone growth, putting growing children at an increased risk for redeposition into the brain[3]. The purpose of this narrative review is to identify sources of lead exposure and provide an outline of the methods used to conduct environmental and human assessments of lead concentration levels. These are first steps to reducing lead exposure.

Methods: A literature search was conducted using databases including PubMed and grey literature published by public health agencies and professional associations.

Results: This review identified the main sources of lead causing human health concerns as: soil pollution originating from leaded gasoline emissions and chipping leaded paint; industrial emissions from formal and informal electronic waste recycling sites, smelting sites and abandoned mine discharge; water contamination including the use of leaded plumbing systems; and consumer products including food, toys and jewellery. Environmental assessment methods included different analytical and procedural techniques depending on the lead source. Human assessment methods commonly used include a detailed environmental health history and measuring the blood lead level.

Conclusion: This review yielded a guide in the form of a 3-step roadmap designed for use by regional public health and environmental agencies. This will allow local authorities to begin the process of reducing human lead exposure via primary prevention and may also be used to direct the planning of screening programs, remediation processes and other policies.

Funded By: This project was completed voluntarily.

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Abstract #:	6
Presenter:	Paul Greidanus
Supervisor:	Tham, Edythe
Title:	Assessment of a Novel MRI liver T1 Mapping Sequence (PROFIT1) in Fontan Patients: Towards Early Detection of Fontan-Associated Liver Disease
Authors:	Paul Greidanus, Richard Thompson, Joseph Pagano, Edythe Tham
Theme:	Children's health and well-being

Introduction: The Fontan procedure is the final surgical stage for congenital heart disease (CHD) patients with single ventricles, routing the systemic venous return directly to the lungs while the single ventricle pumps blood to the body. A long-term complication is Fontan-associated liver disease (FALD) due to a combination of chronic congestion from increased venous pressures and ischemic damage during the multiple surgeries a Fontan patient undergoes. Fibrotic myocardial remodelling may further increase backup and contribute to liver pathology. Liver biopsy is the gold standard for diagnosis of FALD as non-invasive tests such as shear wave ultrasound or liver assays have known limitations. Biopsies, however, are invasive and may not detect patchy disease. MRI T1 (longitudinal relaxation time) mapping of the liver provides quantitative assessment of fluid overload and diffuse fibrosis that may overcome these limitations.

Hypothesis: Our hypothesis is that liver T1 will be elevated in Fontan cohort compared to CHD and normal controls.

Methods: Cross-sectional cohort study of 22 patients within three cohorts: 5 Fontans/single ventricle (8.6±4.7 y), 8 biventricular CHD (13.6±3.1 y), and 9 controls (13.4±5.1 y) who had structurally normal hearts. Ventricular volumes and ejection fraction (EF) were calculated from the systemic ventricle. Myocardial native T1 mapping at a mid-ventricular short axis were quantified using an established cardiac sequence (MOLLI) in both the septum and free wall of the systemic or dominant ventricle. Liver T1 was measured with a new liver-specific T1 mapping MRI method (PROFIT1 - Proton Density Fat Fraction Imaging with Water-Specific T1) from several axial slices at the widest dimension of the liver. Whole-liver average values were calculated, avoiding blood vessels. Cohort means were compared with Kruskal Wallis test and Dunn's posthoc test.

Results: All groups had normal EF (Fontan EF-52±12%; CHD LVEF-59±6%; control LVEF-59±5%)) and myocardial T1 values (septum: Fontan-1034±50ms, CHD-1009±50ms, control-1005±22ms), and (free wall: Fontan-1008±88 ms, CHD-989±141 ms, control-970±23 ms) with no significant differences between groups. The Fontan cohort had significantly higher liver T1 (789.9±69.8 ms) compared to control (669.5±69.7 ms) and CHD (683.5±55.7 ms) (p=0.0147); control and CHD did not differ.

Conclusion: Fontan patients with normal ventricular function and no evidence of myocardial fibrosis displayed higher liver T1 values compared to CHD and control. The data suggests T1 mapping of the liver using PROFIT1 is feasible and discriminates Fontan patients from CHD and control. PROFIT1 may prove to be a useful early, non-invasive marker for detecting FALD.

Funded By: Motyl Endowment Cardiac Sciences Summer Studentship Award

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Abstract #:	88
Presenter:	Leah Hammond
Supervisor:	Andersen, John
Title:	Neonatal follow-up clinics support early identification of cerebral palsy
Authors:	Leah Hammond, Kathleen O'Grady, John Andersen
Theme:	Children's health and well-being

Background: Cerebral palsy is the most common form of childhood physical disability. Recent international expert panels and diagnostic guidelines have highlighted the importance of early identification and intervention in cases of cerebral palsy. Early identification allows children to receive cerebral palsy-specific interventions during critical developmental windows, optimizing opportunities for functional improvements. The Glenrose Rehabilitation Hospital has developed a close alliance with neonatal follow-up clinics (NNFCs) in Northern Alberta to support earlier identification of children at high risk of a cerebral palsy diagnosis. In this study, we investigated whether referral to a NNFC was associated with earlier diagnosis and initiation of rehabilitation services for children with cerebral palsy in Northern Alberta.

Methods: Three hundred and sixty-one children with cerebral palsy born between 2007 and 2019 were identified through the Canadian Cerebral Palsy Registry. All participants received services at the Glenrose Rehabilitation Hospital. One hundred and thirty-one (36.2%) were referred to a NNFC after discharge from the neonatal intensive care unit. The remaining 230 (63.7%) received usual care. Retrospective chart reviews were conducted for each child to identify Gross Motor Functional Classification System (GMFCS) scores, age at diagnosis, and age at initiation of rehabilitation services. Independent samples t-tests were used to compare age at clinical care timepoints across groups.

Results: Of children referred to NNFC, 48.0% were not independently ambulatory (GMFCS ≥ III), relative to 27.9% of children receiving usual care. Children referred to NNFC were diagnosed with cerebral palsy at a significantly younger age (M=18.57 months, SD=8.33 months) than children receiving usual care (M=21.79 months, SD=13.64 months; t(216.043)=2.194, p=0.029). Likewise, children referred to NNFC began receiving rehabilitation services at a significantly younger age (M=8.29 months, SD=5.23 months), than children receiving usual care (M=18.36 months, SD=13.69 months; t(142.899)=5.521, p=0.000).

Conclusions: In this study, we found an association between follow-up at an NNFC and earlier achievement of clinical care timepoints for children with cerebral palsy in Northern Alberta. These findings should be interpreted with caution. Children with greater gross motor impairment were over-represented in the NNFC sample, which may bias NNFC participants to earlier identification. However, the significant differences found here suggest that the Glenrose Rehabilitation Hospital's collaboration with Northern Alberta NNFCs has produced a pathway towards earlier identification and intervention for children with cerebral palsy.

Funded By: Funding for this project was generously provided by the Canadian Institutes for Health Research, Glenrose Rehabilitation Hospital, the National Centres of Excellence, and the Women and Children's Health Research Institute.

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Abstract #:	117
Presenter:	Guillermo Hasbun
Supervisor:	Castro Codesal, Maria L
Title:	Comparing NIV Adherence in Children with Neuromuscular Disease Presenting Early or Advanced Stage Sleep Disordered Breathing
Authors:	Guillermo Hasbun, Prabhjot Bedi, Halima Abuoun, Maria Castro-Codesal
Theme:	Children's health and well-being

Introduction

Children with neuromuscular diseases (NMDs) often develop sleep-disordered breathing (SDB) due to loss of upper airway muscle tone and weakness of respiratory muscles. Commonly, children with NMD initially develop SDB exclusively during Rapid Eye Movement (REM) sleep due to associated physiological muscle atonia. With disease progression, SDB affects both REM and non-REM sleep stages. While non-invasive ventilation (NIV) is the standard treatment for advanced SDB in children with NMDs, the use of NIV in earlier stages of SDB (REM-SDB) is less demonstrated and therapy adherence is unclear. This study aims to compare NIV adherence between children with early SDB (REM-SDB) and advanced SDB (NREM-SDB).

Methods

A dataset of children 0-18 years with a diagnosed NMD receiving NIV in Edmonton was used. An apnea-Hypopnea Index (AHI) ratio between REM and NREM sleep ≥ 2 was used to define the cases (REM-SDB pool). Conversely, an AHI ratio between REM and NREM sleep < 2 was used to define the controls (NREM-SDB pool). An independent sample t-test was used to determine differences in mean percentage of days with NIV use ≥ 4 hrs and mean nightly NIV hours in a 4-week period.

Results

Nine cases and 5 controls with 16 and 8 adherence reports, respectively, were included in the analysis. Case and control groups were homogenous in age, sex, underlying condition, and technology-related characteristics. There was a significant difference in the percentage of days with NIV usage ≥ 4 hours between cases (77% ± 8.9) and controls (93% ± 2.7). However, the average daily hours of NIV used was not significantly different between cases (9.2 ± 1.3) and controls (9 ± 0.4).

Conclusion

Children with REM-SDB and NREM-SDB both had high rates of NIV adherence, with no differences in mean nightly NIV hours. However, children with REM-SDB had lower days with sufficient NIV use (>4 hrs) suggesting less willingness to use the therapy compared with children with NREM-SDB.

Funded By: Northern Alberta Clinical Trials and Research Centre Summer Student Award (NACTRC)

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Abstract #:	7
Presenter:	Rose He
Supervisor:	Hornberger, Lisa K
Title:	Seeing Heart to Heart - Accuracy of Fetal Echocardiography in the Prenatal Diagnosis of Congenital Heart Disease
Authors:	Rose He, Kim Haberer, Jayani Abeysekera, Aisling Young, Luke Eckersley, Angela McBrien, Isabella Adatia, Rashiv Sharma, Michelle Rushfeldt, Lisa K Hornberger
Theme:	Children's health and well-being

Introduction: The ability to detect congenital heart disease (CHD) before birth via fetal echocardiography (FE) - the use of sound waves to image a baby's heart while in the mother's womb - has greatly developed since its conception in the 1950s and has been shown to largely improve the care of both the pregnant mother and affected baby. However, there have been few studies examining the accuracy of FE, which is key in providing accurate family counseling, including decisions regarding continuation/termination of pregnancies and preparation of anxious parents for the baby's care after birth. Moreover, it is also essential for planning the best location, mode and timing of delivery as well as the newborn's medical and surgical care. This approach has led to improved survival of newborns, especially those with severe CHD. We sought to determine the accuracy of FE in defining details of the cardiac anatomy associated with 12 major subtypes of CHD, and the factors that may contribute to more accurate diagnoses, namely gestational age at first FE, serial assessment, and improvement over the years. Methods: We queried the fetal database at the University of Alberta Fetal & Neonatal Cardiology Program from 2007-2018. Discrepancies between prenatal (most accurate exam) and postnatal echo/surgery and/or autopsy (when available) were categorized as: 1) no difference 2) minor difference with no impact on clinical outcome (eg.aberrant right subclavian artery) 3) difference that has a minor impact on surgical care (eg.vascular ring) 4) major differences which impacts the acute care and surgical outcomes of the baby (eg.ductal dependency). Cases that fell in categories 1 and 2 were considered "accurate", while those in categories 3 and 4, which impacted or inadequately predicted postnatal outcome, were deemed "inaccurate." Results: Of the 827 CHD cases diagnosed by FE in our program, 589 had confirmation of the CHD diagnosis (573 postnatal echos and 16 fetal autopsies. The accuracy of FE was 89.3% for all CHD combined, ranging from a high of 100% accuracy in the diagnosis of single ventricle lesions to the lowest of 71.1% for heterotaxy. With respect to gestational age, we found 94.1%(206/219), 87.1%(210/241), and 86.2%(100/116) accuracy for cases evaluated at 16-24, 25-33, and 34-40 weeks, respectively (p=.022), excluding 13 cases between 10-15 weeks where fetal echo is known to have low accuracy. In regards to serial assessment, the number of "inaccurate" cases were halved when there was more than one study, decreasing from 16.2%(single study) to 8.1%(multiple studies). In fact, 91.9% of pregnancies with multiple studies had an accurate prenatal diagnosis, nearly a 10% increase from the 83.6% of pregnancies with only a single study(p=.0036). Finally, we compared data from 2007-2011 with 2012-2018 and found that there was an accuracy of 83.5% in the earlier period versus 92.7% in the latter (p<.001).The "inaccurate" cases decreased from 16.5% to 7.3%. Conclusion: FE has high accuracy at our institution, although there remains challenging lesions to diagnose. The optimal time for FE is between 16-24 weeks and serial assessment is beneficial. These findings will help shape future FE practices to improve provided care to CHD patients and their families.

Funded By: This WCHRI summer studentship award has been funded by the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute.

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Abstract #:	34
Presenter:	Shelby Henry
Supervisor:	Hicks, Elizabeth
Title:	A systematic review and meta-analysis of studies assessing the risk of respiratory-related healthcare visits associated with wildfire smoke exposure in children 0-18 years old.
Authors:	Shelby Henry, Elizabeth Dennet, Maria-Beatriz Ospina, Anne Hicks
Theme:	Children's health and well-being

Introduction

Changes to the earth's climate influence extreme weather events which contribute to natural disasters across the globe, including wildfires. The wildfire burning season is expected to increase, with fires increasing in frequency, size, and intensity. Smoke produced by wildfires is comprised of small particles and toxic gases that are harmful to human health when inhaled. It has been suggested that children may be at an increased risk of negative respiratory effects from wildfire smoke due to their smaller airway size and continuously developing lungs. The primary objective of this systematic review was to synthesize the data from studies investigating the risk of respiratory-related healthcare visits specifically in children aged 0-18 years old following exposure to wildfire smoke. The secondary objective was to synthesis data from studies reporting respiratory symptoms in children following exposure to wildfire smoke.

Methods

A health sciences librarian (LD) conducted a systematic search in relevant databases. The search combined a list of keyword synonyms for wildfires with a search hedge for pediatric studies. A google search was conducted and the Pediatric Environmental Health Specialty Units (PEHSU) and Environmental Protection Agency (EPA) websites were screened to identify grey literature. Reference lists of included articles and reviews were reviewed for additional studies. Peer-reviewed primary research on the topic of wildfires and pediatric respiratory health was reviewed. Studies were included if they contained differentiated pediatric data (0-18 years old), reported outcomes of respiratory related healthcare visits or respiratory symptoms, and focused on exposure to wildfire of any vegetation. Studies were excluded if they were case-report or case series methodology, included prescribed burns or wildfire secondary to a primary disaster, or focused solely on burns, mortality, birth outcomes, or pregnancy related outcomes. Following title and abstract screening and full text review, the remaining studies were screened for bias using the OHAT Risk of Bias Rating Tool for Human and Animal Studies.

Results

The initial search produced 1977 results, and after duplicates were removed, a total of 967 results remained. All 967 results had their titles and abstracts screened for relevance with 913 studies being excluded. Reference screening identified 2 additional studies, and no grey literature was identified. The remaining 56 studies continued on to full text screening; 8 were excluded due to no respiratory outcomes, 11 were excluded due to no pediatric data (or undifferentiated data), 7 were excluded due to prescribed burn or other exposure, 4 were excluded due to case-series/report or review methodology, 3 were excluded due to no full text available, 1 was excluded due to only assessing birth outcomes, 5 were excluded due to repeated data and 17 continued to assessment of risk of bias. One study was identified as having high risk of bias and was excluded from the analysis. As such, the remaining 16 studies were included in this review. Trends suggest that mucosal irritant and respiratory symptoms are acutely increased in children with significant smoke exposure. Quantitative and qualitative analyses are underway.

Funded By: RHSCN Summer Studentship

Abstract #:	95
Presenter:	Jens Herzog
Supervisor:	Waskiewicz, Andrew
Title:	Studying TSC2 mutations effects on mTOR regulation during eye development
Authors:	Jens A. Herzog1, Kevin H. Yoon1, Xaverie MacLennan1, Andrew J. Waskeiwicz123
	1 Department of Biological Sciences, University of Alberta
	2 Neuroscience and Mental Health Research Institute, University of Alberta
	3 Women & Children's Health Research Institute, University of Alberta
Theme:	Children's health and well-being

Introduction

Superior coloboma is a genetic blinding disorder present at birth. It is caused by a gap in upper eye tissue, which we believe fails to close during eye development. Our lab has identified many genetic variants from sequenced genomes of superior coloboma patients. These variants can be studied to detect the developmental causes of superior coloboma. My work focuses on a promising candidate mutation in Tuberous Sclerosis Complex 2 (TSC2). TSC2 is a regulator of mammalian target of rapamycin (mTOR) signaling. mTOR regulates a wide array of cellular functions through mTOR complex 1 and 2, including cell growth, division, death, and protein creation. TSC2 is a primary inhibitor of mTOR complex 1 activity, so in the absence of functional TSC2 mTOR activity is elevated. Previous scientific studies of tuberous sclerosis complex patients with mutations in TSC2, are also sometimes diagnosed with colobomas. We propose that tsc2 plays a role in proper closure of the upper eye by regulating mTOR and aim to discover the cellular mechanisms involved in the process.

Methods

The genetic pathways of vertebrate eye development are highly conserved between humans and zebrafish (Danio rerio), as eyes evolved in a shared common ancestor. This means that zebrafish, can be used as a model to study the genetics of human eye development. An initial study of tsc2 function blocked normal tsc2 function using morpholino oligonucleotides.

Results

Knocking down tsc2 with morpholino oligonucleotides caused a delay in the closure of the gap in the upper eye in 60% of zebrafish embryos. This preliminary data disrupting tsc2 in zebrafish, suggests that tsc2 mutations cause superior coloboma.

Conclusions

The specific functional role of TSC2 in the upper eye is largely unknown, beyond the general roles it plays mTOR signalling. With current genetics techniques we can create a model of superior coloboma in zebrafish to study the role of mTOR signalling in the eye. I am currently using CRISPR-Cas9 mutagenesis to create specific mutations targeted to knock out the zebrafish tsc2 gene function. From reviewing the initial sequencing of human patients other mTOR pathway regulators with mutations were discovered and will also be targeted for CRISPR-Cas9 mutagenesis. These would provide an excellent tool for further experiments assessing the effect on mTOR activity in the eye and identifying what specific functions are being changed. Once the model has been created, we can assess, cell growth, division, and death. By looking at each aspect of mTOR signalling during the window where the gap in the upper eye opens and normally closes, in healthy fish and our tsc2 mutants we will determine the biological mechanism contributing to superior coloboma and better understand the role of mTOR in eye development.

Funded By: WCHRI

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Abstract #:	154
Presenter:	Chelsea Hobbs
Supervisor:	Larsen, Denise J
Title:	The Lived Experiences of Hope for Pregnant Persons Following the Loss of Their First Pregnancy
Authors:	Chelsea L. Hobbs & Denise J. Larsen
Theme:	Pregnancy and developmental trajectories

Introduction: Approximately one in five pregnancies result in pregnancy loss. Though a common experience, pregnancy loss is often not acknowledged socially, and the personal and family impact minimized. This creates isolation regarding a deeply challenging and psychologically stressful experience and for some, the loss of a child represents one of the most traumatic experiences possible. Across the grief literature, hope is identified as an important companion, helping those who face profound loss find a future in which they wish to re-engage. A key contributor to healthy living, hope is consistently linked with life satisfaction and strongly tied to positive life outcomes. The study of hope and its relation to psychological healing has grown exponentially over the last four decades, though little has been done in the field of pregnancy loss in direct relation to hope.

Proposed Research: The purpose of this qualitative study is to explore the lived experiences of hope for pregnant persons following the loss of their first pregnancy. An explorative study, the project will result in a rich description and understanding as lived by pregnant persons who have experienced the loss of a pregnancy. This will develop a foundation of knowledge in this area as well as inform practice by deepening the understanding of individuals' subjective experiences of pregnancy loss. The research question is: How do pregnant persons experience hope following the loss of their first pregnancy?

Methodology: Interpretative phenomenological analysis (IPA) is the research methodology chosen for the proposed study. IPA is a methodology concerned with the lived experiences of being human and IPA researchers focus on how participants make sense of and ascribe meaning to an experience of particular importance to them. A sample size of six to eight participants will be purposefully recruited from health clinics that support perinatal loss within the Edmonton area. The selection criteria are: unintended loss of a first pregnancy that occurred prior to 20 weeks of gestation; no identified fertility problems; wanted the pregnancy; at least one-month post pregnancy loss; self-describe as having difficulty following the loss; self-describe as currently adapting to the experience; have not conceived again and are not currently pregnant; are articulate; are willing to speak about the pregnancy loss experience and hope. Data will be collected through two one-hour, in-depth, semi-structured face-to-face interviews. Interviews will explore experiences following pregnancy loss that were supportive of hope, may have challenged hope, and any role hope played in recovery from the experience. Data will be analyzed according to the six steps used in IPA and data analysis will be coordinated and managed using the ATLAS.ti computer program for qualitative data analysis.

Implications: Findings are expected to describe how pregnant persons experience hope following the loss of a pregnancy. This research will inform professionals including psychologists, physicians, nurses, midwives and doulas on how to best support individuals to grow through and beyond pregnancy loss and deepen society's understanding of an often overlooked, misunderstood and unacknowledged reproductive experience.

Funded By: Funding for this project has been provided by the Bereavement Society of Alberta, the Faculty of Graduate Studies and Research and the Department of Educational Psychology at the University of Alberta, and the Government of Alberta.

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Abstract #:	35
Presenter:	Summer Hudson
Supervisor:	MacLean, Joanna E
Title:	Long-term non-invasive ventilation in children with Down syndrome: a systematic review
Authors:	Summer Hudson, Melanie Lewis, Joanna E MacLean
Theme:	Children's health and well-being

Introduction: Down Syndrome confers susceptibility to multiple sleep-related breathing disorders, for which long-term non-invasive ventilation (NIV) is a common treatment option. While there is a large body of evidence for the use of long-term NIV in the broader pediatric population, work specific to its use in children with Down syndrome is more limited. Understanding the benefits and challenges of long-term NIV use in this population is important for informing patient-centered care as well as fiscal health policy around equipment funding and family support. This study aims to systematically review the current state of evidence on this topic.

Methods: This systematic review is an extension of a scoping review. The search strategy used Medical Subject Headings (MeSH) and free-text terms for "child" and "non-invasive ventilation". MEDLINE (Ovid), Embase (Ovid), CINAHL (Ebsco), Cochrane Library (Wiley), and PubMed were systematically searched for the period of 1990-2019. Included studies examined NIV use for at least three months in three or more children with Down syndrome.

Results: 21 articles met inclusion criteria and included 359 children with Down syndrome. Designs were mostly observational. Only 7 studies were undertaken exclusively in children with Down syndrome. Long-term NIV use was mainly used for the treatment of obstructive sleep apnea (OSA) and was frequently used for residual OSA following adenotonsillectomy and as a bridge to improvement in children who outgrew OSA with age. Satisfactory NIV adherence was documented in children with Down syndrome. Specific neuropsychological and cardiac benefits of long-term NIV use may be seen in this population, though data on outcomes specific to children with Down syndrome is scarce.

Conclusion: Children with Down syndrome can successfully use long-term NIV, however with no comparative studies, it is unclear whether they face more challenges with its use. With limited studies focusing on outcomes, the benefits of long-term NIV for children with Down syndrome remain difficult to define.

Keywords: non-invasive ventilation, continuous positive airway pressure, bilevel positive airway pressure, Down syndrome, obstructive sleep apnea

Funded By: This project was undertaken as a summer volunteer and received no funding support.

Abstract #:	25
Presenter:	Nataliia Hula
Supervisor:	Davidge, Sandra
Title:	The Role of Endothelin-A Receptors in the Increased Cardiac Susceptibility to Ischemia/Reperfusion Insult in Adult Offspring Exposed to Prenatal Hypoxia
Authors:	Nataliia Hula, Jennie Vu, Anita Quon, Raven Kirschenman, Floor Spaans, Christy-Lynn M. Cooke, Sandra T. Davidge
Theme:	Pregnancy and developmental trajectories

Introduction: Fetal hypoxia is a common consequence of complicated pregnancies that triggers the development of cardiac dysfunction in the offspring. We showed that prenatally hypoxic offspring have impaired cardiac tolerance to an ischemia/reperfusion (I/R) insult, however, the mechanisms remain unclear. During a cardiac I/R insult, there is increased endothelin-1 (ET-1) release. Activation of endothelin-A receptors (ETAR) by ET-1 leads to cardiac dysfunction, while activity of endothelin-B receptors (ETBR) is essential for cardiac recovery after I/R. Inhibition of ETAR during I/R has been shown to improve post-ischemic cardiac function; however, whether the ET-1 pathway contributes to the enhanced susceptibility to I/R injury in prenatal hypoxia-exposed offspring, is unknown. We hypothesize that prenatal hypoxia increases cardiac ET-1 and ETAR levels, thus impairing cardiac tolerance to I/R, and inhibition of ETAR during I/R improves post-ischemic cardiac recovery in adult offspring.

Methods: Pregnant Sprague-Dawley rats (n=4-6/group) were exposed to normoxia (21% O2) or hypoxia (11% O2) from gestational day 15-21 (term=22 days). Offspring were aged to 4 months, and cardiac function was assessed ex vivo using the isolated working heart technique. Hearts were subjected to an I/R insult (25 min. ischemia with 40 min reperfusion), or were snap frozen (non-ischemic control). To assess the contribution of ETAR receptors to cardiac dysfunction, an ETAR antagonist (ABT-627) was infused 20 min before the I/R insult. Left ventricle tissues (non-ischemic and post-I/R) were assessed for ET-1, ETAR and ETBR levels by Western blotting (analyzed as % of mean of non-ischemia). Data were compared by two-way ANOVA with Sidak`s post hoc test; $p<0.05$ was considered significant.

Results: In males, I/R decreased cardiac ET-1 levels compared to non-ischemic hearts (128.5±16.4% vs 89.8±10.4%; p=0.02). Exposure to prenatal hypoxia increased ET-1 levels in non-ischemic (99.9±9.4% vs 157±27.6%; p=0.04) and post-ischemic hearts (62.8±6.2% vs 116.8±12.3%, trend: p=0.055) compared to the normoxic group. In females, I/R increased ET-1 levels compared to non-ischemic group (124.7±16.8% vs 327±39.4%, p=0.001) with no effect of prenatal hypoxia. I/R did not affect ETAR and ETBR expression, while prenatal hypoxia decreased ETBR levels in male offspring only (101.2±5.8% vs 72.6±3.9%, p=0.001). ABT-627 induced an extreme reduction in cardiac recovery after I/R in prenatally hypoxic males (60.5±16.3% vs 4.4±2.6%, p=0.009), without effect in normoxic males. In contrast, ABT-627 tended to improve cardiac recovery after I/R, in the female hypoxic group only (53.5±10.6% vs 87±5.6%, p=0.052).

Conclusion: Prenatal hypoxia resulted in an increased cardiac ET-1 levels and decreased ETBR expression in male offspring only, thus suggesting that prenatal hypoxia affects the cardiac ET-1 system in adult offspring in a sex-specific manner. Interestingly, in the prenatal hypoxia groups only, ETAR inhibition impaired cardiac recovery after I/R in males, while it improved cardiac recovery after I/R in females. This suggest that ET-1 function via ETAR may be essential for cardiac ability to tolerate I/R in prenatally hypoxic males, while it contributes to cardiac dysfunction in females.

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Abstract #: 48
Presenter: Robin Humble
Supervisor: MacDonald, Shannon
Title: The Association Between Access to Public Health Vaccine Services and Childhood Immunization Status

Authors: Ms. Robin Humble

Dr. Shannon MacDonald

Dr. Eve Dubé

Dr. Julie Bettinger

Dr. William Fisher

Dr. Vineet Saini

Dr. Devon Greyson

Dr. Holly Wittemann

Theme: Children's health and well-being

Introduction/background: Childhood vaccination coverage in Canada remains below national targets, contributing to periodical outbreaks of vaccine-preventable diseases. Access to health services is a key determinant of health, however, structural barriers may impact the ability of some families to access vaccine services. The aim of this study was to explore the association between urban-rural residence and health system barriers to public health vaccine services and the immunization status of children at 2-years-old.

Methods: This cross-sectional study used an email survey of a national panel of parents who had at least one child aged 24-59 months (N = 2014). Binary logistic regression analysis assessed the relationship between exposure variables: Urban-rural residence, as measured by population size (<1 000, 1000 to 29 999, 30 000 to 99 999, and >100 000) and a categorical composite variable measuring access to vaccine services derived from the following variables: timing of appointments and availability; clinic operating and contact hours; convenience of vaccine services and/or clinic wait times; and, knowledge of vaccine schedules. The outcome variable was immunization status at 2-years-old, measured as: incomplete vaccination (only some vaccines received) or all recommended vaccines received.

Results and analysis: We found that structural barriers to accessing childhood immunizations was statistically significantly associated with incomplete vaccinations received by 2 years-of-age (OR 4.017, CI 95% 1.938-8.326), as compared to receiving all vaccinations, after controlling for urban-rural residence.

Conclusions and implications for policy, practice or additional research: Results suggest that as the number of structural barriers to accessing immunization services increases, the chances that not all recommended vaccines are received also increases. Addressing health systems barriers to immunization services will support parents and caregivers seeking to immunize their children, thereby increasing vaccine coverage and decreasing risk of infectious disease outbreaks. Initiatives may include interventions such as increasing communication methods and appointment scheduling/time-allotment.

Funded By: Funding provided by Canadian Immunization Research Network and Alberta Health

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Abstract #:	118
Presenter:	Ali Hussain
Supervisor:	Kumar, Manoj
Title:	Implementation of Minimally Invasive Surfactant Therapy (MIST) in Preterm Infants with Respiratory Distress Syndrome (RDS) - A Quality Improvement (QI) Project
Authors:	Ali Hussain MBBS FCPS, Jag Bhogal MD MSc, Brenda Hiu Yan Law MD MSc, Manoj Kumar MD MSc
	Department of Pediatrics, University of Alberta
Theme:	Children's health and well-being

Introduction: Respiratory distress syndrome (RDS) is common in premature infants. Treatment of RDS includes endotracheal instillation of surfactant. In stable infants, InSurE (Intubation-Surfactant-Extubation) protocol is commonly used to minimize the duration of invasive ventilation. However, InSurE protocol still exposes infants to potential adverse effects associated with endotracheal intubation (e.g. airway trauma) and mechanical ventilation. Minimally Invasive Surfactant Therapy (MIST), uses a thin catheter inserted under laryngoscopy to deliver surfactant to preterm infants stabilized on non-invasive ventilation (e.g. nasal CPAP). Evidence from randomised trials show that the MIST technique reduces the need for mechanical ventilation (MV) in this population, and reduces the incidence of bronchopulmonary dysplasia (BPD) and intraventricular haemorrhage (IVH). We aimed to implement MIST at our Level III neonatal intensive care unit (NICU).

Method: Our project is being conducted at the Royal Alexandra Hospital in Edmonton, Alberta. Inclusion criteria: Preterm infants, born at >29 weeks gestation, with RDS, weighing > 1000g, and requiring the first dose of surfactant within 72h of birth. Exclusions: Hemodynamically unstable infants, and/or severe RDS (FiO2 > 50%). Implementation is planned in three phases:

Phase 1: Develop local MIST guidelines, and to collect the baseline information on infants receiving surfactant via InSurE protocol;

Phase 2: Introduce training, and implement MIST in the NICU via a selected team;

Phase 3: To establish MIST as preferential mode of providing surfactant to all eligible preterm infants.

We will record data on the following outcomes and compare our results to those reported in pre implementation phase and in literature: Need for MV within 72h of birth, respiratory complications including BPD, IVH, Necrotizing Enterocolitis, Retinopathy of Prematurity, length of hospital stay, time to full feeds, and NICU mortality.

Results: This is an ongoing project. Guidelines and training materials were developed in preparation for on-unit implementation. A small group of experienced intubators were trained to perform MIST using a flexible 16G catheter under either direct laryngoscopy or video laryngoscopy. As of September 2020, 9 infants had MIST attempted, with a median GA of 30 weeks (IQR 29.9-32.4), and a median birth weight of 1450g (1269-1905). Seven procedures (78%) were successful in delivering surfactant via MIST, 2 reverted to InSurE.

Conclusion: MIST has the potential to decrease exposure to mechanical ventilation in preterm infants with RDS. Ongoing monitoring of failure rates, complications, and clinical outcomes is needed to ensure appropriate patient selection and adequate on-unit training.

Funded By: No intra or extramural funding obtained for this project.

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Abstract #:	12
Presenter:	Geraldine Huynh
Supervisor:	Turner, Justine M
Title:	Mealtime Support: A pilot cohort study of an Effective, Cost-saving Outpatient Hunger-Based Feeding Program for Tube Dependency

Authors:	Geraldine Huynh MD, Alysha Vishram OT, Carol Graham-Parker RD, Matthew Carroll MD, Justine Turner MD

Theme:	Children's health and well-being

Background: Tube feeding is essential for children who cannot meet nutritional requirements orally. Over time this can lead to tube dependency with negative impacts on the quality of life of children and families.

Objective: We aimed to examine the efficacy of a multidisciplinary child-led, hunger-based approach called "Mealtime Support" at the Stollery Children's Hospital in Edmonton. Nutritional outcomes, parental satisfaction and cost implications were evaluated over 9 months per child.

Methods: The ambulatory meal program was delivered 2-3 times a day, for 2 weeks, by an occupational therapist and dietitian, under medical supervision. Hunger was promoted by reducing tube fed calories by 80% prior to commencement. Caregivers completed 12-question subjective surveys pre and post intervention. Micro-costing methods compared costs between the program and ongoing tube feeding.

Results: From 2016 - 2017, 6 children were enrolled and 5 completed the program. At 1-month post intervention, 4/5 of the children were 100% orally fed. Parents reported improvement in mealtime struggles (p-value = 0.005), reduction in worry about their child's eating (p-value = 0.005) and improvement in their child's appetite/variety foods eaten (p-value = 0.004). Over 3 years potential cost savings were estimated at $75,000. By 6-months, all feeding tubes were removed.

Conclusions: Mealtime Support was safe and successful in reducing tube dependency and cost-effective compared to no intervention or hospital based programs. There is a need to develop and fund Canadian outpatient feeding programs.

Funded By: none

Abstract #:	116
Presenter:	Peter Anto Johnson
Supervisor:	Schmolzer, Georg M
Title:	Feasibility of Doppler ultrasound for heart rate assessments during neonatal resuscitation: results from a swine model of neonatal asphyxia
Authors:	Peter Anto Johnson, Nicolò Morina, Tze-Fun Lee, Megan O'Reilly, Po-Yin Cheung, Georg M. Schmölzer
Theme:	Children's health and well-being

Introduction:

Heart rate (HR) is the most significant parameter to assess a newborn's clinical status at birth. Assessment of HR is used to decide which interventions are performed and its effectiveness during resuscitation. Current neonatal resuscitation guidelines recommend pulse oximetry and electrocardiography (ECG) for HR assessment, however these techniques are limited by high latency and poor signal quality during severe asphyxia at birth. Most recently, the Doppler ultrasound, which utilizes high frequency sound waves to detect pulsatile blood flow changes, has been proposed as an effective alternative HR assessment technology during neonatal resuscitation. We aimed to evaluate the accuracy and feasibility of the Doppler ultrasound for HR assessment in a porcine model of neonatal asphyxia. We hypothesized using the Doppler ultrasound would provide a similar accuracy to ECG, the clinical gold standard.

Methods:

Newborn piglets (n=20, 1-3 days, 1.7-2.4 kg) were anesthetized, intubated, mechanically ventilated, and subjected to 30 min of hypoxia, followed by asphyxia. Asphyxia was induced by clamping the endotracheal tube and disconnecting the ventilator until asystole was confirmed via carotid blood flow. During asphyxia, HR assessments were performed using a USCOM 1A (USCOM Ltd, Sydney, Australlia) Doppler ultrasound device. The Doppler transducer was placed on the animal's suprasternal notch to detect aortic outflow, which is used to measure HR. Measurements were performed every 30 sec throughout asphyxia and compared to ECG. Bland-Altman analysis was conducted to measure the level of agreement between these measurements.

Results:

ECG recordings provided a mean (SD) HR of 70 (28) bpm, while the mean (SD) HR measured using Doppler ultrasound was 69 (27) bpm. Bland-Altman analysis revealed a mean difference (95% limits of agreement) between Doppler-US and ECG HR of 1.5 (−16 to 19) bpm and intraclass correlation coefficient of 0.93. Although HR could be obtained with a shorter latency and good accuracy throughout asphyxia, the use of Doppler ultrasound had certain limitations including the presence of motion or gasping artifacts during ventilation that could produce false peaks and a decrease in peak size, which was observed with progressing bradycardia.

Conclusion:

Our data suggests using Doppler ultrasound for HR assessment during neonatal resuscitation is accurate and feasible. However, clinical trials are warranted to evaluate its feasibility in human infants requiring resuscitation.

Funded By: Women & Children's Health Research Institute (WCHRI), Stollery Children's Hospital Foundation, SickKids Foundation, Canadian Institutes of Health Research (CIHR), & Heart and Stroke Foundation Canada

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Abstract #:	135
Presenter:	Wisdom Kate
Supervisor:	Weinfeld, Michael
Title:	Assessing the potential role of polynucleotide kinase phosphatase in the cGAS-STING pathway
Authors:	Wisdom Deebeke Kate, Mesfin Fanta, Michael Weinfeld.
Theme:	Lifelong women's health

Introduction

Although conventional radiotherapy (RT) has proven useful in the management of breast cancer, with up to 83% of patients benefiting from it either with a curative or palliative intent, some patients still develop loco-regional recurrence following RT. A paradigm shift in the use of RT comes from our recent understanding that the use of high dose stereotactic body radiation therapy can boost the immune system against tumours at both irradiated and non-irradiated sites. This has prompted the need for a novel approach to effectively use RT together with immune checkpoint inhibitors to control tumour growth and consequently reduce the burden of tumour recurrence and metastasis. Since DNA damage has been implicated in the activation of the type 1 interferon (IFN) response, this opens the possibility of using DNA repair inhibitors to augment the activation of the immune system. As a result, we aim to unravel a new role for the DNA repair protein, polynucleotide kinase phosphatase (PNKP) in the type 1 IFN response. PNKP is a DNA end-processing enzyme that possesses both 5'-kinase and 3'-phosphatase activities. Because the cytosolic 3′-5′ exonuclease, TREX1, is unable to digest DNA with a 3′-phosphate, we hypothesise that knockdown of PNKP and simultaneous irradiation of breast cancer cells will increase the levels of cytosolic DNA, which would consequently potentiate the cGAS-STING pathway and type 1 IFN response, leading to immune clearance of cancer cells.

Methods

For analyses of the effects of PNKP depletion, cells grown in DMEM/F12 complete media were treated with a PNKP inhibitor or transfected with siRNA against PNKP. Transfection media was changed 24 hours later and cells were maintained in fresh media for an additional 16-24 hours prior to ionizing radiation exposure. Western blotting, immunofluorescence, and RT-qPCR were used to analyse changes in protein or gene expression levels. We determined cellular responses using MTS assay and crystal violet staining as surrogate markers of proliferation and viability, respectively.

Results

Our results show that siRNA-mediated knockdown of PNKP in the breast cancer cell line, MCF7, following irradiation led to elevated levels of STAT1 phosphorylation (an indication of cGAS activation) and an upregulation of the IFN stimulated genes compared to the wild type cells. This observation is consistent with the results obtained in the colorectal cancer cell line, PNKP CRISPR knockout HCT116. We have also shown that PNKP-depleted cells exposed to radiation display significantly more cytosolic DNA than wild type cells. Moreover, we have shown that PNKP is present in the micronuclei of irradiated cervical cancer cell line, HeLa, which might suggest that PNKP may be involved in dephosphorylating the ends of DNA fragments, making them amenable to TREX1 digestion.

Conclusion

The results above provide strong evidence for the involvement of PNKP in the cGAS-STING pathway, and that PNKP inhibition might help to potentiate the type I IFN response leading to enhanced immunogenic targeting of breast tumours. Findings from this study will provide further support for the development of an inhibitor against the PNKP enzyme for clinical applications in combination with radiotherapy against breast tumours.

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- FoMD 75th Anniversary Award
- U of A Doctoral Recruitment Award

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- Antoine Noujaim Graduate Entrance Award

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Abstract #:	8
Presenter:	Amanpreet Kaur
Supervisor:	Eckersley, Luke
Title:	Trends in the prenatal detection of major Congenital Heart Disease in Alberta from 2008 to 2018 - a population based study
Authors:	Amanpreet Kaur, Lisa K Hornberger MD, Deborah Fruitman MD, Luke G Eckersley MBBS PhD
Theme:	Children's health and well-being

Introduction: Fetal echocardiography has permitted the detailed diagnosis of most forms of congenital heart disease (CHD) for the past 2-3 decade; however, until more recently, the majority of affected newborns with CHD were not identified before birth. With improvements in obstetrical ultrasound guidelines, particularly in the past decade, we have witnessed enhanced detection of certain CHDs. In the current study, we examine at a population level trends in prenatal detection of major CHD in the province of Alberta. We hypothesize that while most major defects associated with 4 chamber and outlet anomalies have demonstrated a substantial increase in detection, arch and pulmonary venous anomalies remain a challenge.

Methods: We retrospectively identified all fetal and infant cases of major CHD requiring surgical intervention within the first year encountered in our province from January 1, 2008, to December 31, 2018 using provincial fetal, echocardiography and surgical databases. Fetal and postnatal databases were linked, identifying those with and without a prenatal diagnosis including fetal cases not resulting in a live birth and palliated newborns. We categorized CHD subtypes based on the obstetric ultrasound cardiac views required for detection: Groups 1) 4 chamber view, 2) Outflow tract view, 3) three vessel or other non-standard cardiac views.

Results: Of 1476 cases with major CHD encountered in Alberta, 331/611 (54%) were prenatally diagnosed from 2008 - 2012, and 562 / 865 (65%) from 2013 - 2018 ($p<0.001$). There were improvements in prenatal diagnosis rate in all groups: Group 1 (2008 - 2012 70%, 2013-2018 81%, $p=0.002$), Group 2 (2008 - 2012 53%, 2013 -2018 62% $p=0.027$), Group 3 (2008 - 2012 25%, 2013 - 2018 40% $p=0.007$). Whilst the majority of Group 1 conditions remained at a stable and high fetal diagnostic rate (~90%), the fetal diagnosis of Group 2 and 3 conditions improved between 2008 - 2012 and 2013 - 2018: Coarctation (Group 3) 28% vs 43% $p=0.021$; Atrioventricular Septal Defects (Group 1) 35% vs 66% $p<0.001$; Transposition of the Great Arteries (Group 2) 39% vs 58% $p=0.034$, Vascular Rings 25% vs 61% (0.089). Total anomalous pulmonary venous drainage remains a challenge, with only 1 prenatal diagnosis in the study period. Interestingly the diagnostic rate of Tetralogy of Fallot remained stable (47% vs 45%).

Conclusions: The rate of fetal detection of outflow tract and arch abnormalities has significantly improved in the past decade, particularly for Transposition of the Great Arteries, Atrioventricular Septal Defects and Coarctation of the Aorta. Further analysis will focus on socioeconomic and geographic determinants of fetal diagnosis in this large population-based dataset.

Funded By: Unfunded

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Abstract #:	136
Presenter:	Hedieh Keshavarz-Bahaghighat
Supervisor:	Seubert, John
Title:	Eicosanoid profiling of human dilated cardiomyopathy tissues demonstrates changes in lipid metabolism
Authors:	Hedieh Keshavarz-Bahaghighat, Ahmed M. Darwesh, Mathew Edin, Darryl Zeldin, Hao Zhang, Gavin Y. Oudit, John M. Seubert
Theme:	Lifelong women's health

Proposed research project: Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality in both men and women worldwide. Dilated cardiomyopathy (DCM) is a heterogeneous disease characterized by ventricular chamber dilation and depressed systolic function in the absence of homodynamic abnormalities and coronary artery diseases. Although efforts have been made to understand the role of sex differences in CVD, sex differences have seldom been considered as an independent factor in prognosis and pathogenesis of DCM. The long-chain n-3 and n-6 polyunsaturated fatty acids (PUFA) are important fatty acids obtained from dietary sources serve as precursors to large family of eicosanoids. The metabolism of n-3 and n-6 PUFA into a plethora of bioactive eicosanoids occurs through three primary enzymatic systems such as cyclooxygenases (COX), lipoxygenases (LOX) and cytochrome P450 (CYP) enzymes. Epoxylipids derived from the metabolism of PUFAs demonstrate cardioprotective effects and are readily metabolized by soluble epoxide hydrolase (sEH) to diol products, which reduces many beneficial effects and increases formation of potentially adverse products. As such, targeting sEH to increase epoxylipid bioavailability can be regarded as a therapeutic approach in CVD. Interestingly, while sexual dimorphism in sEH expression and activity has been documented in peripheral organs, no studies have addressed sexually different properties in DCM.

Methods/Results: Human left ventricular specimens were procured from patients with DCM and non-failing control (NFC) hearts. LC-MS/MS was used to characterize eicosanoid profiles, which demonstrated differences between DCM and NFC hearts as well between males and females with DCM. Cyclooxygenase (COX)-derived prostanoids, including prostaglandin (PG) E2, 8-iso-PGF2□, and PGD2, and COX-derived hydroxy fatty acids, 9- and 13- hydroxy-octadecadienoic acid (HODE) were significantly higher only in male DCM hearts. Furthermore, male DCM hearts demonstrated significantly higher levels of the diol metabolites, 5,6- and 8-9 dihydroxyeicosatrienoic acids (DHETs) compared to NFC. In addition, CYP-derived metabolite, 12,13- epoxyoctadacamonoenoic acid (EpOME) was found substantially higher in male DCM hearts. While a notable increase in sEH-derived toxic diols, 9,10- and 12,13-dihydroxyoctadecenoic acid (DiHOME) was observed in both male and female DCM hearts compared to NFC. Interestingly, male DCM hearts showed markedly higher levels of DiHOMEs compared to their female DCM hearts. Importantly, there was a significant increase in sEH protein expression in DCM hearts. Mitochondrial abnormalities have a significant role in CVD progression. DCM hearts demonstrated marked decreases in mitochondrial respiration, increased expression of mitochondrial caspase-1 and thioredoxin-interacting protein (Txnip) and NLRP3. Thus, providing evidence of mitochondrial dysfunction and inflammasome formation.

Conclusion: Together, the data demonstrate altered eicosanoid profiles in DCM hearts correlating with changes to sEH expression and suggestive of a less favorable profile in males than females. Preliminary data suggested mitochondrial abnormalities in DCM hearts are associated with an innate immune response.

Funded By: This study was supported by a grant from the Heart and Stroke Foundation to JMS. HKB has been funded by generous supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research.

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Abstract #:	137
Presenter:	Aakankshya Kharel
Supervisor:	Ross, Sue
Title:	The effect of vaginally and orally administrated probiotics on the vaginal health of menopausal women
Authors:	Aakankshya Kharel, Meghan Sit, Sue Ross, Beate Sydora
Theme:	Lifelong women's health

Introduction:

Menopause is often accompanied by a myriad of symptoms, including vaginal health issues. An appealing treatment to alleviate such issues are probiotics, as they are shown to provide general health benefits and have fewer side effects compared to conventional treatments for menopausal symptoms. The primary goal of our study was to investigate the effects of probiotics, specifically on vaginal health issues associated with menopause. A secondary goal was to investigate the difference in outcomes based on the method of probiotic administration.

Methods:

Our systematic review followed PRISMA guidelines. We searched 8 biomedical and nutrition-related databases using keywords related to menopause, menopausal symptoms, and probiotics from inception to May 2020. Articles were collected into COVIDENCE in order to remove duplicates and to apply our inclusion and exclusion criteria. The final selection included only studies that investigated the effect of probiotics on the vaginal health of menopausal women.

Results:

A total of 766 non-duplicate articles were collected from the 8 databases, supplemented with citations from relevant reviews. Ultimately, 9 articles were chosen for data extraction. Seven of the nine studies used postmenopausal participants, while one study used perimenopausal participants and one study used participants experiencing surgical menopause. The average age of participants was 59.6 years ± 5.4 years. The 9 studies used varying numbers of Lactobacillus strains as part of the intervention, with 8 using specifically L rhamnosus. Five studies administered probiotics orally while four administered probiotics vaginally. The average starting dose/week and CFU/dose were 10.5 ± 3.5 doses per week with 1.75E9 ± 2.62E9 CFU/dose for the oral group, and 10.5 ± 4.0 doses per week with 7.38E8± 1.18E9 CFU/dose for the vaginal group. Main outcome measures of the studies were: colonization of the vaginal area with intervention strains (n=2), improvement in pH levels (n=4), urinary tract health (n=2), and scores in bacterial vaginitis/Nugent Score (n=4), as well as general benefit to vaginal health (n=9). 3/5 studies of oral and 4/4 studies of vaginal treatment reported a benefit in at least one outcome measure.

Conclusion:

Cumulative data from our review suggests that probiotics may benefit the vaginal health of menopausal women, especially if administered vaginally. However, due to the limited number and quality of studies available, further research is necessary in order to establish the exact therapeutic and/or preventative value of probiotics on the vaginal health of menopausal women.

Funded By: University of Alberta's Undergraduate Research Initiative.

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Abstract #:	55
Presenter:	Mahdieh Khodaei
Supervisor:	Lou, Edmond HM
Title:	A New Ultrasound Method to Extract Bone Information to Identify Cases with Curve Progression in Adolescents with Idiopathic Scoliosis (AIS)
Authors:	Mahdieh Khodaei, Tehzeeb Sayed, Thanh-Tu Pham, Lawrence H Le, Eric Parent, Doug Hill, Kyle Stampe, Sarah Southon, Edmond Lou
Theme:	Children's health and well-being

Introduction

Adolescent idiopathic scoliosis (AIS) is a three-dimensional spinal deformity which affects 2-3% of children. The gold standard to determine the curve progression is to measure the change of the spinal curvature, called the Cobb angle, on radiographs. However, only approximately 15% of scoliosis cases show progression. Therefore, radiographs taken on cases showing no progression in retrospect are unnecessary. The radiation exposure from radiographs is associated with increased cancer risk. Approximately 27 to 38% of children with AIS present with osteopenia or low bone mineral density which are associated with curve progression. Our team has developed a reliable new ultrasound (US) method which can extract bone information using a reflection coefficient (RC) acquired from the spine. This pilot study was conducted to determine if the RC value acquired from the lumbar spine area can distinguish children with AIS showing curve progression or not.

Methods

One-hundred consented children with AIS (86F, 14M, aged 13.6±1.7 yrs, Cobb angle 10° to 55°) were randomly selected from our database. All had been scanned by an US imager in standing position and followed-up at 9.1± 6.2 months after their baseline scan. The Cobb angle measurements from the radiographs obtained at the same visits as ultrasound images were used to determine if the curve progressed. A change in Cobb angle ≥6° indicated progression. Fifty cases with and 50 without progression were selected for this pilot study. The rater was blinded about which case was with or without progression. The RC value, the quantity of reflected US signals from the lamina area, was measured from the lowest lumbar level (L5). When the US signals reflects from a vertebra, most reflected signals are from the lamina region as it is relatively flat area. The L5 vertebra was chosen because it has the least axial vertebral rotation thereby preventing loss of reflected signal. The recorded signals, from 5 consecutive US frames within the center of each lamina area, were exported. Each frame was less than 1 mm apart. The average RC value of these 5 left and 5 right measurements was recorded. The differences between cases with and without progression were analyzed using Student's t test using an alpha level of $p<0.05$. A receiver operating curve (ROC) was used to determine the cut-off value to best discriminate cases with and without progression.

Results

The mean±SD of the RC for cases with and without progression were 1.53±0.61 (0.37 to 2.95) and 1.81±0.47 (1.03 to 2.93), respectively. There was a statistically significant difference between groups with and without progression ($p<0.05$). The cut-off value from the ROC analysis was 1.74 with an area under curve of 0.66 ($p=0.007$), a sensitivity of 0.68 and a specificity of 0.58.

Conclusion

There was a statistically significant difference on the RC values between groups of AIS with and without curve progression. The RC value of the cases with curve progression was generally lower which suggests the bone was weaker. Future studies may examine the role of the RC within a multi-variable prognostic approach for progression.

Funded By: The authors gratefully acknowledge the funding supports from Scoliosis Research Society (SRS) and the Women and Children's Health Research Institute (WCHRI).

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Abstract #: 96
Presenter: Yana Kibalnyk
Supervisor: Voronova, Anastassia
Title: The role of Ankrd11, a KBG syndrome risk gene, in cardiovascular development
Authors: Yana Kibalnyk, Daniela Roth, Maria Alexiou, Dylan Terstege, Jonathan Epp, Daniel Graf and Anastassia Voronova

Theme: Children's health and well-being

KBG syndrome is a rare neurodevelopmental disorder characterized by global developmental delay, intellectual disability, and heart and brain defects. The disorder is caused by the haploinsufficiency of the chromatin regulator ANKRD11 (Ankyrin Repeat Domain 11), which controls global gene expression by regulating histone acetylation levels. While KBG syndrome patients display multiple heart defects, which often require surgery, the role of ANKRD11 in heart development is not known. To address this gap, I am using a mouse model with conditional knockout of Ankrd11 in the neural crest, a tissue that contributes to heart structures that are abnormal in KBG patients. My results demonstrate that embryonic neural crest conditional knockouts of Ankrd11 (Ankrd11lox/lox;Wnt1Cre2 or Ankrd11ncko) display a congenital heart defect termed truncus arteriosus, where the aorta and pulmonary trunk fail to separate, as well as a common origin of the brachiocephalic and left common carotid arteries. This suggests a failure of the neural crest to initiate the formation of the aorticopulmonary septum. Moreover, µCT (micro computed tomography) imaging and 3D reconstruction reveals that Ankrd11ncko embryos show severely enlarged hearts. Together, this indicates that the heart defect causes deficient blood circulation. Since in utero blood flow impairment can lead to insufficient brain oxygenation and abnormal neural development, I am also analyzing the brain vasculature in these embryos for potential compensatory increase in blood vessel density. I am using fluorescent labeling of intact vasculature coupled with the tissue clearing technique CLARITY to image the brain 3D blood vessel network. My initial results suggest Ankrd11ncko embryos may have aberrant brain vasculature development. Future work will include characterization of any abnormalities in cardiac cell types (myocytes, fibroblasts and macrophages), an in-depth analysis of deficient blood flow and any resulting brain development anomalies. In summary, I show that Ankrd11 contributes to development of cardiac neural crest-derived tissues, which may have implications for brain vasculature and function. This advances our knowledge of the origins of KBG syndrome and the role of chromatin regulators in cardiovascular and neural development.

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Abstract #:	71
Presenter:	Janet Kim
Supervisor:	Mackie, Andrew S
Title:	Compliance with Quality Metrics for Outpatient Cardiology Follow-up of Kawasaki Disease: A retrospective cohort study
Authors:	Janet Kim, Alyssa Chappell, Andrew Mackie
Theme:	Children's health and well-being

Introduction: Kawasaki disease (KD) is a small to medium vessel arteritis that primarily affects children less than 5 years of age. The most important complication of KD is the development of coronary artery aneurysms (CAA), which predispose to angina, myocardial infarction, and sudden cardiac death. The American College of Cardiology recently published quality metrics addressing the outpatient management of KD. Our objective was to evaluate the quality of ambulatory KD follow-up at the Stollery Children's Hospital using these published KD metrics.

Methods: A retrospective medical review was conducted of all children either a) hospitalized at the Stollery Children's Hospital with a primary diagnosis of KD or "suspected" KD between January 2017 - March 2020, or b) seen in the outpatient cardiology clinic during this time frame with a diagnosis of KD that preceded January 2017.

Results: There were 114 eligible patients (64% Male; mean age at diagnosis 3.5 years). The proportion of discharged KD patients who were placed on Aspirin through at least 6 weeks after onset was 95%. However, the proportion who received echocardiographic evaluation within 3 and 6 weeks of hospital discharge was only 33% and 67%, respectively. First outpatient assessments explicitly stated the presence or absence of fever since hospital discharge 53% of the time. The proportion of KD patients with no history of CAA who received an exercise recommendation for no restrictions from physical activities was 62%.

Conclusions: This study identified areas requiring improvement, in particular performance of echocardiography within 6 weeks of discharge, outpatient documentation of absence of fever, and recommendations re: no restriction from physical activities. The creation of a dedicated KD follow-up clinic may help address these findings.

Funded By: Alberta Innovates Summer Research Studentship

Abstract #:	80
Presenter:	Danielle Klassen
Supervisor:	Storey, Kate E
Title:	Within and beyond school walls: Exploring the impact of APPLE Schools on the school and broader community environments
Authors:	Danielle Klassen, Claudine Champion, Genevieve Montemurro, Jenn Flynn, Kim Raine, Kate Storey
Theme:	Children's health and well-being

Introduction

Schools are important settings to promote health behaviours for children and youth during critical developmental years. Health and education are closely connected and it has been shown that healthy kids learn better. School-based health promotion efforts have increasingly used the evidence-based comprehensive school health (CSH) approach which recognizes the interconnected domains of the school, home, and community environments. Previous research has identified the effectiveness of CSH; CSH has been shown to improve health and academic outcomes of students. However, there is limited research on the context of the health promoting environments that CSH addresses both within and outside the school. This study sought to address this gap. The purpose of this study was to examine the impact of a CSH intervention, APPLE Schools, on the school and community environments from the perspectives of school staff.

Methods

This qualitative study used instrumental case study and focused ethnography methods to guide data generation. The setting of the case (Fort McMurray, Alberta) was chosen as the city has readily adopted APPLE Schools; all 21 elementary schools in the city are APPLE schools. Within Fort McMurray, three schools were purposively selected. A walking interviewing approach (i.e., 'go-alongs') was used to observe the setting (i.e., schools) while probing for participants' experiences and interpretations at the same time. One go-along in each school (n=3) was conducted (average length=3 hours), and a total of 15 individuals were interviewed (n=5 teachers, n=4 administrators, n=3 school health champions, n=1 educational assistant, n=1 administrative assistant). Interviews were supplemented by field notes and photographs. All interviews were audio-recorded and transcribed verbatim. Data was analyzed using an inductive, thematic approach.

Results

Findings suggest the impact of APPLE schools has spread both within and beyond school walls. Four main themes were identified: 1) APPLE schools look different, 2) APPLE Schools build champions, 3) APPLE Schools builds community partnerships, and 4) APPLE Schools honours community culture. Participants indicated that APPLE Schools supported a shift in philosophy of the whole school community and was seen as impactful across multiple settings.

Conclusion

This study demonstrated how school and community environments are influenced by CSH. Notably, community stakeholders are critical partners with schools. Their engagement is crucial to sustain healthy initiatives and provide additional funding and resources. Findings will be used to improve school-based health promotion interventions by understanding how school-community partnerships can support and improve the health outcomes of children.

Funded By: Public Health Agency of Canada, WCHRI Graduate Studentship

Abstract #:	49
Presenter:	Jason Kreutz
Supervisor:	Hartling, Lisa
Title:	Considerations for adapting child health knowledge translation tools for Indigenous communities: a qualitative study
Authors:	Kreutz JR, Elliott SA, Wright KS, Scott SD, Hartling L
Theme:	Children's health and well-being

Introduction - The Alberta Research Centre for Health Evidence (ARCHE) and the translating Evidence in Child Health to enhance Outcomes (ECHO) research groups have developed a number of parent knowledge translation (KT) tools. These tools help families and caregivers understand common childhood illnesses and make informed decisions around when to seek urgent care. One set of KT tools developed is a series of videos to help parents know how to manage common acute childhood illnesses at home and when to contact emergency services. While these videos were developed in collaboration with parents, they are currently only available in English, and may not adequately represent all communities. It is unclear whether the videos in their current form and language are useful for a wider scope of populations, including different Indigenous groups. The purpose of this study was to understand if and/or how two of our KT tools could be adapted for use with Indigenous communities.

Methods - Health care providers (HCPs) serving Indigenous patients or communities in Alberta were invited to participate. Participants were asked to review two videos (on croup and acute otitis media), complete an online consent form and demographic survey, and participate in a one-on-one semi-structured interview via Zoom. Interviews were audio-recorded and transcribed verbatim. Interview data were coded using NVivo 12 software and analyzed using thematic analysis. The study was approved by the University of Alberta's Health Research Ethics Board and all participants provided informed consent prior to data collection.

Results - Eighteen HCPs (15 females) aged 21-70 years from various health professions (e.g., doctor, registered nurse, licensed practical nurse) participated. HCPs served patients in rural communities (n=4), urban communities (n=6), or both (n=8). HCPs reported working with Indigenous communities for 11 years on average. Eight HCPs self-identified as Indigenous. Four key themes (and their corresponding subthemes) were identified as important when considering how to adapt KT tools for Indigenous communities: 1) Accessibility (Tangible resources and Relationships); 2) Relatability (Environmental contexts, Individual representation, and Culture); 3) Knowledge Translation Design (Formatting, Plain language, and Translations); and 4) Relationship Building (Understanding community needs, Consultations while adapting tools, and Spreading information).

Conclusion - This study is a critical first step in identifying how to adapt existing KT tools for Indigenous communities. Careful consideration of the themes identified in this study will be essential for informing the development of KT tools for Indigenous populations. Including Indigenous perspectives in the continuing refinement of KT tool content and delivery will increase relevance and accessibility of the messaging.

Funded By: This study was funded by the Alberta Innovates Summer Research Studentship (SRS) program.

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Abstract #:	119
Presenter:	Kimberly Kroetch
Supervisor:	Rosychuk, Rhonda
Title:	Multistate models of the flow through emergency departments of children presenting with asthma in Alberta, Canada
Authors:	Kimberly Kroetch, Brian Rowe MD, Rhonda Rosychuk PhD
Theme:	Children's health and well-being

Objectives

Asthma is a serious condition with a higher prevalence in children, and the severe cases can require immediate treatment in the emergency department (ED). For every 30-minute delay in treatment of acute exacerbations of asthma in the ED, the odds of hospital admission increase by 20% for children. It is therefore crucial that children presenting to an ED with asthma symptoms do not experience long delays. The purpose of this study is to deconstruct the total length of stay in an ED into stages and analyze the effect of covariates on the transition times for children presenting with asthma.

Methods

ED presentations for asthma made by residents of Alberta, Canada aged 2 to 17 between January 1, 2019 and December 31, 2019 were extracted from the National Ambulatory Care Reporting System database. Data extracted included demographic and ED presentation characteristics. Four stages of an ED presentation were considered: start, physician initial assessment (PIA), disposition decision, and ED departure. The transition times between each of the ED stages were modelled using Cox proportional hazards models in a multi-state model with transition-specific covariates.

Results

8,270 ED presentations by 6,598 unique patients were analyzed. Time to PIA was longer when time to PIA crowding metric was above 1h (HR=0.32, 95% confidence interval [CI]=0.30,0.34), for tertiary (HR=0.65, 95%CI=0.61,0.70) and urban EDs (HR=0.77, 95%CI=0.70,0.84), for patients in the winter (hazard ratio [HR]=0.84, 95%CI=0.78,0.89), and for patients triaged less urgent/non-urgent (HR=0.89, 95%CI=0.84,0.95). It was shorter for patients arriving by ambulance (HR=1.22, 95%CI=1.04,1.42) and for patients in the summer (HR=1.12, 95%CI=1.05,1.20). Times from PIA to disposition decision were longer for tertiary (HR=0.47, 95%CI=0.44,0.51) and urban (HR=0.69, 95%CI=0.63,0.75) EDs, for patients triaged as resuscitation/emergent (HR=0.51, 95%CI=0.48,0.54), and for patients arriving by ambulance (HR=0.78, 95%CI=0.70,0.87). They were shorter during the evening shift (HR=1.11, 95%CI=1.04,1.18), in the spring (HR=1.11, 95%CI=1.03,1.19), and in the winter (HR=1.08, 95%CI=1.00,1.18). Times from disposition decision to ED departure were longer for patients who were admitted (HR=0.16, 95%CI=0.13,0.20) or transferred (HR=0.42, 95%CI=0.35,0.50), for tertiary EDs (HR=0.93, 95%CI=0.92,0.94), and for patients triaged as less urgent/non-urgent (HR=0.98, 95%CI=0.98,0.99), and longer when the crowding metric was over 1h (HR=0.98, 95%CI=0.97,0.99).

Conclusions

Characteristics of an ED presentation were found to impact all transition times. Age was the only patient characteristic to affect a transition, and it only impacted time to PIA. ED crowding demonstrated strong effects on time to PIA, but not on the later two transitions.

Funded By: National Sciences and Engineering Research Council of Canada (NSERC) Undergraduate Student Research Award, Women & Children's Health Research Institute Summer Studentship Award, NSERC Discovery Grant

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Abstract #:	115
Presenter:	Ediger Krystyna
Supervisor:	van Manen, Michael
Title:	What is teamwork? A qualitative study on the perception of teamwork in a specialized neonatal resuscitation team
Authors:	Krystyna Ediger MD, Marghalara Rashid PhD, Brenda Hiu Yan Law MD MSc
Theme:	Children's health and well-being

Introduction: Neonatal resuscitation is common; approximately 10% of infants require resuscitation at birth, with 1% receiving more extensive measures such as endotracheal intubation and chest compressions. Effective and timely neonatal resuscitation is a team-based activity involving many decisions, tasks, and procedures conducted in a high-stress environment. Non-technical factors, such as teamwork, is increasingly recognized as having an impact on how well neonatal resuscitation is performed, and therefore on the outcomes of at-risk infants. Existing studies on teamwork in neonatal resuscitation have focused on quantifying interpersonal behaviors and the effect of team-based training on these behaviors; there are limited qualitative studies on healthcare providers' own perception of teamwork in this specialized environment. Further, there are limited studies on the perceptions of teamwork within a multidisciplinary neonatal resuscitation team in a high-resourced, tertiary perinatal centre.

Methods: In this descriptive qualitative study, semi-structured interviews were conducted with members of the multidisciplinary neonatal resuscitation team at the Royal Alexandra Hospital in Edmonton, Alberta, from July to September 2020. This team specializes in attending high risk deliveries of preterm infants and at-risk term infants (e.g. fetal distress, congenital anomalies, etc) in a regional referral center. Participants included registered nurses, registered respiratory therapists, neonatal transport nurses, neonatal nurse practitioners, neonatal-perinatal medicine resident physicians and neonatologists. Thematic analysis was used to create data-driven codes and identify key themes through an iterative consensus-building process.

Results: Nine participants were interviewed, representing all disciplines. Participants have a range of clinical experience (median 7 years, IQR 5-21). Seven themes were identified, including: 1) Team composition (including experience, familiarity and role delegation); 2) Effective communication; 3) Team Leadership (i.e. the importance of the team leader and their effect on team functioning); 4) Hierarchy (i.e. impact of hierarchy within the team on performance and on speaking up); 5) Team training (including simulation and multidisciplinary training); 6) Debriefing (i.e. the importance of debriefing of critical events to assist with learning, coping and interpersonal interactions); and 7) Physical Environment (i.e. the effect of the physical environment on team co-ordination.) Themes were shared across disciplines and range of experience.

Conclusions: By exploring team members' perception of teamwork in a multidisciplinary neonatal resuscitation team, seven themes were identified. These themes align with existing frameworks of effective clinical teamwork. Themes will be used to inform a sequential exploratory mixed-methods study on barriers and mediators to effective teamwork during neonatal resuscitation.

Keywords: neonatal resuscitation, teamwork, qualitative

Funded By: NA

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Abstract #:	63
Presenter:	Takaaki Landry
Supervisor:	Persad, Sujata
Title:	Validation of a role for Active Beta-Catenin (ABC) in promoting Metastatic Phenotype in Osteosarcoma
Authors:	Takaaki Landry, Noureen Ali, Elizabeth Garcia, Jonathan Bush, Danielle Cohen, Rebecca Deyell, Mary Hitt, David D. Eisenstat, Sujata Persad
Theme:	Children's health and well-being

Introduction: Osteosarcoma (OS) is an aggressive primary bone malignancy with peak incidence in children/young adults <25 years of age. The 5-year event-free-survival for patients with localized disease and metastatic disease is ~65% and ~25%, respectively. Despite intensive chemotherapy, metastasis of osteosarcoma occurs in 15-20% of cases. This goes to show that there is an urgent need for identifying prognostic markers to facilitate risk stratification.

The Wnt/β-catenin (β-cat) pathway plays a crucial role in skeletal development and is deregulated in OS. However, its role in OS, especially in OS progression remains unknown. We investigated the role of the β-cat pathway, specifically the transcriptionally active form of β-cat, Active Beta Catenin (ABC), in OS progression. ABC constitutes a unique pool of β-cat that is dephosphorylated at Serine 37 and Threonine 41 at the N-terminal domain.

Objective: The focus of our study was to determine if ABC is a prognostic biomarker that correlates with metastatic dissemination at disease progression.

Methods: Two sets of paired cell lines, SaOS2/SaOS2-LM7 and HOS/HOS-143B were utilized for this study. Using a pEGFP-β-cat fusion construct plasmid, we carried out site directed mutagenesis to the N-terminal S33, S37, T41 and S45 in order to mimic endogenous ABC [GeneArt, Invitrogen]. The pEGFP-ABC and pEGFP-β-cat constructs were then transfected into SaOS2 and HOS cells and subject to Western Blot analysis and immunofluorescence.

We also carried out immunohistochemical analysis (IHC) on 30 OS patient samples to determine whether nuclear ABC levels were correlated to "aggressive" disease.

Results: Initial observations from both paired cell lines indicated that endogenous nuclear ABC levels, but not β-cat, increase with OS progression. SaOS2 Cells transfected with pEGFP-ABC and pEGFP-β-cat plasmid constructs via immunofluorescence showed similar activity to that of the endogenous ABC and β-cat: endogenous and pEGFP-ABC were both seen to translocate to the nucleus while both the endogenous and pEGFP-β-cat remained cytosolic or membrane bound.

We analyzed whether nuclear ABC levels were correlated to aggressive OS, as determined by metastasis at diagnosis or resection (30 patients) via IHC. We observed a significantly greater number of patients with metastatic disease at diagnosis (p=0.029, two tailed) or at the time of resection (p=0.007, two tailed) showing high nuclear levels of ABC (>25% nuclear positivity) compared to samples which did not show metastasis at diagnosis or resection.

Conclusion: This strong correlation between high nuclear ABC levels and metastatic disease helps propel our research to further work with the plasmid constructs to determine whether ABC has potential to be used as a reliable prognostic marker.

Funded By: Women and Children's Health Research Institute Grant

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Abstract #:	9
Presenter:	Guillaume Leclair
Supervisor:	Atallah, Joseph
Title:	Neurodevelomental Outcomes After Neonatal Surgical Intervention For Cyanotic Tetralogy Of Fallot And Other Lesions With Right Ventricular Outflow Track Obstruction
Authors:	Guillaume Leclair, Charlene M. T. Robertson, Gwen Y Bond, Gonzallo Guerra, Konstantin Averin, Joseph Atallah
Theme:	Children's health and well-being

BACKGROUND

Neonatal cardiac surgery carries a significant risk for adverse neurodevelopmental outcomes. There is limited data on these outcomes for the cohort of patients with right sided obstructive congenital cardiac lesions requiring repair in the neonatal period. This study determined the perioperative, re-intervention and 2-year neurodevelopmental outcomes for survivors of neonatal cardiac surgery for Tetralogy of Fallot (TOF) and pulmonary atresia with a ventricular septal defect (PA/VSD).

METHODS AND RESULTS

A single center consecutive cohort of 77 Children underwent neonatal surgery for TOF (41) and PA/VSD (36) at 6 weeks old or younger between 2006 and 2017. Median (IQR) age at surgery was 20 (11-36) days, 46 (60%) were male and 14 (18%) had chromosomal anomalies. Confluent pulmonary arteries were present in 35/36 patients with PA/VSD and all TOF patients. Only 13 patients underwent initial shunt palliation while the majority underwent primary complete repair. Post-operative in hospital mortality was 3.9% (3/77) and two-year mortality was 7.8% (6/77). Mortality was significantly higher in children undergoing a palliative shunt as their first surgery (23%). Freedom from re-intervention by cardiac catheterization or surgical intervention at 2 years was 36%. Infants and children in the PA/VSD group required interventional cardiac catheterization (50%) more frequently than in the TOF group (21.9%) (P=0.016). Functional and neurodevelopmental assessment for 69/71 survivors was completed at a mean (SD) age of 22.6 (4) months using the Bayley Scales of Infant and Toddler Development III. Mean (SD) neurodevelopmental outcome scores were 83.4 (16.5) for cognitive skills, 82.2 (18.7) for language skills, and 81.4 (18.1) for motor skills. Cognitive, language, and motor delay, defined as a score < 70, was identified in 25%, 25% and 23% of patients, respectively. Sensorineural hearing loss, cerebral palsy, and epilepsy were each present in 3 children (4%) while visual impairment was present in 2 (3%). Demographic, pre-operative, operative, and post-operative variables suggestive of correlation to lower neurodevelopmental scores by univariate linear analysis ($p \leq 0.05$) were complemented with multivariate linear analysis. Preliminary analysis suggests chromosomal anomalies ($p<0.001$), and post-operative complications, including for re-operations and cardiac catheterizations ($p=0.02$) are associated with lower cognitive skills , language skills, and motor skills. Children without chromosomal anomalies were subsequently analyzed separately by multivariate analysis and complications continued to be associated with lower neurodevelopmental outcomes ($p=0.01$-0.03). Analysis is ongoing.

CONCLUSION

Patients with cyanotic tetralogy of Fallot and PA/VSD requiring neonatal repair have a relatively high 2-year mortality and need for interventional cardiac catheterization. The later being more commonly in PA/VSD. Their neurodevelopmental outcomes are below normative values and the rates of cognitive, language and motor delay are high. Children with post-operative and procedural complications have lower neurodevelopmental outcomes.

Funded By: This study is possible thanks to: The Western Canadian Complex Pediatric Therapies Follow-up Program

This study is pending submission for a WCHRI grant for statistical analysis support.

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Abstract #:	13
Presenter:	Marissa Ledger
Supervisor:	Kozyrskyj, Anita
Title:	Maternal immigration status and C. difficile colonization in Canadian infants
Authors:	Marissa L. Ledger, Meghan B. Azad, Allan B. Becker, Piush J. Mandhane, Theo J. Moraes, Malcolm R. Sears, Stuart E. Turvey, Padmaja Subbarao, James A. Scott, Anita L. Kozyrskyj
Theme:	Children's health and well-being

Introduction: Nearly 50% of infants are colonized with C. difficile in the first year of life. While colonized infants are asymptomatic, C. difficile colonization is a marker for gut dysbiosis and is associated with poor health in later life. Recent work has demonstrated links between maternal depression and stress, and gut microbial dysbiosis in infants. In the CHILD birth cohort, immigration to Canada has been linked to maternal depression with increased risk with time lived in Canada. We aimed to investigate the association between maternal immigration status and C. difficile colonization in infants.

Methods: A subset of 2,196 mother-infant pairs from the CHILD Cohort Study (www.childstudy.ca) were included in the analysis. C. difficile was detected by qPCR in stool samples collected from infants at 3-months and 1-year of age. Uni- and multiple variable logistic regression were employed to determine associations between maternal ethnicity and duration of residence in Canada with the C. difficile colonization status of infants.

Results: In 3-month old infants, C. difficile colonization rates were 22.3% if their mothers were Asian (13% subjects, mean 16.16 years in Canada), Hispanic (2% subjects, mean 15.02 years in Canada), Black (1% subjects, mean 9.95 years in Canada), or Middle Eastern (1% subjects, mean 16.39 years in Canada) compared to 32.3% in those of White mothers (76% subjects, mean 28.49 years in Canada). At 3 months, infants of Asian ethnicity were half as likely to be colonized with C. difficile (OR=0.47, 95% CI: 0.31-0.69), independent of breastfeeding status, birth mode, and total gut microbial diversity. Infants whose mother's had lived in Canada 3-5 years and 5-10 years were at much lower risk for C. difficile colonization at this age compared to those who had lived in Canada more than 10 years (OR=0.40 and 0.37, respectively; 95% CI: 0.18-0.81 and 0.18-0.68, respectively), adjusted for the same covariates. Time lived in Canada was no longer an important predictor of colonization at 1 year.

Conclusion: Despite residence in Canada for 5 to 10 years being associated with higher risk for persistent depression, this does not appear to translate to higher risk for C. difficile colonization in infants; rather infants born to mothers who lived in Canada more than 10 years were at greater risk.

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Abstract #:	56
Presenter:	Christy Lee
Supervisor:	Alexander, R Todd
Title:	Mutations in the serine protease FAM111A cause hypocalcemia by increasing CaSR expression and activity
Authors:	Christy Lee, Rebecca Tan, Todd Alexander
Theme:	Children's health and well-being

Ca^{2+} levels are tightly regulated in the blood; when blood levels are high, the calcium sensing receptor (CaSR) in the parathyroid is activated thereby inhibiting PTH secretion, which acts to lower blood Ca^{2+} levels. Activating mutations in the CaSR gene causes autosomal dominant hypocalcaemia (ADH), which is characterized by low blood Ca^{2+} levels and hypoparathyroidism. ADH patients also commonly suffer from seizures. We identified a 6-year-old girl who was presented to the emergency with seizures. Work up confirmed hypocalcemia and hypoparathyroidism, ***i.e***. ADH, but she did not have a mutation in the CaSR gene. Instead, using whole exome sequencing and trio analysis we identified a ***de novo*** FAM111A gene mutation. FAM111A mutations are known to cause Gracile Bone Dysplasia and Kenney Caffey Syndrome, both of which are often fatal. Both diseases are characterized by a phenotype similar to ADH, but also short stature and bone abnormalities. Our patient has normal height and normal bones, however, her other clinical characteristics are consistent with the FAM111A mutation causing her disease. We therefore aim to understand how FAM111A regulates calcium homeostasis and why children with mutations in FAM111A have an ADH like phenotype. As little is known about FAM111A, we first performed ***in silico*** analysis using the BioGPS and Human Protein Atlas databases to determine the expression of FAM111A in tissues of mice and humans. In particular, we examined expression in the small intestine, kidneys, parathyroid gland, and bones, as these tissues participate in calcium homeostasis. Our findings show that while human FAM111A expression is mainly in the thymus, mice express the gene mostly in bone. Furthermore, ***in silico*** analysis predicts FAM111A to be a serine protease. We therefore hypothesized that mutations in FAM111A cause ADH, potentially by reducing serine protease activity leading to decreased CaSR degradation, and thus increased CaSR expression and therefore activity. To examine if the FAM111A mutation increased CaSR expression, a mouse model containing the same mutation was created with CRISPR/Cas9. Wildtype and mutant mice were housed in metabolic cages to collect urine and feces for three days, then euthanized to collect tissue and blood. We observed no significant difference between the CaSR levels of mutant and wildtype mice at the mRNA level using qPCR techniques. However, by immunoblot, there was a significant increase in CaSR expression in mutant mice at the protein level. Furthermore, at both the mRNA and protein level, FAM111A expression doubled in mutant mice. Thus, our work suggests that mutations in FAM111A increases FAM111A and CaSR expression, secondary to reduced protease activity leading to the phenotype of ADH that we observe in our patient. Other work in the laboratory is examining calcium homeostasis in these animals.

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Abstract #:	155
Presenter:	Jia Hang Li
Supervisor:	Bourque, Stephane
Title:	The effect of perinatal iron deficiency on neonatal cardiac development
Authors:	Jia Hang Li, Ronan Noble, Claudia Holody, Stephane Bourque
Theme:	Pregnancy and developmental trajectories

Background - Iron deficiency (ID) is the most common nutritional disorder globally, and pregnant women are among the most vulnerable groups. ID during pregnancy can alter developmental trajectories and predispose offspring to cardiovascular diseases. We have previously shown that ID causes tissue-specific patterns of hypoxia and mitochondrial dysfunction in male but not female offspring. Recently, we found evidence of cardiac dysfunction and impaired mitochondrial function in the hearts of neonatal ID rats, specifically reduced ejection fraction and mitochondrial respiration. Given that the perinatal heart is highly metabolically active and undergoing rapid developmental changes, we hypothesized that perinatal ID would disrupt cardiomyocyte maturation postnatally.

Methodology - Female Sprague Dawley rats were fed either an iron-restricted or an iron-replete diet before and during pregnancy. On postnatal days (PD)1, 4, 14, and 28, heart ventricles were collected from male and female pups. Protein markers of cardiomyocyte maturation (α-MHC : β-MHC ratio) and damage (cTnI/T) were quantified by Western Blot. Cardiomyocyte cross-sectional area, dimensions of the heart, and collagen deposition were assessed by Mason's trichrome staining. All data were analyzed by 2-way ANOVA.

Results - Male and female ID pups had reduced hemoglobin at PD1 and 14 ($P<0.0001$, both) but recovered by PD28. ID pups were also growth restricted at all time points ($P<0.001$, both) and had increased relative heart weights at PD1 and PD14. cTnT levels were decreased in ID pups of both sexes at PD28 ($P=0.02$), but not at other time points. α-MHC : β-MHC ratio was decreased in ID pups on PD 14 and 28 ($P=0.01$ and 0.03, respectively). Absolute cardiomyocyte sizes were not different between control and ID pups of both sexes. However, male, but not female ID pups had overall increased cardiomyocyte sizes relative to their heart weights in the left and right ventricle ($P=0.0002$ and 0.0005, respectively) on PD14 and 28. ID pups of both sexes had overall larger septal cell sizes relative to heart weight ($P=0.02$, both) on PD14 and 28. Analysis of heart dimensions and collagen deposition are ongoing.

Conclusions - Our preliminary results show that neonatal ID hearts displayed signs of increased cardiomyocyte damage and impaired maturation. Histological analysis of neonatal ID hearts revealed enlarged cardiomyocytes relative to heart weights, which may contribute to the development of long-term cardiac dysfunction. Results for the remaining histological analyses will provide insights into the mechanisms by which perinatal ID affects cardiac development and long-term cardiovascular health.

Funded By: AIHS Summer Studenship Award, CIHR, WCHRI

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Abstract #: 89
Presenter: Yutong Li
Supervisor: Voronova, Anastassia
Title: Hepatoma Derived Growth Factor (HDGF) as a potential treatment for neurodevelopmental disorders
Authors: Yutong Li, Adrianne Watson, Anastassia Voronova

Theme: Children's health and well-being

Oligodendrocytes, the myelinating cells of the central nervous system (CNS), perform vital functions in neural protection, communication and efficient information transmission. Moreover, oligodendrocyte lineage cells have been recently implicated in cognitive functions. Thus, it is not surprising that oligodendrocytes and/or myelin are often perturbed in children with neurodevelopmental disorders (NDDs). Recent studies suggest developmental oligodendrocyte formation and myelination can be targeted to restore cognition and behaviour in mouse models with NDDs (Barak et al. 2019 Nat Neurosci). Oligodendrocytes are formed by neural stem cells (NSCs) via a 2-step process: 1) NSC to oligodendrocyte precursor cell (OPC) commitment; and 2) OPC to oligodendrocyte differentiation. Our lab has demonstrated that this developmental oligodendrocyte formation from neural stem cells (NSCs) is regulated by factors secreted by a special type of neurons, termed inhibitory neurons (Voronova et al. 2017 Neuron). While HDGF was identified to be a candidate molecule secreted by the inhibitory neurons, its role in the developing brain or NSCs is not known.

To address this, I isolated NSCs from murine postnatal brain subventricular zone (SVZ), an NSC rich area that is known to generate oligodendrocytes throughout life. NSCs were cultured in the presence or absence of HDGF added to minimal media, which allows for oligodendrocyte differentiation and permits the observation of exogenous ligands on this process. I used antibodies specific for proliferation and oligodendroglial differentiation to analyze the effect of exogenous HDGF on these processes.

My results demonstrate HDGF increases the number of mature myelinating oligodendrocytes that express myelin basic protein (MBP), but does not affect the formation of non-myelinating (immature) oligodendrocytes or OPCs. I further show HDGF achieves this by increasing i) proliferation of NSCs and OPCs; and ii) differentiation of OPCs. Future studies will address whether HDGF increases oligodendrocyte formation and overall myelination in vivo.

My results demonstrate a novel role for HDGF in developmental oligodendrocyte formation. Moreover, my data suggest HDGF may be used in future therapeutic strategies to engage NSCs for increased oligodendrocyte formation.

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Abstract #:	103
Presenter:	Natasha Lifeso
Supervisor:	Joynt, Chloe A
Title:	Helping the Helpers: Peer Critical Incident Stress Management for NICU Health Care Providers to Improve Resilience, Burnout and Patient Safety
Authors:	Natasha Lifeso, Matthew Hicks, and Chloe Joynt
Theme:	Children's health and well-being

INTRODUCTION

Health care providers in neonatal intensive care units (NICU) experience critical or distressing events that can overwhelm their usual coping skills and lead to significant stress. Ineffective support for health care providers dealing with critical incidents can lead to poor unit resilience, staff burnout and compromised patient care behaviours. A formalized peer program and process to address critical workplace incidents and support care providers, "Critical Incident Stress Management (CISM)" is used in many first responder professions. While there is growing interest in implementing peer CISM teams in critical care units, there is a lack of research describing the impact of CISM in NICU. This study examined the effect of implementing a multidisciplinary NICU health care provider peer CISM Team on resilience and burnout in a tertiary NICU.

METHODS

Multidisciplinary team members were peer selected and formally CISM trained. Change management strategies were employed to introduce CISM to the NICU. All health care providers were invited to complete an anonymous online or paper survey before and 1 year after NICU CISM Team implementation. The survey contained validated measures of resilience, burnout, and team/safety culture that were analyzed pre and post intervention.

RESULTS

The response rate pre-intervention was 66% (114/172 staff) and 32% post (60/186 staff). Stress recognition significantly improved as fewer staff reported being less effective at work when feeling stressed post incident (74% vs 61%, pre and post CISM respectively, $p<0.05$). Fewer staff reported feeling burned out from their work (41% vs 31%, $p=0.4$) trending towards improved resilience. Communication in the NICU significantly improved as staff indicated debriefing methods met their needs (38% vs 57%, $p<0.05$) and felt comfortable speaking up about safety (66% vs 79%, $p=0.1$). Post-intervention, despite feelings of increased workload indicated by a significant decrease in agreement that "NICU staff levels were sufficient for patient load" (54% vs 33%, $p<0.001$), a majority of staff reported a supportive environment in the NICU (59% vs 77%, $p=0.08$). Work culture significantly improved as staff felt rewarded and recognized for improving quality (13% vs 31%, $p<0.05$).

CONCLUSION

Implementation of a peer CISM team led to improved NICU care provider resilience, stress recognition, team culture all of which can mitigate the effects of increased patient load. Additionally, this research may improve the outcome for children as more resilient staff can improve patient care. Findings from this research and knowledge gained from the CISM implementation process should be shared with other health care environments.

Funded By: Women and Children's Health Research Institute

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Abstract #:	74
Presenter:	Kenji Rowel Lim
Supervisor:	Yokota, Toshifumi
Title:	Exons 45-55 skipping therapy: developing a potential treatment with increased efficacy and applicability for Duchenne muscular dystrophy
Authors:	Kenji Rowel Q. Lim, Yiqing Huang, Rika Maruyama, Stanley Woo, Kasia Dzierlega, Hong Moulton, Toshifumi Yokota
Theme:	Children's health and well-being

Introduction. Duchenne muscular dystrophy (DMD) is a fatal X-linked disease characterized by progressive body-wide muscle deterioration. DMD is primarily caused by large dystrophin gene (DMD) deletions. Exon skipping therapy uses antisense oligonucleotides (AOs) to exclude out-of-frame exons and restore the DMD reading frame, allowing for the production of truncated, partially functional dystrophin. There are three FDA-approved exon skipping AOs for DMD treatment, but these could only treat up to 13% of patients. We aim to develop AOs for skipping DMD exons 45-55, which could treat 47% of patients. We also aim to improve efficacy by conjugating AOs with a cell-penetrating peptide (CPP) to enhance in vivo uptake.

Methods. We previously developed 12 phosphorodiamidate morpholino oligomer (PMO) AOs for skipping DMD exons 45-55, one per exon except exon 48 which required two. We tested minimized derivatives of this cocktail, each having up to 6 PMOs, in immortalized patient-derived cell lines with various mutations. PMOs were transfected 3 days post-differentiation, with total RNA and protein extracted 2 days later to assess exon 45-55 skipping (RT-PCR) and dystrophin protein levels (Western blot). We also carried out a preliminary study by treating mice having an exon 52-deleted human DMD transgene with an exon 51-skipping PMO conjugated to DG9, a novel CPP we previously identified in a zebrafish screen. Mice were given single retro-orbital injections of 64 mg/kg DG9-PMO, 50 mg/kg PMO, or saline, with tissues collected a week later for analysis.

Results. The minimized cocktails significantly skipped DMD exons 45-55 in most cell lines compared to non-treated controls. We observed 34% exon 45-55 skipping on average with one of these cocktails in DMD exon 52-deleted cells, at a level that was not significantly different from the 25% skipping achieved with the 12-PMO cocktail. This corresponded with the production of an average 21% dystrophin of normal levels in this cell line, higher than the 13% observed for the full cocktail. Our preliminary test of the DG9-conjugated PMO revealed that it enhanced exon 51 skipping and dystrophin rescue in treated mice by up to 7-fold and 4-fold, respectively, across skeletal and cardiac muscles compared to the unconjugated PMO. Immunohistochemistry revealed widespread dystrophin-positive fibers in these tissues.

Conclusion. We have developed a minimized exon 45-55 skipping cocktail that significantly rescued dystrophin production in vitro. We have also identified DG9 as a promising CPP that could be conjugated to PMOs comprising this cocktail in order to enhance in vivo efficacy.

Funded By: CIHR, Alberta Innovates, Alberta Advanced Education, WCHRI, Heart & Stroke Foundation, Rare Disease Foundation, BC Children's Hospital Foundation, The Friends of Garrett Cumming Research, and the Muscular Dystrophy Canada HM Toupin Neurological Science Research Chair Fund

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Abstract #:	156
Presenter:	Ricky Liu
Supervisor:	Davidge, Sandra
Title:	Prenatal hypoxia reduces levels of tissue inhibitor of matrix metalloproteinase-4 (TIMP-4) in hearts of adult male offspring
Authors:	Ricky Liu, Nataliia Hula, Anita Quon, Raven Kirschenman, Floor Spaans, Christy-Lynn Cooke, Sandra T. Davidge
Theme:	Pregnancy and developmental trajectories

Introduction: Fetal hypoxia is a common pregnancy complication adversely affecting fetal development and predisposing the offspring to development of cardiac dysfunction in adulthood. We have previously shown that prenatally hypoxic offspring demonstrated impaired recovery of cardiac function after I/R insult. However, the molecular mechanisms underlying the development of cardiac dysfunction in adult offspring exposed to prenatal hypoxia are unknown. Matrix metalloproteinase 2 (MMP-2) is an endopeptidase involved in degradation of intracellular cardiac contractile proteins such as myosin light chain 1 (MLC-1), MLC-2, troponin I (TnI). MMP-2 is activated during an I/R insult due to the oxidative/nitrosative stress associated with I/R injury, and can be inhibited by tissue inhibitors of MMPs (TIMPs). We hypothesize that prenatal hypoxia impairs cardiac recovery after I/R due to increased cardiac MMP-2 expression and decreased expression of cardiac contractile proteins.

Methods: Pregnant Sprague-Dawley rats were exposed to normoxia (21% O2) or hypoxia (11% O2) on gestational days 15-21 (term=22 days). Hearts were isolated from male offspring at 7 months of age (n=2-3/group) and cardiac function after I/R insult were assessed ex vivo using the isolated working heart technique. Hearts were either aerobically perfused for 90 min (aerobic controls) or exposed to the I/R protocol (i.e. aerobically perfused for 30 min followed by 20 min of no-flow ischemia and 40 minutes of aerobic reperfusion) and left ventricle tissues were snap frozen for molecular assessments. MMP-2, TIMP-4, MLC-1, MLC-2 and TnI expression were assessed by Western blotting, and presented as a ratio towards the total protein. Data were compared by two-way ANOVA with Sidak's post hoc test (with two between-subject factors: prenatal hypoxia and I/R) and presented as mean±SEM; $P \leq 0.05$ was considered significant.

Results: MMP-2 levels were not altered by prenatal hypoxia or I/R. TIMP-4 content was significantly lower in offspring exposed to prenatal hypoxia compared to normoxic controls (0.93±0.06 vs. 0.75±0.05, p=0.03; overall effect) and I/R tended to reduce TIMP-4 levels (0.91±0.06 vs. 0.77±0.06, p=0.07; overall effect) in both normoxic and hypoxic groups. Neither prenatal hypoxia nor I/R induced changes in cardiac MLC-1, MLC-2 or TnI levels.

Conclusion: Our results suggest that prenatal hypoxia reduces TIMP-4 levels, which, as TIMP-4 inhibits MMP-2 activity, could suggest an increase in MMP-2 activity. This may provide an explanation for the increased cardiac susceptibility to I/R injury of adult offspring exposed to prenatal hypoxia shown in our earlier studies. Further studies are needed to increase n-numbers, assess MMP-2 activity and to assess whether similar changes would be observed in female offspring.

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Abstract #:	37
Presenter:	Rachel Livergant
Supervisor:	Ospina, Maria
Title:	Canadian Public Health Measures for SARS-CoV-2 Targeting Children During the Early Days of the COVID-19 Pandemic: A Scoping Review
Authors:	Rachel Livergant, Julie Polisena, Omolara Sanni, Brittany Matenchuk, Sana Amjad, Liz Dennet, Igor Zoric, Nisrine Haddad, Andra Morrison, Wilson Kumana, Isaac Bogoch, Vivian Welch, Maria Ospina.
Theme:	Children's health and well-being

Introduction: On March 11, 2020, the World Health Organization declared a global pandemic in response to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the causative agent of the novel coronavirus disease 2019 (COVID-19). Accordingly, health officials in Canada issued public health measures at the federal and provincial/territorial (PT) level to contain and mitigate SARS-CoV-2 transmission in the population and prepare the health systems' responses to COVID-19. Children were identified as a critical group during the pandemic, due to their propensity to act as asymptomatic carriers and transporters of the virus.

Objective: This scoping review describes public health measures implemented at the start of the global COVID-19 pandemic in Canada, with an emphasis on the extent to which issued public health measures targeted children.

Methods: We conducted a comprehensive search strategy of federal and P/T websites on COVID-19 public health preparedness strategies that were released between January 30 and April 30, 2020. Specific measures targeting children under the age of 18 were identified and examined. A mixed-methods approach for analysis of results was conducted, using both quantitative and qualitative methods.

Results: Of the 722 public health measures implemented during the study period, 8.7% (63) targeted children. Prince Edward Island and Quebec issued the most measures (8) while Yukon, Nunavut, Northwest Territories, British Columbia and Manitoba issued the least (three each). The majority of measures focused on school and university closures (28, 44%), with daycare closures the next most common measure (14, 22%). Most of the public health measures targeting children were mandatory orders issued by governments (53, 84%). Non-mandatory measures focused on social supports for children and parents, including daycare provisions for essential workers and recommendations to keep children home from school after travelling in the first few weeks of the pandemic. Most of the public health measures were issued in March 2020 (45, 71%), while none were issued in January and only one measure was introduced in February. Eleven (17%) public health measures aimed at mitigating the psychological, social and/or educational stressors of the pandemic on children.

Conclusion: This scoping review provides insights on the effects of public health measures issued by the Canada federal and P/T governments in the first 90 days of the pandemic on children. Several of these measures directly impacted children's education and care, however, an analysis on the evolution and impact of these measures merits further investigation.

Funded By: This research was funded by the Lois Hole Hospital for Women through the Women and Children's Health Research Institute Start Up Grant (Dr. Ospina). Dr. Ospina is supported by the Canadian Institutes of Health Research as a Canada Research Chair in Life Course, Social Environments and Health.

Abstract #:	28
Presenter:	Rachel Livergant
Supervisor:	Ospina, Maria
Title:	The effect of peripartum synthetic oxytocin exposure on postpartum depression and anxiety: a systematic review
Authors:	Sullivan H; Livergant RJ; Amjad S; Sanni OB; Campbell S; Ospina, MB
Theme:	Pregnancy and developmental trajectories

Introduction: Postpartum depression (PPD) and postpartum anxiety (PPA) are amongst the most prevalent yet treatable disorders affecting women worldwide, occurring in at least one in ten women. Both conditions are associated with poor infant outcomes and adverse maternal-child bonding. Oxytocin is a neuropeptide involved in social bonding, reproduction, maternal behaviours, and stress. Synthetic oxytocin (SynOT) is a medication that is commonly administered during labour and birth. This systematic review identified and evaluated the evidence on the effects of SynOT on depression and anxiety symptoms in the postpartum.

Methods: Comprehensive searches of nine electronic databases were conducted for studies published from database inception to June 2019. Experimental and observational studies reporting on peripartum SynOT exposure and PPD and/or PPA were considered for inclusion. Two reviewers independently screened articles, extracted data, and assessed the Risk of Bias (RoB) of included articles. The primary outcomes of interest in the review were PPD and PPA symptoms. Meta-analysis of primary study outcomes was planned and a descriptive analysis of the results was conducted.

Results: From 758 records identified with the search strategy, two observational studies involving 47 333 participants met the criteria for inclusion in the review. Clinical and methodological heterogeneity of individual studies precluded pooling of results into a meta-analysis. RoB was assessed using the Newcastle-Ottawa Scale for observational studies. Overall, the studies had low and moderate risks of bias. The two studies reported opposing results regarding the direction of the effect for peripartum SynOT on PPD and PPA outcomes. One of the studies found that exposure to peripartum SynOT resulted in 35% higher incidence of PPD and/or PPA compared to women with no exposure within the first year postpartum (Relative Risk: 1.35; 95% Confidence Interval 1.26, 1.41). The other study concluded that SynOT was a protective factor against developing PPD at six weeks and nine months postpartum (Hazard Ratio: 0.65; 95% Confidence Interval 0.45, 0.95).

Conclusion: There is limited and inconclusive scientific evidence on the effect of peripartum SynOT on PPD and/or PPA symptoms. The two relevant studies included in our review present opposing findings, which may be attributable to the significant heterogeneity between them. Large randomized controlled studies are needed to better understand whether administration of SynOT in the peripartum period has an impact on maternal mental health outcomes in the postpartum.

Keywords: postpartum depression; postpartum anxiety; oxytocin; peripartum; maternal health

Funded By: Dr. Ospina is funded by the Lois Hole Hospital for Women through the Women and Children's Health Research Institute Start Up Grant and supported by the Canadian Institutes of Health Research as a Canada Research Chair in Life Course, Social Environments and Health through the Government of Canada.

Abstract #:	125
Presenter:	Samantha Louie-Poon
Supervisor:	Scott, Shannon
Title:	A critical approach to child health research in Canada: exploring the perspectives of Chinese migrant parents
Authors:	Samantha Louie-Poon & Shannon Scott
Theme:	Knowledge translation and decision-making

Background:

International migration is a multi-faceted phenomenon with several intersecting forces. Despite the attraction migration research has received in the past decade, racialized migrants continue to face injustices. Currently, an underexamined division in migration scholarship is the climate of child health research. Particularly, how the research process is simultaneously shaped by and shapes existing systems of power. In Canada, a Western-centric focus remains the dominant framework for conducting child health research. As a result, the products from this research become unsuitable for racialized migrant end-users. This is problematic as it limits the capacity for Chinese migrant parents to promptly identify and manage symptoms of their child's acute health condition. Thus, attending to power relations in the process of child health research is a pressing healthcare and human rights concern.

Aims:

The objectives of this project are to: (i) attend to power relations in acute child health research from the perspective of Chinese migrant parents, and (ii) reduce acute health inequities among Chinese migrant children.

Methods:

This project will be a multi-phase study. Phase 1 will be a scoping review to identity gaps in acute child health research for Chinese migrant parents. The findings from phase 1 will inform the focus and scope of phases 2 and 3. At ASSIST Community Services Centre in Edmonton, AB, homogeneous purposive sampling will be conducted on the basis of race and migrant status for the recruitment of participants (n=12 to 16) for phases 2 and 3. Participant inclusion criteria includes: refugee or immigrant status of Chinese origin, parent or caregiver, arrived to Canada <10 years, English and/or Chinese (Mandarin or Cantonese) speaking. Employing a qualitative descriptive design in phases 2 and 3, data collection will be conducted using focus groups [FG] (n=6 to 8 per FGD). In phase 2, unstructured FG's will explore Chinese migrants' perspectives on power relations with acute child health research products. Phase 2 findings will inform the scope of phase 3. Semi-structured FG's in phase 3 will explore solutions to improve the process of acute child health research. Content analysis using open coding techniques will be used to analyze data from phases 2 and 3.

Expected outcomes and Conclusion:

The expected outcomes are to: (i) understand Chinese migrant parents' perspectives on power relations in acute child health research products, and (ii) explore solutions to navigate power relations in acute child health research processes in Canada. Through the expected outcomes of this project, the United Nations mission pursuant to improving the health of all children will take significant strides in becoming a reality.

Funded By: Operating costs associated with this research will be funded by my supervisor's (S. Scott) grant: Integrating evidence and parent engagement to optimize children's healthcare. CIHR Foundation Grant.

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Abstract #:	26
Presenter:	Samuel (Sammy) Lowe
Supervisor:	Pabayo, Roman
Title:	Greater inequalities make anxious neighbours: investigating the link between neighbourhood income inequality and maternal mental health
Authors:	Samuel Lowe, Darcy Reynard, Ambikaipakan Senthilselvan, Candace Nykiforuk, Sheila McDonald, Roman Pabayo
Theme:	Pregnancy and developmental trajectories

Background - Mental illness presents a substantial public health burden in Canada, with women and mothers experiencing particularly high levels of anxiety and depression disorders. The social determinants of health, such as the unequal distributions of income, have been identified as potential risk factors for adverse mental health outcomes. Previous research into the relationship between income inequality and mental health has been largely cross-sectional, with mixed results. Very few of these studies have focused on mothers as a distinct population. This study addresses these gaps in current knowledge by analyzing longitudinal relationships between neighbourhood-level income inequality and anxiety and depression symptoms among a cohort of pregnant women and mothers from Calgary, Alberta.

Methods - We analyzed longitudinal data from the All Our Families community-based cohort (n=2,461). From 2008-2014, respondents were asked to complete questionnaires at six time points from <25 weeks pregnant to three years postpartum. Mental health outcomes were assessed using the Spielberger State Anxiety Inventory (anxiety), and the Edinburgh Postnatal Depression Scale and the Centre for Epidemiological Studies-Depression Scale (depression). Continuous mental health scores were standardized using the percent of maximum possible scaling method to assess changes in symptoms, and dichotomized using cut-offs to determine the odds of elevated symptoms. Multilevel growth curve modelling was used to quantify the associations between neighbourhood-level income inequality (expressed as gini coefficients) and anxiety and depression symptoms over time, adjusting for individual and neighbourhood-level factors. We repeated the analyses excluding those who had elevated anxiety or depressive symptoms at baseline to adjust for prior experience with elevated symptoms.

Results - Being exposed to higher neighbourhood income inequality was significantly associated with higher levels of anxiety symptoms among the sample of mothers. A standardized deviation increase in the neighbourhood gini (z-score) was associated with higher anxiety symptoms over time (β=0.0011, 95% CI=0.00007-0.0022, p=0.037), and the association remained significant after adjusting for individual and neighbourhood covariates. Linear combination estimates suggest that this association does not become significant until 26.6 years following baseline. The association was stronger and more immediate among mothers who did not report elevated anxiety symptoms at baseline. Among this subsample, a standardized deviation increase in neighbourhood gini (z-score) was associated with increasing anxiety symptoms over time (β=0.0016, 95% CI=0.00038-0.0028, p=0.010), with estimates indicating that the association became significant after five years following baseline.

Conclusion - Income inequality within neighbourhoods negatively impacts the mental health of pregnant women and mothers who live there. Further research is needed to better understand the mechanisms through which inequality influences maternal mental health, and how interventions aimed at reducing income inequality benefit mental health.

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Abstract #:	120
Presenter:	Chang Lu
Supervisor:	Cutumisu, Maria
Title:	Healthcare Providers' Perceptions and Longitudinal Performance in the RETAIN Digital Neonatal Resuscitation Simulator
Authors:	Chang Lu, Simran K. Ghoman, Maria Cutumisu, Georg M. Schmölzer
Theme:	Children's health and well-being

Background: Frequent simulation-based education is recommended to improve health outcomes during neonatal resuscitation, but is often inaccessible due to time, resource, and personnel requirements. Digital simulation presents a potential alternative, however its effectiveness and reception by healthcare professionals (HCP) remain largely unexplored.

Objectives: This study explores HCPs' attitudes towards a digital simulator, technology, and mindset to elucidate their effects on neonatal resuscitation performance in simulation-based assessments.

Methods: The study was conducted from April-August 2019, with 2-month (June-October 2019) and 5-month (September 2019-January 2020) follow-ups at a tertiary perinatal centre in Edmonton, Canada. Fifty HCPs completed a demographic survey, pre-test, two practice scenarios using the RETAIN neonatal resuscitation digital simulation, a post-test, and an attitudinal survey (100% response rate). Participants repeated the post-test scenario after two-months (86% response rate) and completed another post-test scenario using a low-fidelity table-top simulator (80% response rate) five-months after the initial study intervention. Participants' survey responses were collected to measure attitudes towards digital simulation, technology, and mindset. Knowledge was assessed at baseline (pre-test), acquisition (post-test), retention (2-month post-test), and transfer (5-month post-test).

Results: Fifty neonatal HCPs participated in this study (44 females and 6 males; 27 nurses, 3 nurse practitioners, 14 respiratory therapists, and 6 doctors). Most participants reported technology in medical education as useful and beneficial. Three attitudinal clusters were identified by a hierarchical clustering algorithm based on survey responses. Although participants exhibited diverse attitudinal paths, they all improved neonatal resuscitation performance after using the digital simulator and successfully transferred their knowledge to a new medium.

Conclusions Digital simulation improved HCPs' neonatal resuscitation performance. Medical education may benefit from incorporating technology during simulation training.

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Abstract #:	138
Presenter:	Jimmy Lu
Supervisor:	Lemieux, Joanne
Title:	Determining the role of rhomboid protease GlpG in pathogenic bacterial colonization: a potential solution to recurring bacterial infections in women and children
Authors:	Jimmy Lu1, Elena Arutyunova1, Heather Armstrong2, Steven Verhelst3, Eytan Wine2, M Joanne Lemieux1
	1 Department of Biochemistry, University of Alberta
	2 Department of Pediatrics, University of Alberta
	3 Department of Chemistry, KU Luven
Theme:	Lifelong women's health

Extra-intestinal pathogenic E. coli (ExPEC) colonization occurs naturally in the gut, however, when these strains spread to other niches, it leads to pathologies such as skin and urinary tract infections (UTI). If untreated, UTIs can spread even further to the kidneys resulting in pyelonephritis. In the case of pregnant women, UTIs can result in vertical transmission to neonates leading to sepsis and morbidity, which is a significant problem in developing nations. Currently UTIs are one of the most common bacterial infections in children and the treatments available today are limited to antibiotics, however this can lead to recurring infections as bacteria become resistant. In order to investigate new, antibiotic-free therapeutics, a deeper understanding of the mechanism behind UTIs and bacterial infections is necessary. Recent studies have shown that glpG, the rhomboid protease gene, is essential for ExPEC colonization in the mouse gut. This suggests that GlpG could be a potential target to inhibit bacterial colonization as a means to combat bacterial infections. Our lab has had a long-standing interest in GlpG and the rhomboid protease family, a class of intramembrane serine proteases, and have solved crystal structures and developed kinetic assays for these enzymes.

Our preliminary data shows overexpression of the GlpG protease leads to a significantly higher level of invasion in epithelial cells compared to lab strains of E. coli. What's more, we have quantified mRNA levels of the glpG gene in various clinical isolates of E. coli and have shown that certain ExPEC strains have higher mRNA levels relative to non-pathogenic strains. Together, these results suggest that GlpG may be a strong drug target to combat UTIs. In order to test if GlpG can be inhibited, we developed an assay to first measure GlpG activity in living E. coli cells. Using inhibitors specific to GlpG (sub-micromolar IC50), we have shown that enzymatic activity is inhibited up to 50% in live cells. These inhibitors will be optimized using molecular GlpG-inhibitor modeling/crystallography to achieve greater inhibition of GlpG. This will be used to facilitate rational antibiotic-free drug design to treat UTIs.

Funded By: Women and Children's Health Research Institute (WCHRI)

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Abstract #:	81
Presenter:	Kailie Luan
Supervisor:	Kassiri, Janani (Jay)
Title:	Midline Epileptic Discharges and Seizures in Pediatric Epilepsy: Case Series and Review
Authors:	Kailie Luan MD; Natarie Liu MD; Janette Mailo MD; David Barry Sinclair MD; Janani Kassiri MD, PhD
Theme:	Children's health and well-being

INTRODUCTION: Pediatric medically intractable epilepsy accounts for approximately 10-30% of pediatric epilepsy. It can be a major problem, leading to recurrent seizures and severe long-term consequences of the developing brain. Epileptic discharges localized to the midline vertex are rare in pediatric epilepsy and not well understood. Previous studies have suggested that seizure onset often occurs within the first ten years of life with abnormal neuroimaging studies in 30-40% percent of patients. However, the electroclinical correlation, pathological findings underlying the epileptogenic zone, and long-term outcomes of children with midline seizures have not been adequately described. The objective of our study was to understand the etiology of midline epileptic discharges using radiological and clinical features, and to define post-surgical seizure outcomes in these patients.

METHODS: Ethics approval was obtained and we reviewed clinical charts, electroencephalography (EEG) records, and neuroimaging studies of eight pediatric patients with epileptic discharges localized to the midline vertex (Fz, Cz, Pz) on EEG at the University of Alberta's Comprehensive Epilepsy Program. The seizures were classified according to the International League Against Epilepsy criteria and semiology. Patient demographics, age, sex, seizure types, etiology of seizures, Magnetic Resonance Imaging results reported by a neuroradiologist, underlying and/or coexisting neurological diagnosis, additional presenting clinical signs and symptoms and, seizure outcomes in these patients were obtained.

RESULTS: In our cohort of eight patients, simple partial and complex partial seizures were the most prevalent seizure types experienced by 87% of patients with midline discharges. Age of seizure onset was within the first 10 years of life in seven out of eight of these patients. Heterogenous radiological and pathological etiologies were found in children with midline seizures. However, focal cortical dysplasia (FCD) type II was the most common and present in 50% of patients. These children often had normal neuroimaging studies and medically intractable epilepsy. However, seizure freedom was achieved following surgical resection of the epileptogenic zone in these patients.

CONCLUSIONS: In this small case series we demonstrated that patients with midline epileptic discharges on EEG are associated with intractable focal seizures and early seizure onset. However, neuroimaging studies are typically heterogenous or reported as normal in these patients. Surgery may be beneficial for seizure control in children with midline discharges as the most common pathology found in our study was FCD. These results have the potential to treat otherwise intractable epilepsy by localizing midline epileptic discharges early, defining the epileptogenic zone for surgical resection, and achieving seizure freedom with favourable neurological outcomes in children with this electroclinical syndrome.

Funded By: Comprehensive Epilepsy Program

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Abstract #:	51
Presenter:	Richard Mah
Supervisor:	Bourque, Stephane
Title:	Perinatal Iron Deficiency Causes Sex Dependent Alterations in Renal Retinoic Acid Signaling and Development
Authors:	Richard Mah, Andrew Woodman, Claudia Holody, Ronan Noble, Robin Clugston, Stephane Bourque
Theme:	Children's health and well-being

Introduction: Iron Deficiency (ID) is the most common nutritional deficiency worldwide with pregnant women most at risk. Perinatal ID has been associated with reduced nephron endowment and renal dysfunction later in life. It is unclear which mechanisms dictate changes observed in nephron formation. The retinoic acid (RA)-ret tyrosine receptor kinase pathway plays important roles in nephron endowment, and ID is known to impact the metabolism of vitamin A - the precursor of RA. Therefore, we investigated how ID affects RA signalling. We hypothesized that perinatal ID disrupts offspring RA signaling, thereby causing a reduction in nephron endowment.

Methods: Six-week old Sprague Dawley dams were fed an iron-restricted (3-10 mg/kg) or iron-replete (37 mg/kg) diet two weeks prior to and throughout gestation. Offspring kidneys were collected on postnatal day (PD)1 and PD28. Nephron endowment was determined by acid maceration and microscopy. Expression of RA synthesizing enzyme raldh2, RA receptor rarα, RA metabolizing enzyme cyp26b1, and transcriptional target of RA and effector of nephrogenesis ret, were measured by RT-qPCR. Additionally, PD1 expression of kidney morphogenic factors Wilms tumor 1 (wt1) a "master regulator" of kidney development and gdnf a ligand of ret required for both growth and branching of the ureteric bud in kidney development was also measured. Data are analyzed by two-way ANOVA for the effects of perinatal ID and offspring sex.

Results: ID resulted in neonatal anemia and decreased birth weight ($P<0.05$). On PD28, males but not females had a reduced number of nephrons due to ID ($P_{interaction}=0.006$). On PD1 raldh2 and rarα were overexpressed due to ID in male but not female offspring ($P_{interaction}<0.05$). PD1 expression of cyp26b1 was increased due to ID ($P_{ID}=0.03$), but ret expression was not altered. On PD28, raldh2 expression was increased by ID ($P_{ID}=0.04$), but rarα expression was not altered. PD28 expression of and cyp26b1 was increased in females versus males ($P_{sex}<0.05$). The morphogenic factor wt1 was upregulated at PD1 due to ID ($P_{ID} = 0.006$) as was gdnf ($P_{ID} = 0.001$). Expression of ret at PD28 was increased by ID ($P_{ID}=0.005$).

Conclusion: These results suggest perinatal ID causes increased expression of proteins within the RA pathway, morphogenic factor pathway, and the downstream target ret. Dysregulation of important nephrogenic signalling pathways such as the RA pathway may underlie reductions in nephron endowment in perinatal ID males.

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Abstract #:	109
Presenter:	Nilusha Malmuthuge
Supervisor:	Kozyrskyj, Anita
Title:	Abundance of mucin degraders in early-infancy gut microbiota predicts child overweight
Authors:	Malmuthuge N, Azad MB, Becker AB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL
Theme:	Children's health and well-being

Background: Almost one in three children and youth are overweight or obese in Canada. Factors creating an imbalance between energy intake and expenditure such as genetics, diet, physical activities, and gut microbiota lead to overweight/obesity. Mucin degraders (Akkermansia, Ruminococcus, Faecalibacterium, Roseburia, Bacteroides, and Bifidobacterium) successfully colonize the large intestine and effectively harvest energy from indigestible dietary materials. A higher abundance of gut microbiota efficient in harvesting energy for host increases the risk of overweight/obesity. Identifying key gut microbiota in developing overweight/obesity has gained increasing interest with evidence suggesting long-term effects of early life microbiota. This study investigated associations between the abundance of mucin-degrading gut microbiota in 3-month-old infants and body-mass index in toddlers (1 & 3 years).

Methods: This study used a subset of (n=1435) infants enrolled in Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort to profile gut microbiota at 3 months using 16S sequencing of fecal samples. Body mass index z-score (BMIz) was calculated at one and three years of age. Two methods, logistic regression and random forest decision tree, were used to study the association infant colonization with mucin degraders and BMIz. Logistic regression models were adjusted for covariates obtained by maternal report or from the birth chart.

Results: The random forest approach identified Akkermansia, Ruminococcus, Faecalibacterium and Bacteroides as discriminatory mucin degraders at 3 months of age in classifying infants by BMIz at age 1 year. Unadjusted logistic regression identified Faecalibacterium, Roseburia and Bacteroides as determinants of BMI z-score at this age. Following adjustment for prenatal factors (gestational age, birth weight) and infant diet (3-month breastfeeding, solids introduction at 6 months), BMIz at 1 year of age was positively associated with the abundance of Roseburia (odds ratio [OR] = 1.42, 95% confidence interval [CI] = 1.05-1.94, P = 0.02) and negatively associated with the abundance of Bacteroides (OR = 0.79, 95%CI = 0.66-0.95, P = 0.01) in 3-month-old infants. In exclusively-breastfed infants, lower BMIz at 1 year of age was associated with enrichment of Bacteroides (adjusted OR = 0.74, 95%CI = 0.60-0.89, P = 0.003) and of Ruminococcus (adjusted OR = 0.78, 95%CI = 0.61-0.99). In the absence of exclusive breastfeeding, a high abundance of Akkermansia was associated with reduced BMIz at 1 year (adjusted OR = 0.81, 95%CI = 0.65-0.99). The 3-month abundance of mucin degraders had no association with BMIz at 3 years of age.

Conclusion: The abundance of several mucin degraders in 3-month infant gut microbiota predicted BMIz at 1 year of age. Associations between type of mucin degrader and BMIz varied by breastfeeding status. Our findings suggest that interventions to mitigate childhood overweight/obesity can be started early in life via manipulating the infant gut microbiome.

Funded By: CIHR

women & children's health research institute

Abstract #:	14
Presenter:	Inderdeep Mander
Supervisor:	Wine, Eytan
Title:	How Dietary Fibers Relate to Pediatric Inflammatory Bowel Diseases
Authors:	Inderdeep Mander, Rosica Valcheva, Robyn Dickner, Jeremy Jerasi, Alexandra Petrova, Hien Huynh, Matthew Carroll, Heather Armstrong*, Eytan Wine*
Theme:	Children's health and well-being

Introduction: Rates of pediatric inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn disease (CD) are increasing rapidly. Although the etiology of IBD is unclear, the gut microbiome and diet have been implicated. Dietary fibers pass through the small intestine undigested and are fermented in the large bowel by gut microbes to produce short chain fatty acids (SCFAs), shown to improve the mucosal barrier and prevent inflammation. In a dysbiotic environment, such as in IBD, fermentation processes are likely altered, as commensals are less abundant, potentially resulting in a reduction of SCFAs. Whole fibers are also able to interact with host immune cells in the colon to induce a pro-inflammatory response. These observations may help explain why many IBD patients report sensitivity to dietary fibers.

Hypothesis: The lack of fiber-fermenting microbes populating the IBD gut leads to impaired fermentation, resulting in reduced SCFA production and binding of intact fibers to host cell receptors. This ultimately drives an inflammatory response and continued dysbiosis.

Methods:Previous results have indicated that specific dietary fiber receptor expression is increased in pediatric IBD patient tissues. Because these data suggest that T cells may play a role in sensitivity to unfermented dietary receptors, we studied the response of T cells in vitro to inulin and oligofructose, both unfermented or fermented, by previously identified microbes of interest.

Macrophage and T-cell in vitro cultures were treated with inulin (5mg/mL) and oligofructose (5mg/mL) fibers, and their cytokine response to these whole fibers was assessed using ELISA/qPCR and measurement of IL-1β secretions. Ex vivo patient biopsies were similarly treated and IL-1β secretion and gene expression, were measured using ELISAs/qPCR. These fibers were also pre-fermented with microbes of interest or whole microbe patient intestinal washes. Results were correlated to clinical findings.

Results: Whole intact fibers induced a pro-inflammatory response in macrophage cells when compared to fibers that have been shown to be anti-inflammatory. This pro-inflammatory response was mitigated by pre-fermenting the fibers with P. protogens. Oligofructose also was found to increase IL-1β secretion in UC and CD patient biopsies, compared to non-IBD specimens. This increase was also positively correlated with disease severity. Intestinal washes from severe IBD patients were unable to ferment oligofructose or reduce fiber-associated inflammation in macrophage cell lines, whereas fibers pre-fermented by whole microbe intestinal washes from remission or non-IBD samples displayed reduced IL-1β secretion.

Conclusion: Results from this study demonstrate that a lack of fiber-fermenting microbes and presence of whole fibers can lead to pro-inflammatory responses, both in cell line models in vitro, and patient biopsies cultured ex vivo. However, the presence of appropriate fermenting microbes can reduce fiber-associated inflammation. These findings indicate that a better understanding of microenvironments within the bowel could lead to the development of specific dietary guidelines for IBD patients and could drive microbe-altering therapies and markers of response to treatment.

Funded By: Studentship supported by North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the Vessie Heckbert Memorial Fund.

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Abstract #: 139
Presenter: Siavash Mashhouri
Supervisor: Elahi, Shokrollah
Title: Sex matters: Physiological abundance of CD71+ erythroid cells in females
Authors: Siavash Mashhouri1, Shima Shahbaz1, Petya Koleva1, and Shokrollah Elahi1

1Department of Dentistry, Faculty
Theme: Lifelong women's health

The male-biased research had dominated modern medicine so researchers preferred to use male subjects to prevent the occurrence of variabilities, mostly derived from hormonal changes during the menstrual cycle (estrus cycle in animal studies), pregnancy or after menopause. Sex is a biological variable that directly influences immune system. Males and females differ in their immunological responses to foreign and self-antigens and show distinctions in innate and adaptive immune responses. To appreciate the role of sex as an important variable, we analyzed the frequency of erythroid precursors (CD71+ Erythroid Cells (CECs)) in females versus males in both humans and mice. We and others have shown that CECs have a wide range of immunomodulatory functions and suppress both innate and adaptive immune responses. Interestingly, we found females are physiologically enriched in CECs, in the peripheral blood of human subjects and the spleen of mice. We observed a significantly higher abundance of CECs in both C57BL/6 and BALB/c female mouse strains. In particular, BALB/c mice appear to have higher percentages of CECs compared to C57BL/6 mice. We also characterized CECs for expression of PDL-1, PDL-2, Gal-9, VISTA, CD39, CD73, CD45 and ROS activity in both males and females. In mice, females express more inhibitory molecules like VISTA, PDL1 and 2 in comparison with males, however, there was no significant difference between male and female in human study. Furthermore, we observed that the frequency of CECs increases two folds after the menstruation in humans. Based on our findings, considering the immunomodulatory capabilities of CECs, we suggest that the higher frequency of CECs in females, both mice and humans, should be considered as a new sex biological variable. Furthermore, we speculate that the long-term/life-long presence of CECs in peripheral blood may have immunomodulatory/immunosuppression effects on females immune system.

Funded By: WCHRI

Abstract #:	100
Presenter:	Claire McNiven
Supervisor:	Robinson, Joan L
Title:	Antimicrobial lock solutions for prevention of central venous catheter infections in pediatric patients with intestinal failure
Authors:	Bridget Gibson, Claire McNiven, Meghan Sebastianski, Robin Featherstone, Rabin Persad, Joan Robinson
Theme:	Children's health and well-being

Background: Children with intestinal failure are dependent on total parenteral nutrition (TPN) via a central venous catheter (CVC) for survival. They require long-term use of CVCs and are at high risk of catheter-related bloodstream infections (CRBSI). Prevention of CRBSI is imperative, as they can necessitate catheter removal and access site loss. Eventually there may be no available CVC sites, and a child may die without an intestinal transplant. Antimicrobial locks (AMLs) are solutions instilled in CVCs to prevent CRBSI. There are many different solutions available, but limited evidence guiding the optimal choice, frequency, and duration of prophylactic AML solution in children with intestinal failure. Guidance for appropriate prophylactic AML use has the potential to decrease rates of CRBSI and reduce morbidity and mortality in pediatric intestinal failure patients.

Aim: In children with intestinal failure who require a CVC, does using an AML solution decrease the rate of CRBSI?

Methods: A systematic review of AMLs used for CRBSI prophylaxis in children with intestinal failure was performed to determine the optimal AML(s) choice(s) for use in this population. Randomized and nonrandomized trials, case studies, and cohort studies that used comparator groups (including historical controls) with children (age 0-17) with intestinal failure, who have a CVC (2 days or greater) for TPN were screened. If the data is sufficiently homogenous, both clinically and methodologically, we will pool outcomes in a meta-analysis using a DerSimonian Laird random effects model. If possible, we will do network meta-analyses (NMA), simultaneously pooling common outcomes across multiple interventions.

Results: Primary outcomes of interest are the rate of new CRBSI with AML versus controls, and a comparison of each type of AML versus controls. Secondary outcomes include: unplanned CVC removal (all cause), CVC removal due to CRBSI, recurrence of CRBSI with the same pathogen, all adverse events/side effects attributed to antimicrobial lock solutions by the authors, development of infections with antibiotic resistance at any point (in particular resistance to antibiotics used in the AML solution), length of hospital stay due to CRBSI, need for intensive care, any other morbidities or outcomes that were compared, and mortality.

The initial search done May 2018 identified 849 studies, and an updated search done July 2020 and found an additional 142 studies. Four studies were identified from other sources. Eight duplicates were removed. After screening, 29 studies were included in the systematic review. References were screened from these studies with no additional studies identified. These papers are presently undergoing data extraction. The most frequently studied AMLs in this population were ethanol (14 studies) and taurolidine (11 studies). Tobramycin with tissue plasminogen activator (tPA), tPA alone, and tetrasodium-ethylenediaminetetraacetic acid were used in one study each. One study used gentamicin, vancomycin or amikacin as AML solutions.

Conclusions: This research aims to provide guidance on AML use for CRBSI prophylaxis in pediatric patients with intestinal failure. We will provide data on efficacy and clarify which solutions have the best outcomes.

Funded By: This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

women & children's health research institute

Abstract #:	82
Presenter:	Cory Meeuwisse
Supervisor:	Alexander, R Todd
Title:	The use of Rituximab in Nephrotic Syndrome amongst Canadian Pediatric Nephrologists
Authors:	Cory Meeuwisse, Todd Alexander, Sara Rodrigeuz-Lopez, Catherine Morgan
Theme:	Children's health and well-being

Introduction: Nephrotic syndrome is the most common chronic pediatric kidney disease. For treating frequently relapsing (FR), steroid-resistant (SR) and steroid-dependent (SD) nephrotic syndrome, practice variation is common. Rituximab, a monoclonal antibody, is an emerging therapy for these difficult to treat nephrotic syndromes. Among published literature, there exists a wide diversity in the use of Rituximab in many key areas of therapy and no clear treatment guidelines for nephrotic syndrome. Our goal is to evaluate the practice diversity among Canadian pediatric nephrologists, and we hypothesize that significant variations exist in the use of rituximab in management of this disease.

Methods: A survey was created through the REDCap Program which was distributed across Canada through the Canadian Association of Pediatric Nephrologists (CAPN). All Canadian Pediatric Nephrologists were included in the research group. Responses were de-identified, and data collected electronically through the REDCap database.

Results: There were 47 eligible participants contacted and we received 20 responses. Only one physician specified using Rituximab as a second line therapy, where for other nephrologists it was a third choice, fourth choice, or never used. There was no similarity in responses for when physicians elected to start Rituximab therapy, and there were many variations on B-cell monitoring parameters after initiation of Rituximab treatment. Additional doses of Rituximab were administered anytime between 1 week after the first dose, and 6 months after the first dose. Responses were comparable between responders when identifying barriers to Rituximab use which included financial/funding difficulties, provider familiarity, and lack of knowledge surrounding long term side effects.

Conclusion: Significant practice variation exists in the use of rituximab for difficult to treat nephrotic syndrome, and there is no current practice guidelines to guide this therapy. Many barriers exist for the use of Rituximab, and several were identified including both financial and provider specific reasons. Through this study, we have identified the need to determine the next best step in the treatment of difficult to treat nephrotic syndrome. This need could be met through further research including Rituximab clinical trials and eventual formation of practice guidelines.

Funded By: This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

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Abstract #:	83
Presenter:	Pamela Mellon
Supervisor:	Storey, Kate E
Title:	Sleeping Soundly: Teachers' perspectives on school-based sleep promotion
Authors:	Pamela Mellon, Lauren Sulz, Brian Torrance, Kate Storey
Theme:	Children's health and well-being

Introduction

Insufficient sleep is a growing public health concern. The physical and psychosocial impacts of sleep deprivation in our youth include obesity, diabetes, anxiety, depression, and poorer overall health and immune function. The impacts of inadequate sleep can negatively influence students academically. Given that healthy students learn better, schools have been identified as ideal health promotion settings to influence children's health and wellbeing, including their sleep behaviours. In Canada, many schools have embraced the Comprehensive School Health (CSH) approach. The CSH approach empowers and enables school staff and students to improve their overall health and wellbeing through strategies which promote physical activity, healthy eating, mental health, and sleep. To further our understanding of school-based sleep promotion the objective of this study was to explore teachers' perspectives on sleep behaviours and how teaching practices and school-based sleep promotion facilitate and support, or act as a barrier, to healthy sleep behaviours in students.

Methods

Virtual teacher interviews began May 2020 using qualitative research and Interpretive Descriptive (ID) as a guiding methodology. Teachers were purposively sampled and recruited through provincial education partners, inclusion criteria for participation was a teacher in an elementary school. To date, 11 teachers have been interviewed within the greater Edmonton area. Guided by ID, semi-structured interviews were used as a data generating strategy to allow teachers to share their knowledge based on their individualized roles and contexts. Interviews were audio-recorded and transcribed verbatim. Inductive descriptive thematic analysis was used as the analytic strategy.

Results

Preliminary results indicated that overall teachers felt that school-based sleep promotion is warranted and important. Teachers shared that parents and teachers should work together to promote sleep, given that efforts in the school need to be supported at home. It was perceived that school-based sleep promotion should include both formal (i.e., classroom-based lesson plans) and informal (i.e., day-to-day conversation) strategies for students, and awareness/educational strategies for parents. Teachers also indicated that there is opportunity for improvement in current school-based sleep promotion.

Conclusion

Based on the preliminary results, students would benefit mentally, physically, emotionally and academically from home and school collaboration to educate students and parents on healthy sleep behaviours. This collaboration would improve school-based sleep promotion.

Funded By: WCHRI, PaCET Award; CIHR

Abstract #: 140
Presenter: Alissa Minard
Supervisor: Glover, Mark
Title: Understanding nucleosomal dynamics: the first step in DNA damage response signaling
Authors: Alissa Minard, Rashmi Panigrahi, Mark Glover
Theme: Lifelong women's health

Introduction

Cancer is a major cause of morbidity for Albertans. Specifically cancer that affects the ovary and the breast, is a public health problem of critical proportions that affects women. DNA damage response and histone modifications in chromosomes are frequently altered in cancer, and may contribute to the etiology and progression of tumors. The orderly recruitment and disassembly of DNA damage repair (DDR) proteins at the DNA damage foci are conserved throughout eukaryotic evolution. However, the intricate mechanism of this cascade remains to be defined. Developing therapeutic approaches to combat cancer necessitates a deeper mechanistic understanding of the dynamics of interaction of DNA repair proteins with nucleosomes (the basic unit of chromosome). In humans, H2AX, an histone variant exists, which is necessary for recruitment of DDR factors. This variant has a C-terminal motif that is phosphorylated by DNA protein kinases on serine 139 (forming γH2AX), an indication of DNA double-strand break (DSB) recognition. Formation of γH2AX leads to recruitment of the Mediator of DNA damage checkpoint protein 1 (MDC1), an early player in the DDR pathway. MDC1 knockout phenotypes present significant genomic instability. Structural details underlying the interaction of the phosphorylated C-terminal tail of H2AX with BRCT domain of MDC1 has been previously studied by our lab and others.

Our study aims at investigating the nucleosome dynamics underlying MDC1 and γH2AX containing nucleosome interaction.

Methods

We have been using bacterial cloning and protein purification techniques to produce milligram quantities of recombinant nucleosomes. We have accessed the homogeneity of the assembled complexes using size exclusion chromatography assisted with multi-angle light scattering detector (SEC-MALS). Further we use the small angle X-ray scattering technique to visualize the dynamics of the complexes.

Results

Nucleosomes have previously been prepared by other labs using refolding technique. In this project, firstly, we have developed novel bacterial coexpression-purification system to produce milligram quantities of nucleosomes. Secondly, we developed protocol to prepare nucleosomes containing H2AX, which contain phosphorylated serine 139. Thirdly, we have identified conditions to prepare MDC1 BRCT domain complexed with phosphorylated nucleosome. We have tested the homogeneity of the above complexes using size exclusion chromatography. Next, to understand the nucleosome dynamics associated with this complex, we are performing solution scattering studies.

Conclusion

We have successfully prepared large macromolecular assembly of MDC1-nucleosome, suitable for structural studies. This focused study aims to uncover the enigmatic link between phosphorylation of nucleosomes followed by the interaction with the DDR associated player, MDC1 and the consequential nucleosomal dynamics. The current study will add to existing knowledge on nucleosome dynamics during DDR and thus provide targets for therapeutic intervention especially for the design of DDR specific inhibitors.

Funded By: Canadian Institutes of Health Research (CIHR)

National Institutes of Health (NIH)

Abstract #:	157
Presenter:	Catherine Mitran
Supervisor:	Yanow, Stephanie K
Title:	Exploiting heterologous immunity between P. vivax PvDBP and P. falciparum VAR2CSA for vaccine development
Authors:	Catherine J. Mitran, Lauren M. Higa, Michael F. Good, and Stephanie K. Yanow
Theme:	Pregnancy and developmental trajectories

Plasmodium (P.) falciparum infection in pregnancy can cause preterm birth, low birth weight, spontaneous abortion, maternal anemia and maternal and infant mortality. However, there is no licensed vaccine to prevent malaria infection in pregnancy. We previously discovered that antibodies to an epitope within subdomain 1 (SD1) of P. vivax PvDBP cross-react with the P. falciparum placental antigen VAR2CSA and disrupt interactions between VAR2CSA on infected RBCs and the chondroitin sulphate A receptor in vitro. Here we explored ways to express the epitope as a vaccine. First, we used a cross-reactive monoclonal antibody, called 3D10, to screen >400 overlapping linear and cyclic peptides made using the CLIPS technology from Pepscan. We identified a discontinuous epitope within SD1 that forms the putative recognition site of 3D10. Based on these findings, one linear peptide and one cyclic peptide were conjugated to carrier proteins and used to immunize BALB/c mice. Immune sera were tested for reactivity to VAR2CSA by ELISA. The linear peptide elicited antibodies to self but failed to cross-react with VAR2CSA. A cyclic peptide of the entire 31 amino acid SD1 sequence elicited antibodies to self with titers >2.0 million. Antibodies from just over half of the mice also cross-reacted with VAR2CSA, with titers ranging from 1,600 to 6,400. Interestingly, the cross-reactive antibodies had low avidity for the parent protein, PvDBP. Together, these results demonstrate that the epitope in PvDBP that mediates cross-reactivity to VAR2CSA is discontinuous and requires all segments to elicit antibodies with specificity for VAR2CSA.

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Abstract #:	141
Presenter:	NORAZLIN MOHAMAD
Supervisor:	Cummine, Jacqueline
Title:	Effects of Exercise Therapy on Decreasing Pain in Women with TMD: A Pilot Randomized-Controlled Trial
Authors:	Norazlin Mohamad, Francisca Claveria Gonzalez, Paula Ospina Lopez, Alexandra Budd, Susan Armijo-Olivo
Theme:	Lifelong women's health

Introduction:

Musculoskeletal chronic pain disorders, including Temporomandibular disorders (TMD) are more prevalent in females. TMD affect the masticatory muscles, the temporomandibular joint, and related structures. One of the most promising treatments for improving TMD has been exercise therapy. Preliminary studies showed that treatment directed to the neck may be beneficial in people with TMDs. However, to the best of our knowledge, no previous study has tested the effectiveness of exercises directed to the neck in isolation in people with TMDs. Our pilot study primary aim is to investigate the effects of exercise therapy on pain intensity when compared with a placebo group in women experiencing chronic TMD. Our secondary aim is to also investigate the effectiveness of exercise therapy on jaw disability, maximal neck strength, and neck muscular performance.

Methods: This was a triple blind, two-armed parallel group, placebo controlled pilot RCT. Women with chronic TMD were randomly assigned to receive neck motor control exercises, or a turned-off innocuous transcutaneous electrical nerve stimulation (i.e. placebo). Both groups received 12 sessions of treatment in an 8 week-period. The main outcome was pain intensity measured by a Visual Analogue Scale (VAS). Secondary outcomes were neck performance measured with the Craniocervical Flexion Test (CCFT), maximal neck flexor voluntary contraction and jaw disability. Outcomes were measured at baseline, after 8 weeks of treatment, and 4 months after treatment ends.

Results: Currently, 19 participants have participated in our study; 13 individuals received the placebo arm and 6 individuals received the neck motor control training using visual feedback (MCTF). Changes pre-post treatment on current pain intensity indicated that subjects receiving neck exercises have reduced pain by about 2.85 cm on the VAS, which can be considered a clinically meaningful change.10 Participants in the placebo group had a change of 2.0 cm. Participants in the intervention group showed important improvements after the exercise training in neck muscular performance (CCFT) (31.7 points), maximal neck strength (7.6 Newtons) and improved endurance of the extensor muscles (46.79 seconds). In contrast, the placebo group demonstrated a decreased neck muscular performance with -28 points on the CCFT and barely any improvement on the maximal neck strength.

Conclusions: Our preliminary results are promising and encourage further investigation using a larger sample of women experiencing chronic jaw pain. Findings from this study will also help develop treatment strategies for subjects with TMD as well as providing further insight about possible treatment options for similar musculoskeletal chronic pain disorders.

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Abstract #:	126
Presenter:	Muna Mohamed
Supervisor:	Hartling, Lisa
Title:	Using Facebook to conduct research with the Somali community during a pandemic: lessons learned for stakeholder engagement

Authors: Mohamed M[1], Elliott SA[1], Wright KS[1], Scott SD[2], Hartling L[1]

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[2]Translating Evidence in Child Health to enhance Outcomes (ECHO), Faculty of Nursing, University of Alberta

Theme: Knowledge translation and decision-making

Background: Our knowledge translation (KT) tools provide parents with information about common acute childhood illnesses, and when to contact emergency services. While we created these tools with parent input, it is unclear if they are useful for different populations including specific immigrant and refugee groups. Our objective was to understand if our KT tools (in their current form) are useful for parents and caregivers in the Somali community, and what adaptations could improve their usability. Additionally, in response to social distancing requirements in place due to the COVID 19 pandemic, we evaluated the use of a virtual social platform to remotely connect with Somali parents and caregivers.

Methods: A private Facebook group was created where participants were able to view the KT tools, provide feedback via Redcap surveys, and engage in group discussions about tool usability and format preferences. To qualify for the study, we required that participants were: either immigrants or refugees from Somalia, the parent or caregiver of a child under the age of 18, and able to read and write Somali. All study materials were translated and the Facebook group was set up in Somali. Participants were asked to view and evaluate four KT tools that varied in format and addressed different child health conditions; which included an ebook (Bronchiolitis), whiteboard animation videos (Croup & Visiting the ED), and an interactive infographic (Fever).

Results: Recruitment and data collection is underway; to date we have recruited 12 male participants. Initially we faced difficulty with recruitment, despite use of a snowball sampling approach. Reaching out to the Somali community, a vulnerable immigrant and refugee population, during a pandemic highlighted nuances of engaging with this group. For example, workers from relevant community organizations identified that the Somali community values in-person rapport building to create trust between families and researchers. However, restrictions in place due to the pandemic limited our in-person engagement activities and reduced our ability to personally connect with potential participants. We believed Facebook would provide a user-friendly platform to meaningfully engage with participants in a familiar and secure setting.

Conclusion: Engaging with the Somali community during a pandemic has been challenging. Our experience suggests that Facebook could be a feasible platform to engage with the Somali community, as it is a platform people already use with established networks. However, early engagement and personal interactions are essential for building trust and rapport to facilitate online research participation.

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Abstract #: 111
Presenter: Chelsea Morin
Supervisor: Saleh, Abdullah
Title: Developing a scoring tool for earlier diagnosis of childhood intussusception
Authors: Abdullah Saleh

Chelsea Morin
Theme: Children's health and well-being

Developing a scoring tool for earlier diagnosis of childhood intussusception

Introduction

Intussusception, the telescoping of a proximal segment of bowel into a distal segment of bowel is a common cause of acute abdominal pain in children and infants. In developed nations, diagnosis is made through imaging, typically using radiograph or ultrasound. Developing countries may not always have the tools readily available to use imaging to diagnose intussusception. This often leads to delayed diagnosis and treatment which is associated with higher morbidity and mortality. Our goal is to create a highly specific and sensitive clinical tool, using history and physical exam alone, to diagnose intussusception.

Methods

We completed a retrospective chart review of 179 patients at the Stollery Children's Hospital between 2007 and 2017 who had any of a diagnosis of intussusception, imaging done for "query intussusception", or a surgery performed for intussusception. The emergency records, admission notes, and imaging were reviewed for each patient and the diagnosis of intussusception or "other" was verified. The following data was then extracted: epidemiological factors including date of presentation, date of birth, and gender; history factors including presence or absence of emesis/bilious emesis, irritability and whether it was intermittent, presence of abdominal pain, recent/current viral illness, bloody stools, and diarrhea; and physical exam findings including lethargy, presence/absence of bowel sounds, abdominal distention, abdominal mass, and abdominal tenderness.

Results

We are currently working with a statistician to analyze the data and determine if there is a correlation between any of the epidemiological, history, or physical exam variables and a diagnosis of intussusception. On initial analysis (not yet validated by our statistician), chi squared testing showed a statistical difference in patients with an abdominal mass versus those without an abdominal mass diagnosed with intussusception ($p=0.001$) as well as in patients with lethargy on examination versus those without lethargy on examination ($P=0.00009$).

Conclusion

It is too early to determine whether it will be possible to create a tool to diagnose intussusception without use of abdominal imaging. If we are successful in creating such a tool, a prospective study will be necessary to validate the tool in clinical practice.

Funded By: WCHRI

Abstract #:	110
Presenter:	Sarah Morin
Supervisor:	Chui, Linda W
Title:	Evaluating the sensitivity of multiplex molecular panels in detecting Clostridioides difficile in children
Authors:	Sarah Morin, Brendon Parsons, Colin Lloyd, Stephen Freedman, Bonita Lee, Xiao-Li Pang, and Linda Chui on behalf of the APPETITE team
Theme:	Children's health and well-being

Enteric bacterial pathogens - bacteria that cause intestinal illnesses like hamburger disease, typhoid fever, and cholera can cause high mortality rate especially in children. Due to their underdeveloped immune systems, newborns and young children can easily get sick. Fortunately, many respond in a timely manner to appropriate treatment - such as antibiotics that target the specific bacteria. However, most enteric illnesses present with vomiting and/or diarrhea as the primary symptoms, which can be a challenge in identifying the precise causal agent. Therefore, the need for a rapid diagnostic method has catalyzed a shift from laborious and time-consuming conventional culture methods to multiplex molecular platforms targeting multiple different pathogens with a turn around time of reporting within hours. The Luminex xTAG Gastrointestinal Pathogen Panel (GPP) can simultaneously identify nine different bacterial targets, including disease-causing bacteria commonly found in the stools, such as Salmonella, Shiga toxin-producing Escherichia coli (STEC), Campylobacter, and Shigella. However, this particular panel has a potential major drawback for generating false-positives and false-negative results for the Salmonella target, as shown in one recent publication. More sensitive testing can help mitigate inappropriate treatment, which can also have devastating effects on young children. For example, unnecessary antibiotic use may worsen a child's symptoms and/or give rise to antibiotic-resistant "superbugs".

The purpose of the study was to evaluate the sensitivity of the Luminex xTAG GPP assay for its detection of Clostridioides difficile toxin genes on stools collected by the Alberta Provincial Pediatric EnTeric Infection Team (APPETITE). C. difficile was chosen for this project as it was found in abundance (15% of symptomatic children and 12% of asymptomatic children) in the cohort studied by APPETITE, thus providing a large sample size. The bacterial load of each sample was quantified using an in-house real-time polymerase chain reaction assay. This data was compared to the results from the Luminex xTAG GPP and stool culture, the latter of which remains the gold standard method of diagnosis. Of 361 samples that were positive according to the Luminex, 24 (6.65%) were culture-negative, 8 of which were also negative according to our in-house real-time PCR assay. Of 2703 samples that were negative based on the Luminex, 127 (4.70%) were positive for one or both C. difficile gene targets. Culture has yet to be performed on this second cohort of samples to confirm whether these are false-negatives.

The discordance between these diagnostic methods displays the challenge of assessing a patient's disease. Although molecular assays are more efficient, it is paramount that diagnostic laboratories are aware of their limitations in detecting pathogenic bacteria.

Funded By: Women & Children's Health Research Institute Summer Student Award (WCHRI) and Alberta Innovates Summer Studentship Award

women & children's health research institute

Abstract #:	112
Presenter:	Peris Munyaka
Supervisor:	Willing, Benjamin
Title:	Prevotella in the context of maternal vaccine response and offspring protection against group B streptococcus infection
Authors:	Peris M. Munyaka, Benjamin P. Willing
Theme:	Children's health and well-being

Group B Streptococcus (GBS) is the leading cause of stillbirths, neonatal sepsis, pneumonia and meningitis. Carriage of GBS in the female genital tract is common, but most women lack antibodies to these organisms, remaining susceptible to infection. The use of intrapartum antibiotic prophylaxis is not fully protective and may result to negative impacts. To date, there are no approved vaccines for GBS, although research is ongoing. We are looking for ways to make GBS vaccines more effective through manipulation of the gut microbiota as we found positive correlations between several species of Prevotella and vaccine-specific antibodies. Our aim is therefore to test whether enriching Prevotella in the gut of pregnant mice will enhance maternal GBS vaccine response and increase transfer of protective antibodies to the offspring.

Female gnotobiotic mice at 8 weeks of age (n = 12) will be vaccinated intraperitoneally with a potential GBS vaccine and the mice will be bred immediately after immunization. Another set of 12 mice will receive vehicle as negative control. Half of the vaccinated mice will receive a daily dose of colony forming units of Prevotella (composed of 5 Prevotella isolates generated in our lab that represent species that have been positively correlated with vaccine specific antibodies) via oral gavage throughout the duration of pregnancy, whereas the other half will receive media control containing no live bacteria. The control mice will be treated in a similar manner. Pups (~12 per group) will be challenged with an inoculum of GBS strains present in the vaccine used. The challenge dose will be administered intraperitoneally in a total of 0.05 ml. The number of pups that survive GBS infection will be assessed at 24, 48, and 72 hours after challenge and survival data will be compared using Fisher's test.

We expect that the pregnant mice receiving both GBS vaccine and Prevotella dosing will have elevated antibodies against GBS, compared to those without the Prevotella. Pups from these mice are also expected to exhibit the highest survival rate following the GBS challenge. The study will provide a unique perspective into alternative and safe ways of enhancing maternal, fetal and neonatal protection against GBS, as opposed to the use of antibiotics.

Funded By: WCHRI postdoctoral fellowship - through the Stollery Children's Hospital Foundation.

NSERC Accelerator grant.

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Abstract #: 84
Presenter: Rukhmani Narayanamurthy
Supervisor: Unsworth, Larry
Title: Developing a "cooling chamber" to induce hypothermia in neonatal rats with hypoxic-ischemic brain injury
Authors: Rukhmani Narayanamurthy, Jung-Lynn Jonathan Yang, Edward A Armstrong, Jerome Y Yager, Larry D Unsworth
Theme: Children's health and well-being

The interruption of oxygen and blood supply to the offspring around the time of birth may cause hypoxic-ischemic damage to the newborn's brain and is a risk factor for lifelong neurological impairments and death. Currently, therapeutic hypothermia, the cooling of the infant's head or entire body to 33-35°C for 72 h, is the only treatment to curb the extent of brain damage. However, approximately half of the infants receiving hypothermia will have died or suffer long-term neurological impairments by 12-24 months. The incomplete neuroprotection offered by hypothermia necessitates the exploration of potential pharmacological interventions. The systemic administration of drugs may face challenges due to the drugs' low bioavailability and side-effects. To address these concerns, we propose to combine hypothermia with a novel drug delivery system based on self-assembling peptides that can reversibly transition between nanoparticle and soluble conformations according to temperature. Drugs can be loaded into nanoparticles such that localized hypothermia to the infant's head could induce nanoparticle dissolution and release of drugs to the brain in a targeted, controlled manner. Our goal is to create a device for selective head cooling and to establish the biocompatibility of the self-assembling polypeptide system.

We will use a neonatal rat model of hypoxic-ischemic brain damage subject to hypothermia of the head in a "cooling chamber". The chamber consists of a syringe in which cooled water at a steady state temperature of 28°C will circulate through a coil of tubing fitted onto the rat's head. The objective is to lower the temperature of the brain to 31°C, monitored using a brain thermistor. The rectal temperature, indicative of the core body temperature, will be monitored to ensure that a temperature differential is maintained between the head and the body. The temperature differential will control the dissolution of the self-assembling peptide nanoparticles. Both male and female littermates at postnatal day 7, that are subjected to hypoxic-ischemic brain damage, will be placed in cooling chambers to assess the combinatorial effect of hypothermia and self-assembling peptide nanoparticles that will be administered via intraperitoneal injections. The biocompatibility of the self-assembling peptides will be assessed by immunohistochemical staining of coronal brain sections for markers of apoptosis and microglial activation. The establishment of the cooling chamber and drug delivery platform will set the foundation for future pharmacological pre-clinical studies on neonatal brain damage.

Keywords: Hypoxic-ischemia, hypothermia, self-assembling peptides, neonatal, nanoparticles.

Funded By: CIHR, Maternal and Children Health Scholarship Program

Abstract #:	104
Presenter:	Jasmine Nathoo
Supervisor:	Yohani, Sophie
Title:	Conducting community-based research with Syrian female youth transitioning from high school to post-secondary settings
Authors:	Jasmine A. Nathoo, Sophie Yohani
Theme:	Children's health and well-being

Since 2015, Canada has welcomed almost 45,000 Syrian refugees due to the ongoing conflict in Syria. About half of those arriving are children and youth. Upon resettlement in Canada, Syrian youth are faced with unique integration challenges in social, academic, linguistic, and cultural domains. These challenges are particularly apparent in the school setting, often youth's primary point of contact with Canadian society. Challenges are also distinct and often more pronounced for girls. Early research with Syrian youth suggests that many are highly motivated students with aspirations to attend post-secondary institutions, and research with previously resettled refugee groups points to the benefits of post-secondary schooling for refugee youth. For instance, attending and completing post-secondary is associated with enhanced economic and employment opportunities and civic participation. For females specifically, post-secondary attendance is associated with reductions in intergenerational poverty and improved family well-being. However, this existing research also demonstrates a gap between post-secondary aspirations and post-secondary attendance rates, suggesting that many refugee youth who hope to pursue post-secondary studies do not go on to do so. It remains unclear if this trend also applies to Syrian youth. Currently, little is known about the long-term challenges and needs of female youth from Syria integrating into Canadian schools.

This presentation will describe a research project designed to explore these gaps. This community-based participatory research (CBPR) study will be conducted to address the question: what are the challenges, needs, and strengths of Syrian female youth who are transitioning from high school to post-secondary institutions in Canada? The presentation will focus on the utilization of CBPR methodology along with an arts-based data collection method (Photovoice). The Photovoice method has been used effectively to engage refugee youth in the research process, enhance understanding of their needs, build capacity within the community, and facilitate social change. This presentation will explore the methodological and ethical considerations of designing a community-engaged research project with refugee youth. It will also detail the methodological and ethical considerations of arts-based photography research with youth. Finally, the presentation will also explore the ways in which the project has been adapted to be conducted in an online virtual space.

Funded By: Social Sciences and Humanities Research Council; Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

Abstract #:	158
Presenter:	Jasmine Nguyen
Supervisor:	Riddell, Meghan
Title:	The role of atypical protein kinase c in regulation of endocytosis in the placental epithelium
Authors:	Jasmine Nguyen, Khushali Patel, Sumaiyah Shaha, Meghan Riddell
Theme:	Pregnancy and developmental trajectories

Introduction

The placenta is a vital organ that develops during pregnancy and plays an essential role in delivering nutrients and removing waste products from the growing fetus. This exchange of materials occurs at the placenta's epithelium, which makes up the outer surface of the placenta and is composed of a single, giant, multinucleated epithelial cell called the syncytiotrophoblast (ST). Due to its function as the primary interface between mother and fetus, disturbances in ST homeostasis is a key feature of many placental dysfunctions that can result in major pregnancy complications, such as preeclampsia and intrauterine growth restriction. Because endocytosis is the process by which a variety of substances are internalized by cells, endocytic trafficking must have critical contributions to proper ST functioning, however, data examining endocytosis in the ST is currently limited. Additionally, while atypical protein kinase C (aPKC) has been well-documented to affect endocytosis in many cell types and model systems, there is currently no literature examining the role of aPKC in regulating endocytosis in the ST despite its expression in the syncytium. Therefore, the aim of this project is to examine the potential role of aPKC in ST endocytosis and identify the molecular mechanisms that govern endocytic trafficking in the placenta.

Methods

A choriocarcinoma trophoblastic cell line (BeWo) and first trimester placental explants were used to examine endocytic trafficking in the placenta after treatment with an aPKC pseudo-substrate inhibitor. Conditions and time points were optimized for an endocytosis assay with fluorescently labelled rhodamine-transferrin to mark clathrin-dependent endocytosis after serum-starvation for 30 minutes. Samples were then fixed and permeabilized before additional staining for E-cadherin and the apical cytoskeleton or nuclei. Imaging was done at 63x via confocal microscopy with endosome quantification using Volocity.

Results

Through the optimization of this assay, our preliminary data suggests that treatment with aPKC pseudo-substrate inhibitor decreases the endocytic trafficking of rhodamine-transferrin and may also disrupt the typical localization of E-cadherin in BeWo cells.

Conclusion

Future directions involve replicating these initial findings in placental explants for improved representation of in vivo conditions and use of siRNA targeting specific isoforms of aPKC to identify potential isoform-specific involvement in ST endocytic trafficking. This technique will be used to test further hypotheses regarding the regulation of endocytosis in the ST in response to different conditions or diseases. Understanding the molecular mechanism by which endocytosis occurs under normal conditions in the placenta will allow us to better identify potential causes for placental dysfunction during pregnancy and identify novel targets for treatment.

Funded By: the Stollery Children's Hospital Foundation, the Royal Alexandra Hospital Foundation, and supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute

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Abstract #:	57
Presenter:	Kim-Cuong Nguyen
Supervisor:	Le, Lawrence H
Title:	Delineation of Adolescent Alveolar Bone in Intraoral Ultrasonograph with Machine Learning
Authors:	Kim-Cuong T. Nguyen, Dat Q. Duong, Fabiana T. Almeida, Paul W. Major, Neelambar R. Kaipatur, Thanh-Tu Pham, Edmond H.M. Lou, Michelle Noga, Kumaradevan Punithakumar, and Lawrence H. Le
Theme:	Children's health and well-being

Introduction: Crowding and misalignment of teeth, known as malocclusion, and periodontal disease are two of the three most common dental anomalies and can cause psycho-social problems in children. Severe malocclusion can lead to oral function issues such as difficulty in jaw movement, chewing, speech, and high susceptibility to periodontal diseases which can cause adolescents' tooth loss. Alveolar bone is one of the important periodontal structures to support and hold the teeth. Accurate assessment of alveolar bone level is essential for diagnosis of periodontal disease and orthodontic treatment planning. The evaluation of alveolar bone is typically performed using two-dimensional (2D) intraoral radiography on the mesial and distal surfaces, but not on the facial and lingual surfaces of the teeth. This limitation can be overcome by using cone-beam computed tomography (CBCT), which renders images without tissue superposition. Due to high radiation doses, there is a lack of evidence to support the use of CBCT as a routine and standard method of dental diagnosis, particularly for pediatric patients, who are more vulnerable to radiation. The use of intra-oral ultrasound has received great attention recently due to the advantages of being non-invasive, non-ionizing radiation, portable, and low-cost imaging solution for initial and continuing dental diagnosis. However, the interpretation of alveolar bone in ultrasound images depends on observer's experience, which is a challenge for dental clinicians. This work aimed to automatically segment alveolar bone and locate the alveolar crest using machine learning (ML) approach for intra-oral ultrasound images.

Methods: Thirty adolescent patients (17 males and 13 females, aged 12-17 years), who underwent orthodontic treatment, were recruited and consented in Kaye Edmonton Dental Clinic. The data used for the present study were collected from a total of 51 mandibular and 59 maxillary central incisors. The scanning was performed at 20 MHz using a SonixTablet ultrasound scanner (Analogic, Vancouver, Canada). A subset of 10 unalike images for each tooth with the presence of alveolar bone was acquired and then the data was divided into three sets: training (700), validation (200), and testing (200). The training and validation sets were used to train and tune the ML model to automatically segment the alveolar bone. The alveolar bone crests were also identified on the labeled contours.

Results: Quantitative evaluations of over 200 images from the testing set compared to an expert clinician showed that the ML approach yielded an average Dice score of 85.3%, sensitivity of 88.5%, and specificity of 99.8%, respectively. Alveolar bone crests were also identified with a mean difference of 0.20 mm and excellent reliability (ICC ≥ 0.98) in less than a second.

Conclusion: This study demonstrated an application of ML to assist dental clinicians in the visualization of alveolar bone in ultrasound images. This can help improving the workflow efficiency and accuracy of diagnosis. Future study will involve different types of teeth of orthodontic, periodontal and healthy patients to allow for a more comprehensive assessment of the proposed ML algorithm.

Funded By: The study has been funded by the generous support of the Stollery Children's Hospital Foundation through Women & Children's Health Research Institute; Natural Sciences & Engineering Research Council of Canada; Alberta Innovates-Technology Futures Graduate studentship; and Canada-ASEAN Scholarship.

Abstract #: 113
Presenter: Alexandra Hudson Nicole Tyminski
Supervisor: Silverman, Jason
Title: Parenteral nutrition-associated cholestasis and growth pre- and post-SMOFlipid introduction in neonates and infants with intestinal failure in Edmonton
Authors: Alexandra S. Hudson*, MD HBSc; Nicole A. Tyminski*, MD BSc; Justine M. Turner, MBBS FRACP PhD; Jason A. Silverman, MD MSc FRCPC

*both authors contributed equally

Division of Pediatric Gastroenterology & Nutrition, University of Alberta, Stollery Children's Hospital, Edmonton, Alberta
Theme: Children's health and well-being

Background: SMOFlipid was made available for use in pediatric parenteral nutrition (PN) in Canada, since 2013. While it is thought to have anti-cholestatic properties, data remains limited, including growth outcomes. We aimed to determine if infants receiving SMOFlipid had significantly lower rates of PN-associated cholestasis (PNAC) and improved growth compared to conventional Intralipid.

Methods: We conducted a retrospective cohort analysis. Patients (≤1 year old) with intestinal failure (PN ≥6 weeks) at the Stollery Children's and Royal Alexander hospitals (2010-2018) were identified. Non-parametric tests were used to compare PNAC (conjugated bilirubin (CB) ≥34 umol/L) and growth.

Results: 1777 patients were reviewed; 36 infants (21 SMOFlipid, 15 Intralipid) were included. There were no significant differences in SMOFlipid vs. Intralipid median CB at baseline (29 vs. 6.5 umol/L), six weeks (9 vs. 5 umol/L), PN cessation (3 vs. 4 umol/L), or peak CB (29 vs. 16umol/L). At PN cessation, the proportion of PNAC decreased from 37% to 16% for SMOFlipid and remained stable from 8% to 10% for Intralipid. There were no differences in growth z-scores ($p>0.05$) in either the SMOFlipid or Intralipid group. There was a non-significant difference with higher head circumference z-scores given SMOFlipid compared to Intralipid at both six weeks (-0.93 vs. -2.8) and three months (-0.41 vs. -2.3) ($p>0.05$).

Conclusions: Despite significantly longer PN duration and a trend towards higher baseline CB, overall rates of PNAC decreased with use of SMOFlipid. Non-significant improvement in head circumferences and less time spent in low lipid dose ranges raises the possibility that either the better calorie delivery or fatty acid composition of SMOFlipid may support neurodevelopment, although future research is needed.

Funded By: We would like to thank the Women & Children's Health Research Institute for their funding and support.

Abstract #: 73
Presenter: Chunpeng Nie
Supervisor: Graf, Daniel
Title: BMP-Mediated Metabolic Shifts Are Associated With Mesenchymal Cell Differentiation
Authors: Chunpeng Nie, Pranidhi Baddam, Haiming Lin, Daniel Young, Antoine Dufour, Daniel Graf
Theme: Children's health and well-being

Background: Disorders of mesenchymal tissues such as osteoarthritis have been associated with changes in energy metabolism. Bone Morphogenetic Proteins (BMPs) are signalling proteins controlling mesenchymal cell differentiation and their involvement in energy metabolism has become a major point of interest. Here, we compared the action of BMPs in three mesenchymal tissues: adipose, cartilage, and bone.

Hypothesis: Specific BMPs regulate discrete but common aspects of energy metabolism in all mesenchymal lineages.

Methods and Results: We conducted a scoping review on the role of BMPs in adipose tissue, cartilage, and bone. Searching for "bmp metabolism" and "adipocyte", "chondrocyte", or "osteoblast", we identified 13, 34, and 80 articles respectively. Commonalities were found between BMP-dependent adipocyte and chondrocyte differentiation. BMP2 was associated with increased glycolysis, whereas BMP7 increased oxidative phosphorylation in both chondrocytes and adipocytes. Although there is some evidence that BMPs regulate energy metabolism in osteoblasts, details remained unclear partially due to the heterogeneity of bone tissue. Relating this with our lab results, we compared cartilage from the temporomandibular joint (TMJ) of BMP7-deficient or control mice. A quantitative proteomics screen identified changes to mitochondrial energy metabolism. Indeed, the downregulation of Cox5a and UCP1 in 2- and 4-week-old BMP7-deficient TMJ cartilage was confirmed by immunohistochemistry.

Conclusion: Literature evidence suggests conserved roles of BMPs in the regulation of energy metabolism in different mesenchymal cell types. BMP7 induces similar shifts in metabolic function in chondrocytes and adipocytes. Thus, BMP signalling plays a critical role in mediating differences in energy metabolism associated with functional properties of cartilage and bone.

Funded By:

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Stollery Children's Hospital Foundation

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Abstract #:	10
Presenter:	Ronan Noble
Supervisor:	Bourque, Stephane
Title:	Perinatal Iron Deficiency Causes Dysfunction in Hearts of Neonatal Offspring
Authors:	Ronan Noble, Jason Li, Andrew Woodman, Richard Mah, Ferrante Gragasin, Luke Eckersley, Stephane Bourque
Theme:	Children's health and well-being

Introduction: Iron deficiency (ID) is the most common nutritional deficiency worldwide, and affects an estimated 39% of pregnant women worldwide. ID causes organ-specific patterns of hypoxia, mitochondrial dysfunction and oxidative stress in the fetus, however the effects on offspring heart function have not been studied. By virtue of iron's role in ensuring oxygen delivery to the body, we sought to determine how reduced oxygen carrying capacity associated with anemia during pregnancy and shortly after birth would affect heart function.

Methods: Sprague Dawley rats were fed an iron-restricted or iron-replete diet (control) 2 weeks prior to and throughout pregnancy. After birth, all dams were fed an iron-replete diet. On postnatal day (PD) 4, 14, and 28, male and female offspring cardiac function was assessed by echocardiography.

Results: Maternal iron restriction throughout pregnancy reduced maternal hemoglobin (-31%; P<0.001), offspring Hb was reduced from birth through PD14 (-48%, P<0.001; -25%, P=0.013) and recovered by PD28. ID offspring exhibited growth restriction (-19%; P<0.001), which persisted through PD28 (-30%; P<0.001). When normalized to bodyweight, ID pups had increased heart weights at PD4 (+60%; P<0.001) and PD14 (+72%; P<0.001) and diastolic chamber volumes (+31%, P=0.005; +28%, P=0.056; respectively), and these values recovered by PD28. After adjusting for body weight, ID offspring had reduced ejection fraction at PD4 (-15%; P=0.024) and PD14 (-19%; P=0.004), which normalize by PD28. These changes corresponded to a reduction in oxygen delivery on PD4 (-41%; P<0.001) and PD14 (-31%; P=0.05), and recovered completely by PD28. Finally, there were no changes in any pulmonary or other diastolic parameters measured.

Conclusion: Perinatal ID causes functional changes in the neonatal heart as well as a global increase in relative heart size. With no corresponding increase in cardiac output, these results indicate a systolic dysfunction, which may reflect an inadequate or maladaptive compensation in the wake of perinatal anemia. These findings may have important implications for the short and long-term cardiac health of anemic babies.

Funded By: Women and Children's Health Research Institute, Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada

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Abstract #: 121
Presenter: Camille Noel
Supervisor: Cheung, Po-Yin
Title: Use of Low-dose Dexamethasone for Chronic Lung Disease in Extremely Preterm Infants: A Single-Center Retrospective Cohort Study

Authors: Camille Noel MD1, Po-Yin Cheung MBBS PhD1, Brenda Hiu Yan Law MD MSc1

1Department of Pediatrics, University of Alberta

Theme: Children's health and well-being

Introduction. Chronic lung disease of prematurity (CLD) is the most common major morbidity in extremely preterm infants. Its pathophysiology is multifactorial including lung inflammation. While postnatal use of corticosteroids may decrease lung inflammation, its use is controversial because of possible risks on neurodevelopment. Low-dose dexamethasone is currently used to facilitate extubation in selected ventilator-dependent infants, with considerable practice variations. We aimed to characterize the use of postnatal dexamethasone in extremely preterm infants with CLD and to identify predictors of extubation success (defined as no reintubation within 10 days).

Methods. A cohort of infants <29 weeks gestation, admitted to the Royal Alexandra Hospital Neonatal Intensive Care Unit (Edmonton, Canada) from 2010 to 2018, who received low-dose (0.89 mg/kg) dexamethasone for lung disease, were identified using a hospital pharmacy database. Hospital charts were then reviewed to identify patient demographics, clinical characteristics, timing and respiratory status at the time of the first dexamethasone treatment, respiratory/ventilator parameters before, during, and after each dexamethasone course, and short-term outcomes. To quantify respiratory disease severity and treatment response, oxygen saturation index (OSI) before and 48 hours after first dose of dexamethasone was calculated from fraction of inspired oxygen (FiO2), mean airway pressure (MAP) and oxygen saturation (SpO2) (OSI=FiO2xMAP/SpO2).

Results. Sixty-seven infants were identified (33 females, 49%; gestational age: median 24.6 (24.2-25.6) weeks; birth weight: median 710 (620-770) grams). Median age at start of dexamethasone was 32 (26-43) days with 64% started after 28 days. During the 24 hours before first dose of dexamethasone, median OSI was 10.0 (7.3-12.9) with a median FiO2 of 0.64 (0.53-0.92) and median MAP of 15 (12-17) cmH2O. Thirty-two infants (48%) were successfully extubated with their first course of dexamethasone; these patients had lower OSIs prior to treatment when compared to those who failed to extubate (8.5 vs 11.9, p=0.004; respectively). There was no difference in OSI change after 48 hours of treatment between the two groups (-3.8 vs -4.9, p=0.18). Thirteen infants (19%) received a second course of dexamethasone, with 7/13 (54%) successfully extubated. Seven (10%) died prior to discharge. Of the survivors, 34/60 (57%) developed severe CLD.

Conclusion. In this single-center cohort, low-dose dexamethasone was mostly given to extremely preterm infants with severe lung disease after 28 days, achieving less than 50% extubation success. Successfully extubated infants had less severe respiratory disease as evidenced by lower OSI. Further analysis may identify other predictors of extubation success with dexamethasone treatment.

Funded By: This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

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Abstract #:	142
Presenter:	Ana Paula Pagano
Supervisor:	Prado, Carla
Title:	Innovative approaches to the lack of evidence-based energy requirements for patients with ovarian cancer
Authors:	Ana Paula Pagano, Rajavel Elango, Michael B. Sawyer, Sunita Ghosh, Leah Gramlich, Michael Kolinsky, Carla M. Prado
Theme:	Lifelong women's health

Introduction: Malnutrition - a condition associated with low muscle mass - is common in ovarian cancer and is associated with poor outcomes and shortened survival. Malnutrition is often caused by energy or nutrient intake imbalances. Understanding energy metabolism is essential to provide adequate energy recommendations and help prevent or reverse malnutrition. To date, little is known about energy requirements of women with ovarian cancer and current guidelines are non-specific and not evidence-based. In this study, we aim to explore energy needs of women with ovarian cancer and their changes throughout cancer trajectory, including survivorship, using innovative approaches and techniques.

Research questions: Do energy requirements of women diagnosed with ovarian cancer change throughout the disease trajectory? What are key factors that impact energy metabolism during ovarian cancer? Do ovarian cancer survivors return to their baseline energy needs after they completed treatment (i.e. remission)?

Methods: This is an observational longitudinal clinical study with ambulatory women newly diagnosed with ovarian cancer (stages III-IV [n=36]) who will be receiving anti-cancer treatment at the Cross Cancer Institute, Edmonton, Canada. Participants will be invited to come to the Human Nutrition Research Unit (HNRU) at the University of Alberta to have their energy metabolism measured by sophisticated techniques at 3 timepoints during cancer trajectory: 1) within 30 days before or after starting treatment (baseline); 2) up to 30 days at the end of treatment; 3) up to 30 days post-treatment. Total energy expenditure (TEE), resting energy expenditure (REE), and physical activity levels will be measured in a free-living setting. TEE data will be obtained by doubly labeled water (DLW), with a 15-day urine sample collection. Although DLW is considered a state-of-the-art technique, it does not provide individual components of TEE. As such, REE will be assessed using a whole-body calorimetry unit, and activity energy expenditure using Actical accelerometers (for 1 week at 3 timepoints, concurrently with DLW assessments). Changes in energy metabolism will be studied in light of changes in body composition (Dual energy X-ray absorptiometry). Three-day food records will be collected within the DLW period as a marker of food intake (ESHA-Food Processor v.11.1 [Salem OR, USA]). Laboratory results will be obtained from patient records to further define associations with energy metabolism.

Potential knowledge gained: We will develop an in-depth understanding on energy metabolism of patients with ovarian cancer. To our knowledge, this is the first study investigating whole body energy metabolism in ovarian cancer and the first using more accurate techniques. Our results will provide a unique understanding of energy needs during and beyond ovarian cancer, highlighting the need for adjusting current non-specific guidelines to true patient needs. This knowledge can substantially impact the nutrition care process, optimize nutrition prescriptions and improve patient clinical outcomes.

Funded By: This research has been funded by generous supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute and a CIHR Operating Grant.

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Abstract #:	65
Presenter:	Sai Panidarapu
Supervisor:	Lopaschuk, Gary D.
Title:	Maturation of Cardiac Ketone Oxidation in the Human Newborn
Authors:	Sai Panidarapu, Kim Ho, Qutuba Karwi, Liyan Zhang, Matthew Hodapp, Gary Lopaschuk
Theme:	Children's health and well-being

Introduction:

Neonatal heart failure is a chronic condition in which the heart inadequately supplies blood to the body during the newborn period. In both adults and infants, heart failure is associated with impaired cardiac energy metabolism, that can lead to an "energy starved" heart. Recent studies in adults suggest that supplying the failing heart with ketones-a substrate used to produce ATP-can provide the heart with an extra source of energy. However, it is not clear if this is a viable strategy in newborn heart failure, since very little is known about the maturation of ketone oxidation in the newborn heart. We therefore examined how enzymes of ketone oxidation mature in the human newborn heart.

Methods:

Human heart tissue samples were obtained from male and female patients that were undergoing surgical interventions for congenital heart defects. Biopsied cardiac tissue samples were isolated with parental consent, and frozen; samples collected ranged from newborn to four years of age. As such, an age dependent study was conducted with the following groups: (1-20 days), (21-100 days), (101-200 days), (201 days-1year), (1-2 years), (2-3 years), and (<4 years). Using these groups, western blotting was carried out to probe for protein expression of SCOT (succinyl-CoA:3-oxoacid CoA transferase) and BDH1 (β-hydroxybutyrate dehydrogenase) - integral enzymes of the ketone oxidation pathway.

Results:

Over the course of 3 years, the protein expression of SCOT (the rate-limiting enzyme of ketone oxidation) increased with age, indicative of an age-dependant maturation of ketone oxidation. In a similar fashion, the protein expression of BDH1 was low in the immediate newborn period (1-20 days), but did increase slightly from 21-100 days, and increased further throughout the next 2.5 years.

Conclusion:

The capacity for ketone oxidation is low in the immediate newborn period but does increase with age. As a result, ketones may not be ideal in providing extra energy to the failing human heart in the immediate newborn period.

Funded By: WCHRI Summer Studentship Award, CIHR Foundation Grant

Abstract #: 127
Presenter: Rashmi Panigrahi
Supervisor: Glover, Mark
Title: Insight into the high-resolution structural model of BRCA1-BARD1 RING heterodimer to probe missense variants for breast cancer risk assessment
Authors: Rashmi Panigrahi, Ross Edwards, Sean Tavitgan, Mark Glover
Theme: Lifelong women's health

Introduction: Breast and ovarian cancer is a public health problem of critical proportions that affects women worldwide. Inherited germline mutations in the tumor suppressor gene BRCA1 predispose individuals to early onset forms of these cancers. Loss of BRCA1 function in cells results in hypersensitivity to DNA damage and accumulation of chromosomal aberrations associated with cancer development. These effects are likely due to the central role that BRCA1 plays in the homologous recombination (HR) pathway of DNA double strand break repair. Together with our collaborator Dr. Sean Tavitgan, University of Utah, we are working to understand how missense substitutions in BRCA1 and its partner protein, BARD1, impact protein structure and function. The majority of these substitutions are currently have insufficient clinical data to provide cancer risk assessment. This collaborative project funded by NIH, seeks to develop a sequence variant classification model built on multispecies sequence alignment together with structural modeling of missense variants that will provide a better risk assessment for variants that are currently unclassified. One of the genes of interest for this project is the RING domain of BRCA1. For optimization of the sequence variant classification model, an intricate understanding the three dimensional structure is crucial. As a part of the collaborative project, the Glover lab aims at providing structural insight into the RING domain of BRCA1. Cellular BRCA1 forms a heterodimer with BRCA1-associated RING domain 1 (BARD1) which possess an ubiquitin ligase (E3) function which has been shown to be crucial for the prevention of breast and ovarian cancer development. A high resolution three-dimensional structure of the human BRCA1-BARD1 RING domain heterodimer is not available to provide a basis for structural modelling of missense variants.

Methods: The heterodimer has been recombinantly coexpressed and the purification protocols have been optimized. Size exclusion chromatography assisted with multi-angle light scattering suggest that the protein product purified is an intact heterodimer in the optimized buffer condition. Art Robbins robot has been used to screen a myriad of crystallization conditions. Recently crystals have been observed in a couple of conditions and have tested positive for protein using in house diffractometer.

Results: This study provides the first high-resolution three dimensional structure of the heterodimer using X-ray crystallography. The structure will be used to model various missense substitutions in the BRCA1 RING domain identified as pathogenic alleles in HR genes. Mutations causing loss of three dimensional structure or function are damaging and will be identified using modelling approach.

Conclusion: We have successfully obtained crystals of BRCA1-BARD1 RING heterodimer. These protein crystals are being used for obtaining the first high resolution, three dimensional structure of the complex. Next, the BRCA1 missense variants will be modelled using this structure. This structure based analysis will highlight the role of these mutations leading to breast and ovarian cancer.

Funding: Canadian Institutes of Health Research (CIHR), National Institutes of Health (NIH)

Funded By: Funding: Canadian Institutes of Health Research (CIHR), National Institutes of Health (NIH)

Abstract #:	159
Presenter:	Mazhar Pasha
Supervisor:	Davidge, Sandra
Title:	Maternal aging impacts vascular adaptations to pregnancy
Authors:	Mazhar Pasha, Raven Kirschenman, Amy Wooldridge, Floor Spaans, Sandra T. Davidge, Christy- Lynn Cooke
Theme:	Pregnancy and developmental trajectories

Introduction

Advanced maternal age (≥35 years) increases the risk of pregnancy complications, which may be due to poor cardiovascular adaptations to pregnancy in aged women. Aging is associated with vascular stiffness and endothelial dysfunction. Enhanced oxidative stress with reduced nitric oxide (NO) bioavailability and increased activity of vasoconstrictors, such as endothelin-1 (ET-1), may contribute to these aging-related vascular abnormalities. However, whether these vascular changes linked to aging affect vascular adaptations during pregnancy, and contribute to endothelial dysfunction, remains unknown. We hypothesize that vascular adaptations are impaired by maternal aging, due to altered NO-and ET-1-dependent mechanisms.

Methods

We used non-pregnant and pregnant young (4 months of age) and aged rats (9.5 months of age; equivalent to ~35 years of human age); n=6-10/group. Blood pressure was measured (CODA tail-cuff system) on gestational day 20 (term=22 days), or in aged matched non-pregnant rats, and rats were euthanized. Mesenteric arteries were isolated to assess vascular function ex vivo using wire myography. Endothelium-dependent relaxation to methacholine (MCh) was assessed and L-NAME (pan nitric oxide [NO] synthase inhibitor), or apocynin (inhibitor of NADPH oxidase; an enzyme that induces oxidative stress) were used to assess the contribution of those pathways. Vasoconstriction responses to big-endothelin-1 (bET-1) and ET-1 were evaluated to assess constrictor capacity; CGS (an inhibitor of endothelin converting enzyme: ECE) was used to measure ECE contribution. Data were analyzed by two-way ANOVA with Sidak's post-test, $p<0.05$ was considered significant.

Results

Mean arterial blood pressure (MAP) was highest in aged non-pregnant rats ($p=0.025$). Interestingly, MAP in aged pregnant rats was similar to MAP in both the young groups. Mch-induced vasodilation responses were not different between groups. However, pretreatment with L-NAME (NO contribution to vasodilation) decreased maximum vasodilation in young ($p=0.027$) and aged pregnant rats ($p=0.001$) and decreased MCh sensitivity in young nonpregnant rats ($p<0.0001$), without effects in aged non-pregnant rats. Pretreatment with apocynin (to assess NADPH oxidase activity) increased MCh sensitivity in aged non-pregnant rats only ($p=0.029$). Vasoconstriction to bET-1 did not change during pregnancy but were higher in aged versus young pregnant rats ($p=0.009$); while ET-1 responses were similar between groups. The contribution of ECEs in converting bigET-1 to ET-1 (control vs. CGS curve) was higher in aged pregnant ($p=0.012$) and non-pregnant rats ($p=0.015$), compared to young controls.

Conclusion

A higher MAP in aged non-pregnant rats may be due to a constrictive systemic vasculature. The lower MAP and enhanced NO-mediated vasodilation in aged pregnant rats may reflect adaptations to maintain pregnancy. In contrast, pregnancy in aged rats did not alter other aging-related effects, like the higher bET-1 responses and ECE contribution, highlighting the complex cardiovascular adaptations required for a successful pregnancy in aged rats. Overall, advanced age is associated with altered cardiovascular function in non-pregnant rats, while these changes appear to be compensated during pregnancy

Funded By: Mazhar Pasha is supported by WCHRI Graduate Studentship award. This study was funded by a CIHR Foundation grant and by the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women through WCHRI (CLC-Innovation Grant).

Abstract #: 143
Presenter: Tautvydas Paskevicius
Supervisor: Michalak, Marek
Title: A new protein complex in multiple sclerosis
Authors: Tautvydas Paskevicius, Joanna Jung, Paul Eggleton, Myriam Pujol, Luis B. Agellon and Marek Michalak
Theme: Lifelong women's health

Multiple Sclerosis (MS) is a debilitating disease of myelin that affects over 2.5 million people worldwide, with 100,000 individuals afflicted in Canada. Canada has the highest rate of MS in the world. Most importantly, MS is universally found to be more prevalent in females than in males. MS is most frequently diagnosed in pre-menopausal women with symptoms including weakness, imbalance, fatigue and depression. Women with MS face several gender-specific complications as they have to deal with the effects of MS on hormones, menstruation, pregnancy, childbirth, and menopause. It is well established that multiple sclerosis is most commonly diagnosed in adults at their age between 20 to 50, however more and more children and teenagers are also diagnosed with this condition. In addition to that, it is estimated that a large population of kids with MS have not been diagnosed yet. The disease has a significant impact on children affecting their thinking, emotions, self-image, schoolwork and relationships with others. Unfortunately, there is still no defined cause(s) or cure(s) for the disease, and the development of therapies to slow down the progression of the disease remain challenging. We found that MS patients have unusually high abundance of calnexin (Canx; an endoplasmic reticulum (ER) membrane chaperone) and fatty acid binding protein 5 (Fabp5, a cytoplasmic lipid binding protein) in blood-brain barrier (BBB) endothelial cells. The loss of either Canx or Fabp5 in mice confers resistance to experimental autoimmune encephalomyelitis (EAE), the animal model of MS. Canx-/- mice resistant to EAE is attributed to the cytoplasmic C-tail of Canx. We discovered that Fabp5 interacts with Canx cytoplasmic tail and co-localizes with Canx in brain endothelial cells. We identified that resistance to EAE is due to inhibition of trans-endothelial T-cell migration across Canx-/- or Fabp5-/- brain endothelial cells. Therefore, this suggests the amount of Canx and Fabp5 present may be important in controlling the function of the blood-brain barrier by preventing T-cell infiltration into the brain. Thus, deciphering our proposed link between two ER proteins and MS pathogenesis would greatly contribute towards improving health outcomes for female and pediatric patients that suffer from MS.

Funded By: WCHRI graduate studentship; CIHR

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Abstract #:	160
Presenter:	Khushali Patel
Supervisor:	Riddell, Meghan
Title:	Role of Atypical protein kinase C isoform in regulating placental microvilli
Authors:	Khushali Patel, Ashley Zubkowski, Meghan Riddell
Theme:	Pregnancy and developmental trajectories

Introduction

The surface of the human placenta is covered by a single giant, multinucleate, non-proliferative cell known as the syncytiotrophoblast (ST). The ST layer is the primary maternal-fetal interface that acts as a functionally selective epithelial barrier to aid in transport of nutrients, oxygen and waste. Importantly, the ST is highly polarized with dense microvilli decorating its surface, bathed in the maternal blood. The mechanism controlling ST microvilli formation and maintenance is unknown, however, loss or decrease in ST microvilli have been observed in pregnancy complications such as intrauterine growth restriction (IUGR) and pre-eclamptic placenta. The protein, ezrin, anchors the cell membrane to the actin cytoskeleton, thereby stabilizing the microvillar structure. To accomplish this, ezrin must be activated via phosphorylation. Atypical protein kinase C (aPKC) is known to phosphorylate ezrin in the intestinal microvilli. Two isoforms of aPKC, ι and ζ, are expressed in the ST, however their function has never been addressed. Thus, we hypothesize that aPKC isoform(s) mediate phosphorylation of ezrin and regulates human placental ST microvilli abundance and structure.

Methods

Late first trimester human placental explants were cultured +/- 10μM myristoylated-aPKC pseudosubstrate inhibitor for 4-8hrs in culture media and then collected for western blot analysis or fixed for immunostaining. Western blotting was conducted for phospho-Thr567 ezrin and total ezrin. Immunofluorescent staining was carried out with anti-ezrin and E-cadherin antibodies and fluorescently labelled phalloidin and imaged with confocal microscopy.

Results

Confocal images showed a significant decrease in total ezrin specifically in the apical ST when explants were treated with aPKC inhibitor. Additionally, strong changes in the apical actin cytoskeleton could be seen after aPKC inhibitor treatment suggesting loss or change in the shape of ST microvilli. However, western blot analysis of whole placental lysates did not show a significant change in total or phospho- ezrin expression.

Conclusion

Our preliminary data suggests that aPKC isoforms may regulate ST microvilli by controlling ezrin expression. Future directions include examining ST specific changes in the phospho-ezrin expression after aPKC inhibitor treatment and examining the isoform specific effect of aPKC on ezrin expression using siRNA knockdown. Further, imaging of aPKC inhibitor and siRNA treated explants with electron microscopy will be used to confirm the loss or change in the microvillar structure and abundance. Thus, by understanding the processes regulating normal ST microvilli maintenance, we will be able to identify previously unrecognized mechanisms inducing the development of placental dysfunction, leading to the development of treatments for pregnancy complications and healthier pregnancies in the future.

Funded By: CIHR , WCHRI , Stollery Children's Hospital Foundation , Lois Hole Hospital for Women

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Abstract #:	19
Presenter:	Nicol Patricny
Supervisor:	Pei, Jacqueline R
Title:	Resistance to antisocial peers: A protective factor for adolescents found Not Criminally Responsible on account of Mental Disorder
Authors:	Nicol Patricny, Jacqueline Pei, and Andrew Haag
Theme:	Children's health and well-being

Introduction: From 1941 to 2018, there have been 147 adolescents found Not Criminally Responsible on account of Mental Disorder (NCRMD) in Alberta's history. These adolescents represent a unique developmental subset of the understudied NCRMD population in Canada. They typically experience severe mental health issues, such as psychotic disorders, and are detained in secure forensic psychiatric settings with certain conditions and restrictions in place until they can safely be discharged into the community. To date, most researcher have focused primary on examining risk factors for negative mental health outcomes and reoffending in this population, most of which are static in nature with limited clinical utility. Adolescence is an important developmental period wherein there is a window of opportunity to promote resilience. Our objective was to explore theoretical protective factors, that is, strength-based factors that reduce the risk of negative outcomes and promote healthy developmental trajectories for adolescents found NCRMD.

Methods: Our investigation used data from the Alberta NCR Project-a retrospective longitudinal study of recidivism among the Alberta NCRMD population. We reviewed all available forensic files at Alberta Hospital Edmonton to retrieve information on theoretical protective factors. Based on available data, we were able to include 81% (N = 119) of all adolescents (age 15 to 25 years) ever found NCRMD in Alberta's history for our quantitative analyses. We conducted multiple linear and bivariate logistic regression analyses to determine which hypothetical protective factors were predictive of nonrecidivism within the 35-year maximum follow-up period.

Results: We found one significant protective factor, resistance to antisocial peers, which is characterized by the tendency to keep to oneself or engage with other prosocial peers while resisting the negative influences of antisocial peers in one's environment. Adolescents who demonstrated this protective factor during their warrant were more likely to experience long-term community success, being 3.9 times (95% CI = 1.19-12.77, $p < .05$) more likely to display nonrecidivism for general offences and 5.6 times (95% CI = 1.17-26.48, $p < .05$) more likely to display nonrecidivism for violent offences, as compared to adolescents who gravitated towards antisocial peers. This is equivalent to a medium effect size. Resistance to antisocial peers explained between 6.1%-9.5% of the variance in general nonoffending outcome and 6.5%-11.2% of the variance in violent nonoffending outcome. Compared to individuals without this protective factor, the base rate of recidivism was 19.0% lower for general offences, and 14.8% lower for violent offences.

Conclusion: Our study provides empirical evidence that resistance to antisocial peers is an important protective factor for adolescents found NCRMD. This protective factor could be amenable to change through individual treatment or environmental change. The results provide a theoretical foundation for researchers to explore if health professionals may be able to elicit change in this variable, and if so, what treatment or management strategies may be most effective to promote positive developmental trajectories for adolescents found NCRMD.

Funded By: This WCHRI graduate studentship has been funded through the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

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Abstract #:	124
Presenter:	Thanh-Tu Pham
Supervisor:	Le, Lawrence H
Title:	Development of Machine Learning Algorithms to Automatically Assess Hip Displacement in Children with Cerebral Palsy
Authors:	Thanh-Tu Pham, Minh-Binh Le, Lawrence H. Le, John Andersen, Edmond H. Lou
Theme:	Knowledge translation and decision-making

Introduction: Cerebral palsy (CP) is a leading cause of lifelong physical disability with an incidence of 1 in 500 live births, and it affects over 50,000 Canadian children and their families. The core feature of CP is the early onset neuromotor impairment attributed to a non-progressive lesion or acquired injury to the brain early in development. One third of the children with CP experience hip displacement, which can cause reduced function and severe pain. Hip displacement, which occurs when the femoral head abnormally lies beyond the edge of the acetabulum, is evaluated through anteroposterior (AP) pelvic radiographs as part of clinical surveillance strategies. Reimer's migration percentage (MP) measured on these radiographs is the current gold standard to assess hip displacement. However, manual measurements of MP are subjective and time-consuming. The objective of this study was to develop a machine learning (ML) based method to measure the MP on AP radiographs.

Methods: A total of 122 deidentified AP radiographs of pelvis, acquired as part of a routine hip surveillance program for children with CP, was used for the study. Eight reference landmarks were manually labelled on the radiographs for the MP calculation. A Convolution Neural Network-based ML method was used to detect the eight anatomical landmarks. The radiographic dataset was divided into 3 sets to implement the ML algorithm: 57 for training, 10 for validation and 55 for testing. The mean absolute difference (MAD) and the intra-class correlation coefficient (ICC [2,1]) were used to evaluate the accuracy and reliability of the method using the test set of 110 hips (left and right). The labelled and ML measurements were compared. The sensitivity and specificity of diagnosing hip displacement (MP-threshold of 30%) were also assessed.

Results: The MAD between the manual and ML-based measurements, and the ICC [2,1] of inter-method were 4.5 ± 4.3% (95% CI, 3.7-5.3%) and 0.91, respectively. The sensitivity and specificity for classifying hip displacement were 87.8% and 93.4%, respectively. The ML algorithm took approximately 5 seconds to process the test set of 55 images.

Conclusion: The ML method using the Convolution Neural Networks provided high accuracy and excellent reliability of measuring MP values on children with CP. This method has potential to assist clinicians in the routine assessment of hip displacement in hip surveillance clinical pathways.

Funded By: Glenrose Rehabilitation Hospital Foundation and WCHRI funding of the Northern Alberta Canadian Cerebral Palsy Registry.

Abstract #:	144
Presenter:	Allison Pihelgas
Supervisor:	Sia, Winnie
Title:	The impact of a Postpartum Preeclampsia Clinic on cardiovascular risk factors, patient knowledge and cardiovascular outcomes
Authors:	Allison Pihelgas
	Winnie Sia
	Laura Sevick
	Gabriela Pelinska
Theme:	Lifelong women's health

OBJECTIVES: We aimed to evaluate the efficacy of a Postpartum Preeclampsia Clinic based out of the Royal Alexandra Hospital in Edmonton, AB, in improving patient's knowledge about their own cardiovascular health, healthy behaviours, and medical/ cardiovascular outcomes.

STUDY DESIGN: A case-control cohort study was performed using survey-based data. 470 total surveys were distributed; half to patients who had been discharged from the Postpartum Preeclampsia Clinic from 2010-2019, and half to patients who were seen by the Obstetric Medicine clinic during their pregnancy and had been diagnosed with preeclampsia but were not seen at the postpartum clinic. The survey collected information on patient health behaviours (exercise habits, smoking, weight loss), health outcomes (medications and medical diagnoses), and their knowledge about preeclampsia as a cardiovascular risk factor.

MAIN OUTCOME MEASURES: The primary outcome studied was amount of exercise activities performed per week. Secondary outcomes included return to prepregnancy weight, smoking, and diagnosis of hypertension, diabetes, dyslipidemia, ischemic heart disease, stroke. Narrative data regarding patient feedback on the postpartum preeclampsia clinic is also reported. As well, patients who did not attend the postpartum preeclampsia clinic were asked to report whether they had participated in cardiovascular screening and risk reduction based on information from other sources.

RESULTS At this point a total of 120 surveys have been returned, for a response rate of 25%. These are currently being entered into the RedCap database for analysis.

Funded By: This research project was funded by the WCHRI Obstetrics & Gynecology resident grant.

Abstract #:	85
Presenter:	Megan Pohl
Supervisor:	Bolduc, Francois
Title:	Specific Gamification Elements could be implemented in a Chatbot for Children with Neurodevelopmental Disability

Authors:	Megan Pohl, Mahdieh Yousef, Cory Rosenfelt, Francois Bolduc

Theme:	Children's health and well-being

Families of children with neurodevelopmental disabilities (NDD) need access to a menu of evidence-based options to obtain diagnosis and continuity of care. Our goal is to develop a chatbot that provides relevant online resources for NDD families, educators and frontline healthcare workers. To increase the engagement of families interacting with this chatbot, our research team explored the utilization of gamification. Gamification is the implementation of game-like elements into non-game contexts. Examples of gamification include badges, points, and social networks in health applications. Determining what elements of gamification are most effective in increasing engagement in this population and how they should be implemented is our primary aim. It was predicted that certain elements of gamification would be more effective in increasing engagement than others. A literature review on gamification in healthcare and educational settings was conducted to determine what elements of gamification would be most relevant to our chatbot. From this, and further readings, a research-based focus group question set was constructed. The question set aims to uncover perspectives on the implementation of gamification in the chatbot. To finalize this question set and obtain preliminary perspectives, five virtual focus groups were run on 11 members of an internal parent advisory board. Participants' comments were audio-recorded, coded, and common perspectives were highlighted. The preliminary results show a preference for the implementation of some mechanisms (social networks and goal setting) and a hesitation to others (unlockable content). Additionally, participants raised novel ideas about possible implementation strategies. These results indicate that specific types of gamification in an NDD chatbot may increase engagement amongst users. Further, these findings necessitate continued focus group sessions with our participant population.

Funded By: Natural Sciences and Engineering Research Council of Canada (NSERC), Canadian Institutes of Health Research (CIHR), Women and Children's Research Institute (WCHRI), and Kids Brain Health Network

Abstract #:	105
Presenter:	Neelam Punjani
Supervisor:	Papathanassoglou, Elizabeth
Title:	EXPLORATION OF ADOLESCENT PAKISTANI-DESCENT GIRLS' EXPERIENCES OF DEVELOPING SEXUALITY IN RELATION TO PSYCHOLOGICAL WELL-BEING - AN INTERPRETIVE DESCRIPTION APPROACH
Authors:	Elizabeth Papathanassoglou, Kathleen Hegadoren, Margot Jackson, Saima Hirani, Zubia Mumtaz
Theme:	Children's health and well-being

Background: Adolescence is a critical period in the transition from childhood into adulthood, during the course of which young children aged 11-19 years' experience substantial physical, psychological, social, and emotional changes. Sexual health incorporates a wide range of interlinked mental, physical, and emotional factors. In Alberta, immigrant youth and children account for 31% of the total immigrant population. The experience of developing sexuality and any relationships with their well-being has not been studied among Pakistani-descent adolescents in Canada. Moreover, based on evidence from LMICs revealing specific challenges faced by adolescent girls, it will be interesting to explore the experience of developing sexuality among Pakistani-descent girls.

Aims: The purpose of the proposed study is to explore the experience of developing sexuality and their relationship to psychological well-being in middle- to late- adolescence girls of Pakistani-descent, living in Edmonton, Alberta.

Methods: An Interpretive Descriptive approach will be used to study the experiences of female Pakistani-descent adolescents in relation to developing sexuality and psychological well-being. A purposive and theoretical sampling strategy will be used to recruit adolescent girls (age: 14-19 years) with the collaboration of the Indo-Canadian Women's Association. Participants will be interviewed using a semi-structured interview guide with open-ended questions. Participants will also be asked to create timelines about their life experiences on a sheet of paper. Qualitative data analysis software (NVIVO 12.0) will be used to manage the data and themes and patterns emerging will be identified. As the findings will generate new angles or discoveries, additional literature will be searched from other disciplines to see what other new similar or opposing ideas or perspectives exist within the themes arising in current study.

Anticipated outcomes: It is anticipated that the study will provide preliminary insight into the complex phenomenon of developing sexuality and its relationship to psychological well-being among adolescent girls of Pakistani descent. The study will draw attention to the hidden voices of adolescent girls and will increase awareness about the psychological aspect of sexuality. Recommendations from the study can potentially inform healthcare professionals to address adolescents' sexuality and their psychological well-being and integrate those while providing sexual and reproductive health care services.

Funded By: Women and Children's Health Research Institute

Izaak Walton Killam Memorial Scholarship

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Abstract #:	38
Presenter:	Steven Qiu
Supervisor:	Funk, Gregory
Title:	Enzymes that produce adenosine are differentially distributed in the brainstem respiratory networks: implications for apnea of prematurity
Authors:	Steven Qiu, Robert Reklow, Tuca Alvares, Gregory D Funk
Theme:	Children's health and well-being

Prematurely born infants, due to their immature brainstem networks that produce and control breathing, often have irregular breathing patterns that include frequent periods when breathing stops altogether (apneas). The severity and incidence of this condition, referred to as apnea of prematurity (AOP), increases with the degree of prematurity. Apneas are a problem because they can cause a decrease in blood O2 levels, which triggers an adaptive increase in breathing. However, if O2 levels in the brain are not immediately restored, hypoxia causes a profound inhibition of breathing in premature infants that can become life threatening. Our recent work has shown that during hypoxia, the transmitter ATP is released in the pre-Bötzinger complex (preBötC; brainstem site that generates breathing) and that this stimulates breathing, partially counteracts the hypoxic depression of breathing. ATP, however, is rapidly broken down into adenosine (ADO), which slows breathing and in premature infants it is causally implicated in AOP; e.g., Caffeine, which blocks ADO actions, is the first-line treatment for premature infants with apnea. However, ~20% of infants do not respond to caffeine, so alternatives are needed. The interaction between ATP excitation and adenosine inhibition of breathing is emerging as a key determinant of how much breathing slows in response to oxygen deprivation. Multiple factors determine the balance between the actions of ATP and adenosine. Key among these is a family of enzymes called ectonucleotidases that remove phosphates from ATP, ultimately producing ADO. Our goal was to compare the distribution and activity of ectonucleotidases in the preBötC with those other brain regions. The rational is the therapeutic potential of developing strategies that can shift the balance between excitatory ATP signaling and inhibitory ADO signaling in favor of ATP actions. Ectonucleotidases are central in setting this balance. Thus, understanding the activity and subtypes of enzymes in the preBotC vs other brain regions is key to designing approaches to specifically manipulate ATP/ADO signaling in the preBotC.

The brainstem was isolated from 1-2 day-old mice, cut into 600µm-thick slices at the areas of interest using a vibratome, and tissue punches were taken from the pre-BötC, XII nucleus (a region that contains motoneurons that drive breathing muscles), and a non-respiratory area (NRA) from these tissue slices using a 21-gauge hypodermic needle. Ectonucleotidase activity was assessed using a custom-designed assay that measures the PO4 produced by these punches when incubated with ATP.

The preBötC produced less PO4 than the XII ($p=0.053$, $n=12$), as did the NRA ($p=0.03$, $n=12$). In contrast to expectations, these data suggest that ectonucleotidase activity is not uniform in the brainstem. In addition, these data raise the interesting possibility that lower activity in the preBötC may have evolved to minimize the breakdown of excitatory ATP into inhibitory ADO, which would reduce the risk of respiratory inhibition and apnea. Future goals are to identify the subtypes of enzymes in the preBötC to inform development of therapeutic strategies for apnea of prematurity that focus on reducing ATP breakdown or enhancing ADO removal.

Funded By: AI, WCHRI to SQ

Research support: CIHR, NSERC, WCHRI

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Abstract #:	145
Presenter:	Samina Rashiq
Supervisor:	Dijke, Esme
Title:	Exploring the immune consequences of pregnancy in kidney patients awaiting transplantation
Authors:	Samina Rashiq, Anne Halpin, Patricia Campbell, Dr. Esmé Dijke
Theme:	Lifelong women's health

Introduction: Historical immune (sensitizing) events can make it difficult to find a compatible donor in transplantation. Human Leukocyte Antigens (HLA) are important in donor-recipient compatibility. Three key sensitizing events resulting in exposure to non-self HLA are previous transplant, pregnancy, and blood transfusion. These events can lead to the development of HLA antibodies, which have a negative impact on transplant outcomes. Percent calculated panel reactive antibody (cPRA) is used to define the level of antibody burden in transplant patients. Our aim was to assess whether there are differences in cPRA between males and females on the kidney transplant wait list and to investigate the impact of pregnancy.

Methods: HLA antibody data were extracted from the clinical HLA laboratory database. Data were organised in Excel and analysed using GraphPad Prism. Statistical tests used were the Observed vs. Expected proportions test and the Mann-Whitney test.

Results: As of August 2020, 146 kidney patients were active on the wait list; 66 females and 80 males. The median age for females and males was 56 yrs (range 31-75 yrs) and 58 yrs (range: 24-78 yrs), respectively. Within the female group, 80% has a history of pregnancy. Similar proportions of females and males had previous transplants (32% vs. 42%, respectively) or transfusions (50% vs. 66%, respectively). Overall, females had a significantly higher median cPRA than males (74% vs 20%, respectively; p=0.004). However, if pregnancy as a sensitizing event is excluded, no significant differences were observed in median cPRA between males (n=80) vs. females (n=13). Within the female group, no significant differences were observed between previously pregnant patients (n=53) and females without pregnancies (n=13). However, in those awaiting their first kidney transplant (n=45), previously pregnant patients (n=36) had a significantly higher median cPRA than the no pregnancy group (n=9; median cPRA: 66% vs. 0%, respectively; p=0.004).

Conclusion: Female kidney patients on the waitlist have a higher median cPRA than males, which appears to be associated with pregnancy. This sex-based difference means that it may more challenging to find a compatible kidney donor for females who have been pregnant than females who have not been pregnant as well as males. This finding impacts most female patients on the waitlist as the vast majority has a history of pregnancy. Further studies will include analysis of wait times as well as an evaluation of immune memory in women with a history of pregnancy to help assess their current vs historic immune risk.

Funded By: Alberta Transplant Institute Summer Studentship, Canadian Donation and Transplantation Research Program

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Abstract #:	39
Presenter:	Robert Reklow
Supervisor:	Funk, Gregory
Title:	The life-threatening inhibition of breathing by hypoxia in premature mammals may reflect limited adenosine clearance from the central network that generates breathing
Authors:	Robert J. Reklow, Tucaauê S. Alvares, Daniel B. Zoccal, Alexander W. Toohey, Megan A. Hansen, Sara M. Frangos, Gregory D. Funk
Theme:	Children's health and well-being

Breathing in premature infants often stops briefly (apnea) because the brainstem network that controls breathing is immature (apnea of prematurity, AOP). Apneas cause hypoxia (reduced oxygen levels) triggering the hypoxic ventilatory response (HVR), which comprises an initial increase in ventilation followed by a centrally mediated 2º decrease that is much more pronounced in premature/newborn mammals. In adults, breathing remains above baseline during this 2º phase but in the very young, it falls below baseline leading to a life-threatening feedback loop where the apnea causes hypoxia, which decreases breathing, causing further hypoxia, greater inhibition and so on. Understanding the cause of this powerful hypoxic inhibition of breathing in the very young, one of the major questions in perinatal physiology, could inform new therapies for AOP.

Our work has focused on the transmitter ATP, which is released in the preBötzinger Complex (preBötC, brain region that generates inspiration) during hypoxia where it reduces the 2º depression of breathing. However, extracellular ATP (ATPe) is degraded to adenosine (ADOe), which inhibits breathing and is implicated in AOP; e.g., caffeine blocks the actions of ADO and is the first line treatment for AOP. New therapies are required because ~20% of infants do not respond to caffeine.

We hypothesize that the greater 2º inhibition of breathing in prematurity is due to an immature system for clearing ADOe. ADOe-mediated inhibition stops with its removal from the extracellular space, which depends on i) equilibrative nucleoside transporters (ENTs) that move ADOe across cell membranes down its concentration gradient, and ii) ADO kinase (ADK), an enzyme that keeps the level of ADO inside cells lower than outside so ENTs clear ADOe. How ENT activity develops in the preBötC is unknown. However, the form of ADK that influences ADOe is not functional in the brain until two weeks of age in rodents. To assess the importance of ADOe clearance in the development of the HVR, we used plethysmography to measure the HVR (10% O2) in 0-56 day old (P0-56) wild-type (WT), ENT knockout (KO), and ADKtg mice engineered to have functional ADK throughout life.

In WT neonates (P0-3), it took 7 min in hypoxia for ventilation to fall below baseline; it took only 40 sec in ENT KO mice. Strikingly, ADKtg mice showed the mature response; ventilation remained above baseline levels throughout 10 min of hypoxia. By P12, the HVR had also matured in WT mice, but VE still fell below baseline in the ENT KO mice. To assess the importance of ENT and ADK specifically in the preBötC, we isolated the preBötC network in brain slices from P0-11 mice (~23-40 weeks of human gestation). The ADO-mediated inhibition of preBötC frequency lasted twice as long in ENT KO mice compared to WT, while in WT the ENT inhibitor (NBMPR) significantly increased baseline frequency (10%). Conversely, the decrease in basal frequency caused by ADK inhibition (ABT-702) increased with age (P0-2, 15%; P9-11, 23%). These data suggest that i) ENTs are critical for ADO clearance and reducing the hypoxic respiratory depression throughout life and ii) low ADK activity at birth is a major contributor to the greater hypoxic respiratory depression in early development.

Funded By: WCHRI (Graduate Scholarship), WCHRI and FoMD Bridge Funding; CIHR; Lung Association of Alberta & NWT, CFI, NSERC.

Abstract #:	106
Presenter:	Nicole Rodriguez
Supervisor:	Kozyrskyj, Anita
Title:	Maternal depression impacts infant gut microbial composition dependent on breastfeeding status

Authors:	Nicole Rodriguez, Hein M. Tun, Catherine J. Field, Meghan B. Azad, Allan B. Becker MD, Piushkumar J. Mandhane, Theo J. Moraes, Malcolm R. Sears, Stuart E. Turvey, Padmaja Subbarao, James A. Scott, Anita L. Kozyrskyj
Theme:	Children's health and well-being

Background:

Depressive symptoms are common during pregnancy and are estimated to affect 7% to 20% of pregnant women, with higher prevalence found in those with a prior history of depression, in ethnic minorities, and in those with increased exposure to stressful life events. Maternal depression is often left undiagnosed and its symptoms can increase adverse health risks to the infant including impaired cognitive development, behavioral problems, and higher susceptibility to physical illnesses. There is accumulating research evidence that supports the association between maternal physical health factors to infant gut health. However, specific maternal prenatal psychosocial factors and their effect on infant intestinal microbiota remains an area that is not well understood.

Project objectives:

The objective of the current study is to examine the effect of maternal prenatal psychosocial and physical health on the microbial gut compositions of infants at 3-4 months of age. Specifically, we will investigate the association of maternal prenatal depression status within stratified breastfeeding groups on the infant gut microbiota.

Methods:

The current study employed a large subsample of 996 infants (mean age: 3.7 ± 1.0 months) from the CHILD Cohort Study (www.childstudy.ca). Maternal psychosocial health, specifically depression, was assessed using self-reported questionnaires at the time of recruitment during pregnancy. Additionally, hospital records were used to provide information related to the birth scenario, UTI occurrence, antibiotics, and other factors. The infant gut microbiota at 3-4 months of age has been profiled using 16S rRNA sequencing and characterized by microbial beta-diversity (Bray-Curtis distance) to represent community composition.

Result:

In our study mothers, 6.1% reported prenatal depression, 19.1% had depression in the past and 74.8% indicated never having depression. 29.4% of infants had been exclusively breastfed since birth, 13.8% briefly received formula in the hospital, 34.3% were partially breastfed, and 22.4% were not breastfed. Stratification by infant diet revealed that maternal depression had the strongest effect on infant gut microbial beta-diversity in the partially breastfed ($p = 0.023$) and the non-breastfed group ($p = 0.022$), adjusted for maternal prenatal diet, birth mode, and other covariates. Maternal prenatal diet was crudely associated with gut microbial beta-diversity of non-breastfed infants but not in the adjusted model with maternal depression.

Conclusion:

Maternal depression impacts infant gut microbial diversity, dependent on breastfeeding status at 3 to 4 months. These changes in the microbial composition of infants born to depressed mothers are known to be predictive of metabolic diseases in later life. Early cessation of breastfeeding among depressed moms may ultimately result in a compromised immunity and negative developmental outcomes for infants.

Funded By: Northern Alberta Clinical Trials and Research Centre (NACTRC), Canadian Institutes of Health Research (CIHR), AllerGen NCE

women & children's health research institute

Abstract #:	97
Presenter:	Daniela Roth
Supervisor:	Graf, Daniel
Title:	The chromatin regulator ANKRD11 controls palate and cranial bone development
Authors:	Daniela M. Roth, Pranidhi Baddam, Devyn Godziuk, Sarah-Thea DeSouza, Adrianne E.S. Watson, Tim Footz, Daniel Graf*, Anastassia Voronova*
Theme:	Children's health and well-being

Epigenetic regulation of craniofacial development remains poorly understood. Ankyrin Repeat Domain 11 (ANKRD11) is a chromatin regulator involved in the control of progenitor cell function via fine-tuning of histone acetylation. Loss of function ANKRD11 gene variants or microdeletions of the 16q24.3 chromosomal region containing ANKRD11 gene cause KBG syndrome, a rare autosomal dominant congenital disorder with variable neurodevelopmental and craniofacial involvement. Significant craniofacial abnormalities include a distinct facial gestalt, delayed bone age, tooth and palatal abnormalities as well as hearing loss. The role of ANKRD11 in the developing cranial neural crest has not been established.

Our results show Ankrd11 is broadly expressed in all developing murine craniofacial structures, which are derived from neural crest. Global deletion of ANKRD11 results in embryonic lethality prior to bone formation. To study the postnatal phenotype of ANKRD11 deletion, we induced Cre-Lox recombination in Wnt1+ neural crest cells during embryogenesis. The resultant Ankrd11ncko mice display craniofacial deficiencies that correlate with several clinical features of KBG syndrome patients. These deficiencies included cleft palate, retrognathia, midfacial hypoplasia, delayed calvarial growth, and tooth malformations. Ossification of midfacial bones was reduced and several ossification centers failed to expand and fuse. The cranial base was abnormal with marked reduction of the pre-sphenoid and pterygoid wings. The tips of the developing palatal shelves showed reduced proliferation, though their elevation appeared normal. Osteoblast differentiation was altered. Bone formation was already compromised at mid-gestation, and several osteoblast markers were strongly reduced at birth, indicating potential direct regulation of bone differentiation by Ankrd11. Primary osteoblast cultures supported this hypothesis, as Ankrd11-deficient osteoblasts appear aberrant morphologically and in osteogenic assays.

These data provide novel developmental and mechanistic insight into how ANKRD11, a chromatin regulator, is required for normal bone and in consequence craniofacial development. This study provides the first functional understanding of how ANKRD11 gene mutations or deletions may lead to the craniofacial deficiencies observed in KBG syndrome patients.

Funded By: Gilbert K. Winter Fund, G. Sperber Fund for Dentistry

women & children's health research institute

Abstract #:	64
Presenter:	Nicholas Ruel
Supervisor:	Hammond, James
Title:	SLC43A3/ENBT1 regulation by oxidative stress
Authors:	Nicholas M Ruel, Kerrylei Jabilona, James R Hammond
Theme:	Children's health and well-being

Introduction: Acute lymphoblastic leukemia (ALL) is the most common cancer associated with childhood. 6-Mercaptopurine (6-MP) is a nucleobase analog drug used in the maintenance treatment phase of ALL. 6-MP has numerous side-effects associated with its use, which has both short-term and long-term implications, and this also impacts patient compliance (especially in children). Our lab has established that SLC43A3, which encodes for the equilibrative nucleobase transporter 1 (ENBT1), is expressed in leukemia cells and transports 6-MP, but its regulation is yet to be elucidated. A previous study has demonstrated in microvascular endothelial cells that nucleobase uptake via ENBT1 was significantly decreased upon exposure to oxidative stress. It is well known that oxidative stress is very prevalent in cancer, including leukemia, suggesting that it could impact ENBT1 function and thus 6-MP uptake and therapeutic activity. Therefore, we hypothesize that the ENBT1 function will be reduced by oxidative stress in leukemia cells and thus impact the therapeutic efficacy of 6-MP.

Methods: MOLT-4 cells, a commonly used leukemia cell line, were used for all experiments. The MTT cell viability assay was used to assess the viability of the cells after exposure to compounds that induce oxidative stress, TBHP and menadione, for 15 min, 30 min, and 24 hours. Mechanistically, TBHP causes the generation of hydroxyl radicals on the outside of cells, while menadione generates superoxide radicals intracellularly. [14C]6-MP was used to determine the functional uptake of ENBT1 using our oil stop centrifugation assay for the determination of ENBT1 kinetics (Km and Vmax).

Results: A range of concentrations of TBHP and menadione were tested initially to determine the optimum concentration to use for subsequent studies. Incubation of MOLT-4 cells for 15 and 30 min in TBHP and menadione had significant effects on cell viability only at the highest concentrations tested (85 ± 4% and 71 ± 6%, respectively) Incubation for 24 hours led to higher levels of cell death by TBHP and menadione (Log EC50: -3.877 ± 0.108 and -4.283 ± 0.106, respectively). Based on these data, we used 100 µM TBHP and menadione for 6-MP uptake assays, to ensure that any changes to ENBT1 function were independent of the direct effects of these agents on cell viability. ENBT1-mediated uptake of 6-MP was not significantly altered following incubation with 100 µM TBHP. However, incubation with 100 µM menadione led to a significantly decreased uptake of 6-MP (Vmax: Control - 145 ± 58 pmol/µL/sec; Menadione - 37 ± 10 pmol/µL/sec.

Conclusions: Short term treatment of MOLT-4 cells with menadione, but not TBHP decreased the functional activity of ENBT1. This difference between TBHP and menadione in this regard implies that ENBT1 is more prone to oxidative stress through intracellular generation of free radicals. It is also indicated that this change is not a transcriptional change but an acute change to ENBT1 since our incubation time was relatively short (30 min). Our data suggest that oxidative stress leads to reduced transport capacity by ENBT1 and thus could impact 6-MP therapeutic activity.

Funded By: Canadian Institute of Health Research, Cancer Research Society

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Abstract #: 4
Presenter: Tamara Saez
Supervisor: Davidge, Sandra
Title: Long-term vascular dysfunction in female mice with a history of a pregnancy complicated by dyslipidemia
Authors: Tamara Sáez1,2, Abbey Pagee1,2, Raven Kirschenman1,2, Floor Spaans1,2, Sandra T. Davidge1,2,3

1Department of Obstetrics and Gynecology, 2Women and Children's Health Research Institute, 3Department of Physiology, University of Alberta, Edmonton, Canada.

Theme: Lifelong women's health

Introduction: Dyslipidemia during pregnancy is a risk factor for developing the pregnancy complication preeclampsia. Preeclampsia is associated with maternal vascular dysfunction and an increased risk of cardiovascular complications later in life. High circulating levels of oxidized low-density-lipoproteins (oxLDL) are associated with vascular endothelial dysfunction (via oxidative stress) and also contribute to the development of atherosclerosis. However, whether vascular dysfunction in pregnancies complicated by dyslipidemia persists postpartum and increases the risk of atherosclerosis later in life, remains unclear. We hypothesize that dyslipidemia-induced vascular dysfunction in pregnancy will impair maternal long-term vascular function and will contribute to the development of atherosclerosis.

Methods: Pregnant C57BL/6 mice were fed a high-cholesterol diet (HCD) between gestational day (GD) 13.5 and term (GD19), to increase cholesterol levels and induce vascular dysfunction, as recently reported (Sáez et al. Clinical Sci, 2020). Control pregnant mice were fed a standard chow diet. Non-pregnant females were on the same diets for equal time. At 3 months postpartum (or 3 months after diets) (n=3-7/group), plasma samples were collected to measure oxLDL levels and aortas were isolated to assess ex vivo vascular function by wire myography. Vascular responses to the endothelial-relaxing agonist, methacholine (MCh), were evaluated in the presence or absence of oxLDL (50 µg/mL) or L-NAME (nitric oxide synthase inhibitor; 100 µM). Superoxide levels (an oxidative stress marker) and lipid deposits were evaluated in sections of aorta by DHE and SUDAN-IV staining, respectively.

Results: Plasma levels of oxLDL tended to be increased in postpartum females compared to the non-pregnant group (78.3±12.9 vs 48.9±6.4 mg/dL; p=0.067). Also, HCD reduced maximal (Emax) MCh-induced vasodilation in the postpartum females compared to the control group (65.3±19.0 vs 88.5±7.2%; p=0.02), while no effects of HCD were found in the non-pregnant mice. HCD reduced nitric oxide contribution to vasodilation in the postpartum (183.8±10.5 vs 256.5±13.4 AU; p=0.001) and non-pregnant females (135.4±15.2 vs 252.1±19.8 AU; p=0.04) compared to the respective control group. Pre-incubation with oxLDL reduced maximal vasodilation in aortas from postpartum females previously fed on a HCD compared to control (33.5±1.0 vs 65.3±19.0%; p=0.004); however, no effects of oxLDL were found in aortas from control postpartum or non-pregnant mice. HCD tended to increase aortic superoxide levels in postpartum females (4.5±2.1 vs 3.6±1.1 AU), while it tended to decrease in non-pregnant females (5.5±1.2 vs 3.6±0.6 AU) compared to respective control group (interaction p=0.064). Finally, the HCD caused a slight lipid deposition in aortas from postpartum females compared to non-pregnant mice.

Conclusion: Our preliminary data suggest that HCD given only during pregnancy impairs maternal vascular function later in life, which could be due to increased plasma oxLDL levels and higher superoxide levels in aortas. Our study suggests that vascular dysfunction during gestational dyslipidemia persists after pregnancy, which could play a key role in the development of cardiovascular complications later in life

Funded By: TS is supported by the Women and Children's Research Institute (WCHRI) and Banting-CIHR postdoctoral fellowships. This study was funded by a CIHR Foundation grant and by the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women through WCHRI.

women & children's health research institute

Abstract #:	50
Presenter:	Omolara Sanni
Supervisor:	Ospina, Maria
Title:	Maternal Cannabis Exposure during Pregnancy and/or Breastfeeding and Early Childhood Outcomes: An Overview of Systematic Reviews and Meta-analyses
Authors:	Sanni OB; Belon AP; Sullivan H; Dennett L; Seabrook JA; Ospina MB
Theme:	Pregnancy and developmental trajectories

Introduction

Cannabis is the most used recreational drug worldwide. Evidence suggests that the prevalence of cannabis use during pregnancy increased from 1.2% in 2012 to 3.4% in 2017. The inconsistent evidence on the effect of maternal cannabis exposure on fetal, infant and child health, coupled with the increasing prevalence of cannabis use among women of reproductive age, calls for consolidation of available evidence on the impact of maternal cannabis exposure during pregnancy and/or breastfeeding on fetal and child health.

Methods

Five electronic databases were searched (MEDLINE, Embase, CINAHL, Web of Science and PsycINFO) from database inception up to April 2020 for systematic reviews and meta-analyses assessing the association between maternal cannabis exposure during pregnancy and/or breastfeeding and fetal, newborn and child health. Panoramic meta-analyses were conducted for adjusted effect estimates reported in both meta-analyses and individual primary studies. The AMSTAR-2 tool was used to assess the methodological quality of systematic reviews and meta-analyses, and the level of evidence was assessed using the GRADE assessment tool.

Results

553 records were screened, and nine reviews met our inclusion criteria. Five reviews were conducted in the USA, two in Canada, and one in Italy and Australia. There was no evidence of an association between maternal cannabis exposure during pregnancy and low birth weight (pooled adjusted odds ratio [aOR] for meta-analyses: 1.13 95%CI 1.00, 1.27; I2=0%; pooled OR for individual studies: 1.08 95%CI 0.92, 1.28; I2=31%) or preterm birth (pooled aOR for meta-analyses: 1.15 95%CI 0.88, 1.50; I2=0%). Mean differences (MD) reported in two meta-analyses suggested an association between maternal cannabis exposure during pregnancy and decreased gestational age at delivery (pooled MD -0.2; 95%CI -0.6, 0.2 and -0.1; 95%CI -0.5, 0.3). Pooled estimates reported in two meta-analyses suggested a reduction in birth weight with maternal cannabis exposure (pooled MD -109.4g; 95%CI 180.1, -38.7 and -167.0g; 95%CI -245.0, -90.0). Maternal cannabis exposure during pregnancy and/or breastfeeding was not associated with sudden infant death or IQ. Maternal cannabis exposure during the first month postpartum was associated with a 14-point decrease in the Bayley index of motor development at one year of age. Findings were inconsistent for the association between maternal cannabis exposure and NICU admission, intrauterine growth restriction, APGAR scores, and several neuropsychological outcomes.

Conclusions

Limited evidence suggests varying degrees of associations between maternal cannabis exposure during pregnancy and/or breastfeeding and fetal, neonatal, and childhood health, which underpins the need for further studies assessing these relationships.

Funded By: Dr Ospina is funded by the generous supports of the Lois Hole Hospital for Women through the Women and Children's Research Institute Recruitment Grant.

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Abstract #:	58
Presenter:	Tehzeeb Sayed
Supervisor:	Lou, Edmond HM
Title:	Intra- and inter-rater reliability of ultrasound reflection coefficients to assess the bone strength of the spine for children with adolescent idiopathic scoliosis
Authors:	Tehzeeb Sayed, Mahdieh Khodaei, Edmond Lou
Theme:	Children's health and well-being

Introduction

Adolescent idiopathic scoliosis (AIS) is a three-dimensional (3D) spinal deformity of unknown cause, characterized by lateral curvature and vertebral rotation, primarily affecting girls aged 10 to 18. Approximately 27% to 38% of children with AIS also suffer from osteopenia (low bone mass). Currently, the most common method to assess bone mineral density (BMD) is dual x-ray absorptiometry (DXA), which exposes patients to ionizing radiation and increases cancer risk. A novel non-ionizing radiation method has been developed to assess bone strength using the ultrasound reflection coefficient (RC) index. The aim of this study was to assess the intra- and inter-rater reliability of ultrasound reflection coefficients to assess bone strength for children with AIS.

Methods

Sixty subjects with AIS were recruited with signed consent. Standing 3D ultrasound (US) scans were obtained from each subject. Literature has reported that US signals reflected from the interface between soft tissue and bone can provide the strength properties of the bone. The reflection coefficients and soft tissue thickness were measured at the lowest lumbar vertebra (L5) due to the minimal spinal axial rotation there. During the measurements, the centers of the left and right lamina were identified. The centers of laminae are the relatively flat areas of a vertebra that reflect the most US signal. The RC value and soft tissue thickness were calculated using in-house developed software. This RC measurement was repeated for another 4 US frames which were 2 above and 2 below the first center frame. Two raters (R1 and R2) measured each US image twice with 1 week apart to minimize memory bias. The reliability was analyzed based on the average RC values from the 10 measurements (5 left and 5 right) on each subject.

Results

The average soft tissue thickness and RC values for R1 vs R2 on the 2nd measurements were 3.7±0.5 vs 3.8±0.5 mm and 0.072±0.029 vs 0.078±0.033, respectively. All the intra- and inter-rater ICC [2, 1] reliabilities of both the RC measurements and soft tissue thickness ranged from 0.71 to 0.98, which was indicative of good to excellent reliability. The RC intra-rater reliability ICC [2,1] for R1 and R2 were 0.98 and 0.84, respectively. The RC inter-rater reliability ICC [2,1] for the first and second measurements were 0.86 and 0.85, respectively.

Conclusion

A new US method was developed to measure the RC from spinal US and the results showed that the proposed method was repeatable and reliable. Future analysis of how bone strength correlates with the RC value will be conducted.

Funded By: the Scoliosis Research Society and The Women and Children's Health Research Institute

Abstract #: 146
Presenter: Benjamin Schultz
Supervisor: Menon, Geetha
Title: Practice changes in radiation therapy for locally advanced cervical cancer
Authors: Benjamin Schultz, Fleur Huang, and Geetha Menon
Theme: Lifelong women's health

Introduction: Curative radiotherapy for locally advanced cervical cancer (LACC) requires a brachytherapy (BT) boost following concomitant external beam radiation therapy (EBRT) and chemotherapy. Recent international guidelines recommend attention to dose aims and overall treatment time (OTT), adherence to contouring standards and intensity modulated EBRT, along with an interstitial (IS) addition to BT in MR-based volumetric planning.

Methods: LACC patients treated with EBRT+BT between 01/2013-12/2015 (cohort 1; C1) and 07/2017-06/2020 (cohort 2; C2) at the Cross Cancer Institute were identified. Clinical and treatment details were extracted from health records and analyzed using descriptive statistics.

Results: At EBRT, 56.9% were ≥ stage IIB in C1 (N = 87; median age 64 [31-90] years) compared to 63.5% in C2 (N = 104; median age 68 [24-93], mean EBRT planning target volume 114±117 cc). Intensity modulated EBRT was used in all of C2, while C1 also included 3D conformal EBRT. All C2 patients received a dose of 44.3 Gy EQD2 in 25 fractions to the EBRT planning target volume; mild heterogeneity in C1 (5% treated to 50 Gy EQD2 in 25 fractions). Nodal involvement was similar: 66.6% in C1 and 69.2% in C2. Nodal target doses were more consistent in C2. Mean high risk target volumes at pulsed-dose-rate BT were 42.1±29.8 cc for C1 and 33.4±22.9 cc for C2. Tandem+Ring applicators were used similarly in both groups (68% C1 and 65% C2); 17% C1 and 22% C2 used Tandem+Ovoids. IS usage increased from 20.2% (median 4 [1-4] used per patient) to 81.4% (median 4 [1-11]). All C1 and C2 treatments were MR-planned. Contouring of recommended structures for dosimetry increased from 43% (07/2017-12/2018) to 96% (01/2019-06/2020) in C2; 31% in C1. Mean EBRT+BT dose to target was 87.5±10.6 and 89.0±7.6 Gy EQD2 for C1 and C2, respectively (tumor dose escalation). Dose contribution from ring and ovoids improved from 41.2±11.6 to 36.1±14.2% (vaginal dose de-escalation), while that from IS (11.9±11.8% vs 13.3±11.8%) components remained similar. Median number of BT pulses was 58 for C1 [30-66] and C2 [38-58]. Mean OTT was 49.1±10.3 days for C1, improved to 45.3±5.3 for C2.

Conclusion: International guidelines, for both EBRT and BT, were rapidly integrated in our growing practice, for more consistency. Clinical outcomes will be evaluated in future.

Funded By: Alberta Cancer Foundation partnered with the Cancer Research Institute of Northern Alberta (CRINA-ACF summer studentship)

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Abstract #:	40
Presenter:	Jesus Serrano-Lomelin
Supervisor:	Ospina, Maria
Title:	Geographic inequalities of respiratory health services utilization during childhood in Edmonton and Calgary: a tale of two cities
Authors:	Jesus Serrano-Lomelin, Charlene Nielsen, Anne Hicks, Susan Crawford, Jeffrey Bakal, Maria B. Ospina
Theme:	Children's health and well-being

Introduction. Young children are susceptible to respiratory diseases. Inequalities exist across socioeconomic groups (SES) for a variety of pediatric respiratory diseases in Alberta. However, the geographic distribution of inequalities in respiratory health services utilization in early childhood has not been fully explored. The main aim of this study was to identify geographic inequalities in respiratory health services utilization in early childhood in Calgary and Edmonton.

Methods. We conducted a cross-sectional geographic analysis of data from a retrospective cohort of all singleton live births that occurred in Calgary and Edmonton between 2005 and 2010. We extracted individual data on hospitalizations and emergency department (ED) visits between birth and five years of age associated with a primary diagnosis of acute bronchiolitis, asthma, croup, influenza, pneumonia, other acute lower respiratory tract infections, and/or other acute upper respiratory tract infections. We used dissemination areas (DA) as geographic units of analysis to aggregate all respiratory hospitalizations and ED visits and calculated smoothed standardized prevalence ratios (sSPR) by DA as the main outcome. Eigenvector spatial filters (ESF) were derived to identify areas with low to high sSPR. The association between geographic areas defined by ESF quintiles and sSPR values was estimated in a regression model including area-level SES, nitrogen dioxide (NO2), and particulate matter (PM2.5) as covariates.

Results: A total of 111,056 respiratory health services events were registered by the 119,909 children in the birth cohort. Geographic inequalities in respiratory health services utilization in both cities were identified. There were a 1.4-fold gap in Edmonton and a 1.5-fold gap in Calgary between the areas with the highest and the lowest smoothed SPR. This translates into 40% to 50% more pediatric respiratory health services events in urban areas spatially associated with the highest smoothed SPR compared to areas spatially associated with the lowest smoothed SPR. In Calgary, several small geographic conglomerates scattered across the city had a high demand of pediatric respiratory health services, while areas with a high demand for pediatric respiratory health services in Edmonton followed a regional-cluster spatial distribution.

Conclusion: There are geographic inequalities of respiratory health services utilization in Calgary and Edmonton that are independent of SES, NO2 and PM2.5. Research on other contextual factors (e.g., access to health care) underlying high demands of pediatric respiratory health services is needed.

Funded By: This work was supported by a Respiratory Health Strategic Clinical Network Research and Innovation Seed Grant [2019], and the Lois Hole Hospital for Women through a Women and Children's Health Research Institute Recruitment Award [2016-2021]

Abstract #:	122
Presenter:	Prachi Shah
Supervisor:	Hicks, Elizabeth
Title:	It's All About That Trach! - Using a Modified Delphi Approach to Developing Pediatric Tracheostomy Teaching Tools
Authors:	Prachi Shah, Tamizan Kherani, Trina Uwiera, Anne Hicks
Theme:	Children's health and well-being

Pediatric tracheostomy care is intimidating; regular and emergency care are critical skills. Tracheostomy care training is vital for pediatric patients as they have multiple people involved in their care and are fully dependent on their tracheostomy tubes for breathing. An AHS team is developing an informational tool, the "Tracheostomy Journey", to help families and healthcare providers understand and communicate clearly about pediatric tracheostomy. A needs assessment identified consistent, universal multimodal teaching and communication tools for families, trainees, hospital & home care providers as a primary need. Consistency in training will also improve communication between caregivers and families of these children.

This project provides a structured approach to developing training modules that address learning goals for safe, consistent pediatric tracheostomy care. The project consisted of two components: 1)Update and consolidate basic care checklists completed by families before hospital discharge. 2)Formalize current unstructured emergency training while building new resources to teach families, hospital staff and trainees through goal-oriented simulations.

We consolidated 7 Home Care tracheostomy care checklists and developed 22 simulations to teach specific skills for tracheostomy care to families and clinical teams, incorporating input from multiple stakeholders to consolidate and unify content. The materials emphasize confidence building as learners master each skill. Each module consists of a scenario, preceptor script and debriefing materials to ensure the learning point is addressed. Each is scripted to allow filming so trainees can review scenarios as needed. Simulations were reviewed by physicians, allied health professionals, and trainees.

The materials and supporting documents are set up for evaluation by an expert team via a modified Delphi process, and beta testing with trainees including knowledge and confidence assessment before and after training. These tools are ready for employment and anticipated to improve teaching and communication for families and trainees caring for children with tracheostomy.

Funded By: FoMD Health Professions Education Summer Studentship

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Abstract #:	27
Presenter:	Sumaiyah Shaha
Supervisor:	Riddell, Meghan
Title:	Development of a Physiologically Oriented Placenta Organoid Model
Authors:	Sumaiyah Z. Shaha , Saba Saadat, Meghan Riddell
Theme:	Pregnancy and developmental trajectories

Introduction

The placenta is a fetal-derived organ that supports the exchange of oxygen, nutrients, and wastes between the mother and fetus. The placental surface is uniquely composed of a single giant multinucleate epithelial cell serving as a selective barrier, called the syncytiotrophoblast (ST). Until recently, study models did not accurately represent the complex placental surface and its crucial interactions with underlying placental progenitor cells, cytotrophoblasts(CT). Further, 2D CT cultures are non-proliferative and spontaneously differentiate to ST, requiring constant tissue sourcing. Organoids are simplified 3D tissue models that represent an organs cellular organization allowing for the study of complex multi-cellular processes. Recently, two placental organoid models were developed, however, these models form with inverse orientation where the ST is underneath a CT layer that forms the organoid surface. We propose to develop a 3D self- sustaining placenta organoid model that recapitulates the physiological organization and better exemplifies the complexity of the surface of the placenta.

Methods

CTs were isolated from fresh human 1st trimester placental villi. Villi were trypsinized for cell release and immunopurified via negative selection with CD9, MHC Class I and II. Cell purity was assessed by staining for trophoblastic markers (E-cadherin, p63, GATA-3) and stromal (vimentin) markers. CTs were cultured on collagen IV coated microcarriers in rotational culture to establish cell attachment to beads in defined trophoblast organoid medium for up to 21 days. Organoids were fixed and cellular composition was examined by staining for trophoblast lineage markers (E-cadherin, p63, GATA-3 (CT), human chorionic gonadotropin (hCG; ST), HLA-G extravillous trophoblast), and proliferation was examined by staining for Ki67.

Results

CT isolation procedures yield a pure population of CT cells positive for GATA-3, p63, and E-cadherin (mean values 94%, 95%, and 94%, respectively). Cell to bead ratio, rotational speed, and culture volume were optimized for maximum CT adherence to beads. Marker staining showed that the established placental organoids are positive for CT and ST markers and negative for other trophoblast lineages. They also contain a proliferative cell population up to 20 days in culture.

Conclusions

Our current 3D model forms with physiologically oriented surface ST and an underlying mixed population of proliferative and non-proliferative CT. Future work is needed to develop protocols for passaging, conditions for expansion of the organoids, to characterize the ST structure, and to ensure the organoid genetic signatures are representative of placental tissue. This unique model will be used in the future to study ST specific pathology in pregnancy complications, placental targeted drugs, and unintentional off-target effects of maternal therapies.

Funded By: WCHRI Innovation Grant

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Abstract #: 147
Presenter: Nayiar Shahid
Supervisor: Hammond, James
Title: Characterization of novel HEK293 cell line (HEK293-ENT1KO) to assess the role of equilibrative nucleoside transporter protein subtype-2
Authors: Nayiar Shahid, Chris Cromwell, Basil P. Hubbard and James R. Hammond.

Theme: Lifelong women's health

Background: Equilibrative nucleoside transporters (ENT1, ENT2) mediate the transmembrane flux of endogenous nucleosides and nucleoside/nucleobase-analog drugs that are used to treat breast cancer (5-fluorouracil), lymphoma (cytarabine), endometrial and uterine cancers (gemcitabine) and are also known to treat viral infections in pregnant women (ribavirin, abacavir). ENT1 has been studied the most in this regard due to its relative predominance in most tissues, and the availability of highly selective ENT1 inhibitor, nitrobenzylthioinosine. ENT2, on the other hand, is expressed at relatively lower levels in most cells, with no selective inhibitor. Thus, there is much less information on how these drugs interact with ENT2 or factors that affect ENT2 expression. Interestingly, ENT2 has also been proposed to play a role in ENT1 trafficking to the plasma membrane via hetero-oligomerization, and this appears sensitive to phosphorylation state. An understanding of the role of ENT2 is critical to exploiting its impact on therapies using nucleoside analog drugs.

Objectives: Most cells endogenously express both ENT1 and ENT2 and there has been no human centric model system where ENT2 can be studied in isolation. To address this lack, we developed a novel Human Embryonic Kidney (HEK293) cell mutant (using CRISPR-Cas9) lacking ENT1 and having just ENT2 (HEK293-ENT1KO) as the only functional ENT in this system. We report on the characterization of HEK293-ENT1KO model in terms of ENT2 expression levels, functional activities and selective affinities for a range of known nucleoside/nucleobase compounds (endogenous and therapeutic analogs).

Methods: We assessed transporter function by measuring the initial rates of [3H]2-chloroadenosine uptake (2.5-300µM) and the binding of the specific ENT1 probe [3H]NBMPR. Protein levels were assessed by immunoblotting using ENT-specific antibodies. Compensatory changes in other transporter proteins and adenosine metabolic enzymes were examined using qPCR. Ki values of transport inhibitors were defined using the IC50 derived from concentration-response curve analyses and the Km of the [3H]2-chloroadenosine for ENT2 in this model.

Results: HEK293-ENT1KO cells had a similar level of ENT2 uptake (Km-49±28µM, Vmax-1.3±0.6pmol/µl/s) as wild-type (Km-25±17µM, Vmax-0.6±0.1pmol/µl/s). Neither [3H]NBMPR binding sites, nor ENT1 protein, were observed in HEK293-ENT1KO cells in binding assay and western blot. There relative expression of ENT1 was negligible in ENT1KO compared to the WT. The isolated transporter subtype-2 has shown expected affinities for a range of nucleoside/nucleobase substrates: adenine (2300±750µM), hypoxanthine (340±54µM), gemcitabine (820±79µM), ribavirin (500±140µM) and inhibitors: NBMPR (2.9±0.3µM), dipyridamole (0.5±0.1µM), dilazep (2.6±0.9µM), ticagrelor (11± 2.4 µM).

Conclusion: Our data show that removing ENT1 from HEK293 cells does not impact the expression or function of ENT2. This model can be used to advance our knowledge of pathways that may be exploited to modify cellular function of ENT2 to enhance the therapeutic use of existing and novel nucleoside analogues; specifically the individual role of ENT2 that are relevant to breast and uterine cancers and viral infections in pregnant women.

Funded By: Natural Sciences and Engineering Research Council of Canada (NSERC)

women & children's health research institute

Abstract #:	72
Presenter:	Rishav Sharma
Supervisor:	McBrien, Angela
Title:	Associated genetic and extra-cardiac anomalies and outcomes in prenatally detected tetralogy of Fallot
Authors:	Rishav Sharma, Lisa K Hornberger, Oana Caluseriu, Karen Y Niederhoffer, Christy-Lynn Cooke, Luke Eckersley, Lily Lin, Michelle Rushfeldt, Rose He, Angela McBrien
Theme:	Children's health and well-being

Introduction: Historically, prenatal detection of tetralogy of Fallot (ToF) was poor and around 60% had major extracardiac (ECA) or genetic anomalies. Recently, prenatal detection of ToF has improved, along with a wider range of genetic testing options having become available. Knowledge of outcomes and risk of associated anomalies is crucial for prenatal counselling. We hypothesize that prenatal ToF now has a different risk profile for ECAs and genetic anomalies than previously reported.

Methods: A retrospective study of all fetuses with a diagnosis of ToF in our Fetal Cardiology program from 2012-2019. ToF type double outlet right ventricle was excluded. Pre and postnatal charts and imaging reports were reviewed for ToF subtype, additional cardiac and non-cardiac diagnoses and outcomes.

Results: Of 83 cases, 49 had standard ToF, 24 pulmonary atresia (14 with major collateral arteries, 10 without), and 10 absent pulmonary valve. There was ≥1 ECA in 41% (34/83), including 6% (5/83) with 2 and 4% (3/83) with 3. ECA sub-types were: 10 gastrointestinal, 8 neurological, 8 pulmonary, 7 renal, 4 musculoskeletal, and 8 others. Of 76 with genetic testing, 30% (23/76) had genetic anomalies (39% (9/23) Trisomy 21, 35% (8/23) 22q11 deletion, 9% (2/23) Trisomy 18, 9% (2/23) Trisomy 13, and 9% (2/23) other). Additional diagnoses: 4% (3/76) had VACTERL spectrum, 5% (4/76) had variants of uncertain significance, and 1% had (1/76) placental mosaicism. Right aortic arch was associated with 22q11 deletion (28% (7/25) vs 2% (1/51) $p<0.001$). ToF with atrioventricular septal defect (AVSD) was strongly associated with Trisomy 21 (100%, 3/3 tested). Those with ≥1 ECA were more likely to have a genetic abnormality (47% (14/30) vs 24% (9/38), $p<0.05$). Outcomes were: 22% (18/83) termination, 5% (4/83) intrauterine fetal deaths and 72% (60/83) livebirths, with 1 lost to follow-up. Of live births, there were 3% (2/60) neonatal and 7% (4/60) late deaths, and 90% (54/60) were alive at last follow-up (mean age 3.5±2.4 years).

Conclusion: ECAs are less common in prenatally diagnosed ToF in the modern era, however the rate of genetic diagnoses is similar to previously published data. ToF with right aortic arch and ToF with AVSD in particular have strong genetic associations. Additionally, genetic diagnoses are more common in those with an ECA.

Funded By: This research was completed through the WCHRI summer studentship that has been funded by the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women through the Women and Children's Health Research Institute.

Abstract #:	161
Presenter:	Kristen Simone
Supervisor:	Chandra, Sue
Title:	Optimizing antenatal corticosteroid administration for women at risk of preterm birth: a quality improvement project
Authors:	Kristen Simone, Khalid Aziz, Megan Gleddie, Priscilla Frenette, Heather Robinson, Sue Chandra
Theme:	Pregnancy and developmental trajectories

Introduction: Preterm birth at less than 37 weeks' gestation occurs in approximately 8% of pregnancies in Canada and is associated with perinatal morbidity and mortality, long-term health consequences and socioeconomic burden. Administration of antenatal corticosteroids (ANCS) within 7 days of delivery significantly reduces adverse outcomes related to prematurity including perinatal and neonatal death, respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis and mechanical ventilation. Antenatal corticosteroids administered outside of this window are associated with reduced benefit and potential risks. The Canadian Preterm Birth Network has found substantial variability between sites in the rate of ANCS administration in the week preceding preterm delivery. This project aims to develop and implement a decision making tool to increase the percentage of infants born prematurely who receive antenatal corticosteroids within 7 days prior to delivery.

Methods: Evidence-based Practice for Improving Quality (EPIQ) methods were used to engage a multidisciplinary team to a develop an evidence-based decision making tool to guide the administration of ANCS. The tool was implemented on labour and delivery, triage and antepartum wards at a tertiary care centre after educational presentations were offered to Obstetricians, Maternal Fetal Medicine Specialists, NICU, residents and nursing staff and feedback from these stakeholders was incorporated. The Plan-Do-Study-Act (PDSA) cycle was used as a template to evaluate the change in practice.

Results: A PDSA cycle was completed from July 27-August 6 2020. During this period, 66 eligible patients were assessed with the tool used for 33 patients resulting in a 50% uptake of the tool. 11 out of the 33 patients received ANCS. 6 of those 11 patients delivered with the 7 day window of ANCS administration. The nursing staff gave feedback on the increased clinical workload required to implement this tool.

Conclusion: The use of a decision tool was effective in guiding decision making on whether to administer ANCS. The next PDSA cycle aim to increase uptake of the tool from 50% to 80%. The data sheet will be streamlined in response to feedback and involves an audit card to ask whether steroids are indicated or not, and whether the tool was used to guide decision on ANCS administration.

Funded By: Unfunded

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Abstract #: 17
Presenter: Reshma Sirajee
Supervisor: Hawkes, Michael
Title: Growth Faltering and Developmental Delays in HIV-Exposed Uninfected Infants in Uganda

Authors: Reshma Sirajee, Andrea L. Conroy, Sophie Namasopo, Robert O. Opoka, John Kim, Stephanie Lavoie, Sarah Forgie, Bukola Oladunni Salami, Michael T. Hawkes

Theme: Children's health and well-being

Background: Globally, 1.5 million HIV-infected mothers give birth to children who are HIV exposed but uninfected (HEU). In some HIV endemic nations, HEU newborns represent nearly 30% of all births. Recently, concerns have emerged about HEU children who have increased risk of impaired early linear growth, higher mortality, poor psychomotor and cognitive development delays, hearing loss, and language expression delay, and chronic diarrheal disease. This study examines the early risk factors in HEU infants to predict growth faltering and neurodevelopmental delay at 18 months of age.

Methods: We prospectively followed a cohort of HEU infants from birth to 18 months of age. The height, weight, head circumference, and mid-upper arm circumference (MUAC) were collected and compared to the World Health Organization growth charts. The Malawi Development Assessment Test (MDAT) was performed at 12 and 18 months of age to determine developmental milestones across several domains: gross motor, fine motor, language and social. The Color Object Association Test (COAT) was used at 18 months of age to determine the declarative and immediate memory in HEU infants.

Results: Between March 2016 to December 2018, 375 mother-child pairs were enrolled. Mothers were a median 28 years of age and 32% had a known diagnosis of HIV prior to pregnancy. The cohort included 53% of female infants. Also, 11% of the infants were premature and 7.6% had low birth weight. About 147, 109, and 170 infants completed follow-up at 6 weeks, 12 months, and 18 months of age respectively. Eight infants tested positive by deoxyribonucleic acid polymerase chain reaction (DNA PCR) for HIV and were excluded from subsequent analysis. A total of 197 infants were lost to follow-up at 18 months of age. The final cohort consisted of 170 infants who completed the MDAT at 18 months of age. The number of HEU infants who were stunted (low height-for-age) and underweight increased from 6 weeks to 18 months of age. At 6 weeks, 12 months, and 18 months of age, 32%, 43%, and 58% of infants were stunted and 7.4%, 15%, and 15% of infants were underweight, respectively. Failure to thrive, defined as crossing two major percentile lines downward on the weight-for-age growth chart, was observed in 21% of infants during the first 18 months of life. HEU infants had behavioral scores on the MDAT that were similar to the reference range for normal infants. The mean score on the COAT (declarative memory) at 18 months of age was 5.5 compared to 6.9 in developmentally normal children. The MDAT score at 18 months of age showed cross-sectional correlation with weight- (ρ=0.36, $p<0.0001$), height- (ρ=0.41, $p<0.0001$), head circumference- (ρ=0.26, $p=0.0011$), and MUAC-for-age (ρ=0.34, $p=0.0014$). Failure to thrive was associated with lower MDAT scores at 18 months of age ($p=0.007$). Lower weight-for-height z-scores were associated with lower declarative memory at 18 months of age (ρ=0.32, $p=0.0017$). Low birth weight (<2500g), predicted lower MDAT score at 18 months of age ($p=0.0010$).

Conclusion: In a prospective cohort of HEU infants in Uganda, low birth weight, stunting, and failure to thrive were common and were associated with lower attainment of developmental milestones and lower declarative memory at 18 months of age.

Funded By: We would like to thank the Department of Pediatrics, Faculty of Medicine and Dentistry, Li Ka Shing Institute of Virology, and Women and Children's Health Research Institute for supporting our research work.

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Abstract #:	5
Presenter:	Meghan Sit
Supervisor:	Ross, Sue
Title:	Effect of oral probiotics on menopause symptoms and related risk factors: findings from a systematic review
Authors:	Meghan Sit, Aakankshya Kharel, Sue Ross, Beate Sydora
Theme:	Lifelong women's health

Introduction: Postmenopausal and perimenopausal women may present with a broad range of symptoms and may be at higher risk for particular diseases such as cardiovascular and metabolic diseases and bone health. Probiotic supplements have been shown to be beneficial for several health issues. The objective of this study was to conduct a systematic review in order to explore the current research assessing the effect of oral probiotic supplements on menopause-related symptoms.

Methods: Our systematic review followed PRISMA guidelines. We searched 8 databases including MEDLINE, EMBASE, Cochrane and others for articles published up to May 21, 2020. Menopause and probiotic-related key words were used for database searches. Data was collected onto Covidence. Two reviewers independently screened for experimental studies assessing the effect of oral probiotics supplements alone on postmenopausal or perimenopausal women experiencing menopause-associated symptoms. Data was extracted from the final selection and analyzed descriptively.

Results: 766 non-duplicate records were identified and 16 met the eligibility criteria. Studies were randomized control trials, non-randomized trials, non-controlled randomized trials, and cohort studies. The average age of participants consuming probiotics was 60±5 years. The majority of participants (88%) were postmenopausal with a minority being perimenopausal. Outcome measures included metabolic syndrome, weight and cardiovascular disease risk (n=6), urogenital and vaginal health (n=5), bone health (n=5) and general menopause symptoms (n=1). Lactobacillus and Bifidobacterium probiotics were most commonly used for intervention. 11 studies used a multiple species intervention and 5 studies used a single probiotic species intervention. 4/6 studies investigating metabolic syndrome, weight and CVD risk reported beneficial effects while 1/6 reported no effect and 1/6 reported a limited effect. 3/5 studies assessing urogenital and vaginal health reported positive effects while 1/5 reported no effect and 1/5 reported a limited effect. 3/5 studies reporting on bone health noted a favourable effect and 2/5 reported a limited effect. A single study assessing general menopause symptoms reported no effect after probiotic intervention.

Conclusion: Evidence collected in this systematic review suggests that oral probiotic supplements may serve as a more natural, lower risk alternative therapy for menopause-associated risk factors. There is a lack of research on the effect of probiotic supplements on typical menopause symptoms. Further research on this topic is imperative.

Funded By: Meghan Sit received partial funding from the Faculty of Medicine and Dentistry Office of the Provost and VP (Academic) Summer Student Award and partial funding from research funds provided by WCHRI to the Cavarzan Chair of Mature Women's Health Research.

Abstract #:	59
Presenter:	Katherine Souter
Supervisor:	Graf, Daniel
Title:	Bmp2 expression in cranial sutures does not correlate with active bone growth
Authors:	Katherine Souter, Daniela M. Roth, Daniel Graf
Theme:	Children's health and well-being

Introduction

Cranial sutures facilitate secondary skull growth to accommodate pressure from the growing brain and extracranial forces. Bmp2 promotes osteogenesis, mutations in which have been associated with craniosynostosis (premature cranial suture fusion). Synostosis treatment requires invasive surgical intervention to re-open fused sutures and allow expansion of the developing brain. The precise role of Bmp2 in cranial sutures has not been established, but Bmp2 expression has been detected in excised, obliterated sutures. Extrapolating from the literature, one might assume that Bmp2 participates in active bone formation at the suture front although this has not been formally shown. In this study we characterize the expression pattern of Bmp2 in developing, actively growing, and resting sutures to contextualize the spatial and temporal findings within current knowledge. This is a first step for subsequent functional analysis using specific mutant mice.

Methods

Literature review revealed that Bmp2 plays a key role in osteogenesis and that its specific role in sutures remains unknown. Bmp2 lacZ reporter mice were used to characterize Bmp2 expression in cranial sutures. Bmp2 wt/lacZ (Bmp2lz) and control Bmp2 wt/wt (Bmp2wt) mice were collected at embryonic day 18.5 (E18.5), postnatal day 0 (P0), P7, P14, P30, 1 month, 2 months, and 1 year 2 months and stained with X-Gal. Whole mount stained skulls were documented prior to embedding in paraffin for histological analysis. Nuclear fast red and picrosirius red were used as counterstains. TRAP staining was used to detect osteoclasts.

Results

Whole mount LacZ staining for Bmp2 expression was documented for P15, 1 month, 2 months, 3 months, and 1 year 2 month-old mice. Dynamic expression of Bmp2 was observed; it was strong up to P7 in developing sutures, reduced between P14 and 1 month, and renewed in sutures that have ceased active growth. Histological analysis at E18.5 and P7 showed Bmp2 expression associated with bone/cartilage progenitor cells and ossifying bone, as well as TRAP-positive bone-resorbing osteoclasts. Decreased/absent Bmp2 expression was observed in mature bone. At P7, Bmp2 expression was reminiscent of osteoblast-progenitor cells in the suture mesenchyme, indicating Bmp2 involvement in suture differentiation.

Conclusion

Bmp2 expression was found in frontal and internasal sutures, as well as developing facial bones. Its persistent expression in quiescent, non-growing sutures in late adulthood indicates a hitherto undescribed role of Bmp2 in maintenance of suture patency. This project sheds new light on a well-established osteogenic protein that appears less associated with bone, but rather bone-progenitor cells, or cells maintaining suture patency rather than growth alone.

Funded By: Office of the Provost and VP (Academic) Summer Studentship Award from the Faculty of Medicine and Dentistry (FoMD)

NSERC and Funds for Dentistry

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Abstract #:	148
Presenter:	Jordan Southcott
Supervisor:	Cutumisu, Maria
Title:	Detecting patterns of mental health support utilization by gender with machine learning
Authors:	Jordan Southcott, BSc; Chang Lu, MEd; and Maria Cutumisu, PhD
Theme:	Lifelong women's health

Introduction: Mental illness is one of the most pressing medical challenges facing society, with women being affected disproportionately. Thus, identifying gaps in mental-health support-seeking is important for public health. The goal of this research is to determine if unsupervised machine learning can reveal (1) sex-based differences of mental-healthcare support-utilization in the CCHS-MH dataset and (2) gaps in support-utilization.

Methods: This study constitutes an exploratory analysis of the latest CCHS-MH survey conducted by the Canadian government to assess mental health, which measured support-seeking for any mental-health issue from 24,788 Canadians. The study goal was twofold: to test the effectiveness of unsupervised learning algorithms on categorical psychological survey data and to find patterns of women's utilization and under-utilization of supports for mental-health. Clustering efficacy was measured with Dunn and Silhouette indices.

Results: Of the clustering methods compared (K-Means, Hierarchical Agglomerative, and Fuzzy C-Means), Fuzzy C-Means Clustering yielded the best-fit model for the data. A 4-factor model was found to be optimal based on the Exploratory Factor Analysis, with loadings available in Table 2: Mixed Support, No Support, Social Support, and Family Doctor. Multiple differential effects between men and women were discovered by this clustering.

Conclusions: Fuzzy C-Means Clustering can effectively cluster large datasets of categorical psychological data. Findings suggest that women relied on social support but under-utilized family doctors. We suppose this effect is caused by entrenched sexism in the medical establishment and should be remedied by a greater focus on educational policies to reduce sex-based bias in the field.

Funded By: The SSHRC, NSERC, and Killam.

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Abstract #:	123
Presenter:	Hyelin Sung
Supervisor:	Scott, Shannon
Title:	Evaluating a social media campaign for a parent educational video on bronchiolitis
Authors:	Hyelin Sung, Hannah Brooks, Chentel Cunningham, Shannon D. Scott
Theme:	Children's health and well-being

Introduction

Bronchiolitis is a viral infection, commonly caused by the respiratory syncytial virus (RSV), and mainly affects children under 2. A 12-week social media campaign was developed and conducted from 14 October 2019 to 30 November 2019 to promote and disseminate a research-based bronchiolitis educational video for the 2019 CIHR video competition. The social media accounts used were: Child Health to Enhance Outcomes (ECHO), Alberta Research Centre for Health Evidence (ARCHE), and Translating Emergency Knowledge for Kids (TREKK).

Methods

User interactions were recorded for Facebook and Twitter accounts, website, and YouTube. Metrics were collected monthly for the time periods of baseline (August - September 2019), campaign (October - November 2019), and post-campaign (December 2019 - March 2020). Mean monthly changes and standard deviations were generated for each time period. For comparison, percent differences of mean changes between periods were generated.

Results

During the campaign, user interactions increased for Twitter accounts (ECHO/ARCHE/TREKK) including new followers (25.6%/41.7%/54.7), profile visits (178.7%/96.7%/56.7%), and impressions (87.4%/223.0%/31.4%). There was a general decrease in new followers (-19.4%/-11.8%/-28.0%), profile visits (-61.6%/-53.7%/-43.8%), and impressions (-37.3%/-22.2%/-47.8%) following the campaign compared to the campaign period. Facebook accounts (ECHO/TREKK) experienced an increase in monthly page likes (0.0%/209.1%) and post reach (62.1%/61.2%) throughout the campaign. Post campaign, there was a decrease in page likes (-6.7%/-9.8%), a decrease in post reach for the ECHO Facebook (-1.2%), but an increase in post reach for the TREKK Facebook (21.3%) compared to the campaign period. The ECHO website experienced a decrease in visits (baseline to campaign: -2.8%/campaign to post campaign: -28.2%) but visits to the 'tools' page increased (444.5%) during the campaign and decreased after (-70.2%). The TREKK website experienced an increase in website visits (45.4%) and 'parent and family' page visits (29.8%) and an overall decrease following the campaign (-13.7%: website visits/-32.0%: 'parent and family' page visits). There were 815.5 'tools' page clicks recorded on the ECHO website and 28.5 'parent and family' page clicks recorded for the TREKK website during the campaign.

Conclusion

Overall, there was a visible increase in user interactions throughout the campaign period, suggesting that social media may be a useful method to disseminate our research with end users. However, it requires dedicated planning and resources. Our results demonstrate that once the campaign ended, user engagement levels did not sustain at campaign levels.

Funded By: CIHR, NCE, WCHRI, Faculty of Nursing

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Abstract #:	75
Presenter:	Jonas Szelewicki
Supervisor:	Kassiri, Janani (Jay)
Title:	Concordance between MRI and neuropathology findings in surgically-managed pediatric patients with refractory epilepsy
Authors:	J. Szelewicki, B. Sinclair, N. Liu, A. Tamm, J. Kassiri
Theme:	Children's health and well-being

Poorly controlled seizures in childhood have a detrimental impact on the developing brain. In children with pharmacoresistant epilepsy, surgical resection of epileptogenic foci can be an effective means of achieving seizure control. Neuroimaging is crucial to accurately localize epileptogenic foci and additionally influences pre-surgical patient counselling and post-surgical seizure control. The objective of our study is to compare pediatric epilepsy surgery patients' pre-surgical MRI (either 1.5 or 3 Tesla (T) magnet strengths) findings with their post-surgical neuropathology results and post-surgical seizure outcome. 25 pediatric patients enrolled in the Pediatric Comprehensive Epilepsy Program at the Stollery Children's Hospital from January 1, 2015 to April 30, 2020 were identified for retrospective chart review. Data including patient demographics and history, pre-surgical MRI findings, resected tissue pathology results, and post-surgical seizure outcome at 12 months were collected from electronic medical records, entered into REDCap database, and analyzed. Concordance was defined as complete (identical MRI and neuropathology diagnoses), partial (correct category of neuropathology identified or correct diagnosis on a list of ≥ 2 differential diagnoses on MRI report), or no concordance. Complete, partial and no concordance were observed in 12/25 (48%), 7/25 (28%), and 6/25 (24%) patients, respectively. Excluding patients with focal cortical dysplasia (FCD), complete, partial and no concordance were observed in 10/19 (52.6%), 7/19 (36.8%), and 2/19 (10.5%) patients, respectively. 13 of the original 25 patient cohort currently have post-operative follow-up data available at 12 months. Of these, 11 patients (84.6%) with partial or complete concordance were seizure-free. These data demonstrate that MRI can accurately identify pre-surgical lesions in the majority of refractory epilepsy patients, with the exception of patients with FCD. Exclusive use of higher resolution 3T MRI to identify epileptogenic foci should improve likelihood of accurate lesion identification and radiologic-neuropathologic concordance, optimizing surgical and clinical outcomes.

Funded By: Department of Radiology and Diagnostic Imaging

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Abstract #: 90
Presenter: Rebecca Tan
Supervisor: Alexander, R Todd
Title: Mutations in FAM111A; A potential cause of autosomal dominant hypocalcemia
Authors: Rebecca Tan, Christy Lee, and R Todd Alexander
Theme: Children's health and well-being

Autosomal Dominant Hypocalcemia (ADH) is a childhood disorder resulting in low blood calcium levels and inappropriately low levels of parathyroid hormone (PTH), a hormone which functions to increase blood calcium. In 2014, a nine-year old female presented to the Stollery Emergency Department with seizures and was found to have low blood calcium levels (0.72 mM ionized), low PTH (1.2 nM) and increased urinary calcium excretion. Supplemental vitamin D and calcium were used to treat her. Given her clinical symptoms, the genes known to cause ADH (CASR and GNA11) were sequenced twice, but a mutation that could cause her disease was not identified. Her parents and brother had normal blood calcium, urinary calcium excretion and PTH levels. Therefore, whole exome sequencing was completed on her and her parents. Trio analysis revealed a novel mutation in the FAM111A gene. FAM111A mutations are known to cause Kenny Caffey syndrome and Gracile Bone disease, which are both characterized by low blood calcium levels, low PTH, short stature and bony abnormalities. The patient does not have short stature or bony abnormalities, but her other characteristics are consistent with a mutation in the FAM111A gene causing her disease. We therefore hypothesize that mutations in FAM111A cause a range of diseases that all include low blood calcium and PTH levels. To determine if the novel FAM111A mutation causes ADH, we generated with CRISPR/Cas9 a mutant mouse carrying the same mutation. We hypothesized the mutant mice would have low blood calcium and low PTH on a low calcium diet. FAM111A heterozygous (HET) (Female n=22, Male n=13), homozygous (HOM) (Female n=6, Male n=8), and wild-type (WT) (Female n=9, Male n=18) mice receiving a low calcium (0.01%) diet were placed in metabolic cages to collect 24-hour urine and blood before euthanasia. Blood calcium and PTH levels were not significantly different between wild-type and mutant mice. However, contrary to our hypothesis, the urinary calcium excretion of female mice as assessed as a calcium/creatinine ratio (mM/mM) and 24-hour calcium excretion (mg/day) was significantly ($p<0.05$) lower in mutant HET (0.67 ± 0.13, 0.12 ± 0.03) and HOM (0.72 ± 0.10, 0.13 ± 0.03) than WT (1.17 ± 0.36, 0.20 ± 0.08). Additionally, female mice showed no difference in fractional calcium excretion (%) between WT (1.21 ± 0.66), HET (0.88 ± 0.50) and HOM (0.97 ± 0.41). In male mice, the urinary fractional calcium excretion and calcium/creatinine ratio did not differ between WT (0.54 ± 0.27, 0.59 ± 0.27), HET (0.68 ± 0.35, 0.63 ± 0.16) and HOM (0.46 ± 0.32, 0.44 ± 0.08). However, the 24-hour urinary calcium excretion was significantly ($p<0.05$) lower in HOM (0.08 ± 0.01) than HET (0.15 ± 0.08) animals. The mutant mice may have increased activity of compensatory systems to normalize blood calcium levels. This could include excreting less calcium into the urine, increased breakdown of bone to release calcium into the blood, or increased absorption of calcium from the intestine. Overall, the effect of the FAM111A mutation may be masked by the effects of a low calcium diet. Future work will analyze mice fed a normal calcium (0.83%) diet and may explain the cause of our patient's disorder by demonstrating that mutations in FAM111A cause ADH.

Funded By: This project is supported by the Stollery Children's Hospital Foundation, supporters of the Lois Hole Hospital for Women, and through the Women and Children's Health Research Institute. It is additionally funded by The Canadian Institutes of Health Research.

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Abstract #:	149
Presenter:	Mischa Taylor
Supervisor:	Gokiert, Rebecca J
Title:	The role of social bridges in supporting integration amongst Syrian refugee women
Authors:	Dr. Sophie Yohani, (Project Investigator), Dr. Anna Kirova, Dr. Rebecca Gokiert, Mischa Taylor
Theme:	Lifelong women's health

The unprecedented influx of Syrian refugees arriving in Canada in 2015 onwards with experiences of trauma precipitated an urgency to support their successful settlement and integration. In response, a community-based participatory study was conducted with the Syrian refugee community in Edmonton to explore critical aspects of psychosocial adaptation and integration after trauma using Community Learning for Empowerment Groups (CLEGs). This study, referred to as the ADAPT project (PI: S. Yohani), employs the combined Domains of Integration model (Ager & Strang, 2008) and the ADAPT model (Silove, 2013) as its framework. A key indicator of psychosocial integration within both models is social connections, which is examined in the CLEG project. My thesis research forms a complementary study by exploring the experiences of social connections amongst members of the Syrian refugee community, focusing particularly on social bridging. This presentation will share some of the preliminary findings on social connections that were shared by women participating in the ADAPT project and how my research on social bridging expands on these further. I will present the findings of my thesis research on Syrian's experiences building social bridges and discuss the implications of supporting newcomer women's social connections within the greater community.

Funded By: ADAPT project: SSHRC Insight Grant

My thesis research: SSHRC CGS-M, WCHRI PaCET Grant

Abstract #:	15
Presenter:	Carmen Tessier
Supervisor:	Kozyrskyj, Anita
Title:	EXPLORING THE GUT-BRAIN AXIS: ASSOCIATIONS BETWEEN MATERNAL PRENATAL DEPRESSION, INFANT COLONIZATION WITH C. DIFFICILE, AND CHILD NEURODEVELOPMENT
Authors:	Tessier CA, Obiakor CV, Pei J, Morales-Lizcano NP, Azad MB, Becker AB, Lefebvre D, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Mandhane PJ, Kozyrskyj AL.
Theme:	Children's health and well-being

Introduction

Colonization of the infant gut with Clostridioides difficile (C. difficile) is on the rise. While asymptomatic, colonized infants are at increased risk for atopic disease and other inflammatory conditions. It is unknown why some infants are colonized with C. difficile and others are not. We have previously found that prenatal depressive symptoms were associated with lower infant fecal Immunoglobulin A levels, which were a risk factor for infant C. difficile colonization. Therefore, this study aimed to examine the impact of maternal prenatal depression on colonization of C. difficile in infants at 3 months of age. With increasing evidence of the impact of inflammation on brain development, our secondary objective was to explore the impact of C. difficile colonization on cognition at 1 and 2 years of age.

Methods

This study used a substudy of 406 term infants from the CHILD Cohort Study. Maternal prenatal depression was measured using the CES-D with a cut-off score above 16 describing clinically significant depression. Fecal samples were collected at 3 months during a home assessment. Analysis of C. difficile was performed using qPCR with appropriate primers. Cognition was assessed using the BSID-III administered at 1 and 2 years. Confounding variables were measured by maternal report or retrieved from hospital records. Logistic regressions were used to examine the associations between maternal depression and C. difficile colonization. Linear regressions were used to examine the associations between C. difficile colonization and cognitive scores at 1 and 2 years of age.

Results

In our sample, 42% of the infants were colonized with C. difficile at three months of age. During their third trimester of pregnancy, 24% of mothers experienced clinically significant depressive symptoms. Prenatal depression significantly increased the odds of C. difficile colonization in the infants (Odds Ratio [OR]=1.70, 95% Confidence Interval [CI]= 1.43, 2.78; p=0.034), adjusted for birthmode and feeding status. Colonization of C. difficile in infants was marginally associated with lower cognitive scores at 1 year of age (Beta= -1.94, 95%[CI]= -4.16, 0.28; p=0.087), adjusted for birthmode and feeding status. This finding remained at two years of age (Beta= -2.87, 95%[CI]= -6.04, 0.31; p=0.077).

Conclusion

At 3-4 months of age, infants of mothers who experienced prenatal depression had significantly increased risk of C. difficile colonization in their gut. The colonization of this pathobiont was marginally associated with lower cognitive scores at both 1 and 2 years of age. Our findings further suggest that maternal mood may contribute to alterations in early infant microbiome, which may have implications for the developing infant brain.

Funded By: Research funded by the CIHR microbiome team grant and WCHRI studentship.

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Abstract #:	29
Presenter:	Alexa Thompson
Supervisor:	Charlton, Carmen L
Title:	Universal prenatal HCV screening in Alberta in response to lack of standardized risk-based screening across Canada
Authors:	L. Alexa Thompson & Carmen L. Charlton
Theme:	Pregnancy and developmental trajectories

Introduction: Hepatitis C virus (HCV) is a blood borne pathogen that chronically infects over 250,000 people in Canada, causing liver cirrhosis and hepatocellular carcinoma. Because viral transmission can occur vertically from mother to infant during pregnancy, women who are considered at high-risk for HCV are prenatally screened. However, the definition of "high-risk" is highly variable across the country. We aimed to compare all HCV high-risk factors defined by Canadian provinces/territories and implement a universal prenatal HCV screening program in Alberta to evaluate the effectiveness of the current risk-based screening method.

Methods: HCV high-risk factors were systematically reviewed and compiled from all government-issued provincial/territorial communicable disease and prenatal screening guidelines across Canada. Concurrently, a pilot universal HCV screening program for prenatal women was implemented in Alberta to understand the number of women who may be missed through risk-based screening alone. All prenatal specimens were tested for HCV infections regardless of risk-factor. Prenatal HCV screening data was collected 5 months prior (risk-based screening) and 5 months after implementation of universal screening to compare HCV diagnostic rates. Quantitative analyses were performed using Chi-Square tests and risk ratios (RR) were analyzed across the risk-based and universal screening programs.

Results: Criteria for HCV risk factors were inconsistently defined by all provinces/territories. 17 different risk factors were defined across the entirety of Canada, but only 4 were consistently included in all provincial/territorial prenatal screening or communicable disease guidelines. Over a 5-month period in Alberta, the risk-based prenatal screening program screened 8.1% of all prenatal women for HCV, while the universal program screened 99.9% (RR= 12.3, $p<0.0001$). The diagnostic prevalence of prenatal HCV with the risk-based program was 0.05% while the prevalence with the universal screening was 0.14% (RR=2.6, $p<0.005$). The risk difference between programs was 0.085% (0.026%-0.14%), translating to approximately 47 prenatal women being missed by the risk-based screening program in Alberta every year, with up to 40 of these women developing undiagnosed chronic infections.

Conclusions: The HCV risk-based screening system for prenatal women across Canada is inconsistent at defining HCV risk factors and a universal screening pilot study demonstrated prenatal women are being significantly underdiagnosed with HCV in Alberta. Implementing universal HCV screening would standardize guidelines across Canada and could capture more prenatal women infected with the virus, although cost-effectiveness should be considered.

Funded By: CIHR Canada Graduate Scholarship and the M.S.I. Foundation.

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Abstract #:	162
Presenter:	Barbara Verstraeten
Supervisor:	Olson, David
Title:	Social support improves maternal posttraumatic stress symptoms after a natural disaster: The Fort McMurray Wood Buffalo wildfire.
Authors:	Barbara S.E. Verstraeten, Guillaume Elgbeili, Ashley Hyde, Suzanne King and David M. Olson
Theme:	Pregnancy and developmental trajectories

Introduction: In May 2016, the Fort McMurray Wood Buffalo (FMWB) wildfire devastated the FMWB region in Alberta, Canada, forcing the evacuation of upwards of 88,000 people. Following natural disasters, pregnant and postpartum mothers are vulnerable to developing posttraumatic stress disorder (PTSD)-like symptoms, which may affect the development of their children. Little is known about protective factors. We hypothesized that peritraumatic stress would predict PTSD-like symptoms in perinatal women with social support and resilience acting as moderators.

Methods: Women (n=200) who personally experienced the FMWB wildfire during or shortly before pregnancy were recruited for a randomized controlled trial using expressive writing as an intervention to improve pregnancy and mental health outcomes. At recruitment, peritraumatic experiences and current PTSD-like symptoms were evaluated using the Peritraumatic Distress Inventory (PDI) and the Impact of Events Scale - Revised (IES-R), respectively. They also completed the Social Support Questionnaire Short Form and Connor-Davidson Resilience Scale. Correlation analyses and multiple linear regressions with interaction terms were performed. Significant interactions were probed using the PROCESS macro v3.4. All tests were two-sided with $p<0.05$ considered significant.

Results: Most study participants were highly educated, affluent women in committed relationships. At recruitment on average 10.5 ± 4 months after the fire, i.e. prior to the intervention, 23.5% of participants qualified for possible and 26% ranked as probable PTSD. Greater peritraumatic distress ($r=0.56$) at the time of the fire correlated with more severe PTSD-like symptoms in mothers. High social support satisfaction moderated the relationship between peritraumatic distress and PTSD-like symptoms, however only when peritraumatic distress was below average; at more severe levels of PDI it was not protective. Resilience was not a significant moderator. The timing of exposure during pregnancy, time elapsed since the fire, parity and whether mothers had delivered at recruitment did not contribute significantly to explaining variance in PTSD-like symptomatology.

Conclusions: Social support satisfaction may moderate the effect of peritraumatic distress on the development of PTSD-like symptoms in pregnant and postpartum women after a wildfire. Resilience did not have a moderating influence on this association in this sample. Given the established effects of prenatal maternal stress on fetal and early-life programming, specific attention to women who are pregnant, postpartum or with plans of becoming pregnant during and after a disaster, is warranted. This population should be targeted for early screening and interventions in the immediate aftermath of traumatic experiences with the aim of improving long-term maternal and child outcomes.

Funded By: Canadian Institutes of Health Research

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Abstract #: 163
Presenter: Roberto Villalobos
Supervisor: Davidge, Sandra
Title: Uptake of Syncytiotrophoblast-Derived Extracellular Vesicles by Human Umbilical Vein Endothelial Cells

Authors: Roberto Villalobos-Labra 1,3; Floor Spaans 1,3; Anita Quon 1,3; Sandra T. Davidge 1,2,3

1Department of Obstetrics and Gynecology, 2Department of Physiology, 3Women and Children's Health Research Institute, University of Alberta, Edmonton, Canada

Theme: Pregnancy and developmental trajectories

Introduction: Preeclampsia (PE) is a pregnancy disorder occurring in 5-7 % of all pregnancies that is characterized by new-onset hypertension and/or end-organ dysfunction after 20 weeks of gestation. PE is a major cause of maternal and neonatal mortality, as well as a risk factor for long-term cardiovascular disease in the mother and the offspring. The vasculature of women with PE presents with endothelial dysfunction, which is thought to be key to the development of hypertension and other PE-associated cardiovascular complications. Although the pathogenesis of PE and the factor(s) and mechanism(s) inducing maternal endothelial dysfunction are still not clear, it has been thought that impaired placentation and placental oxidative stress play a major role. This dysfunctional placenta could contribute to vascular dysfunction by releasing high levels of stress-related factors in the maternal circulation, such as syncytiotrophoblast-derived extracellular vesicles (STBEVs). We and others have previously shown that STBEVs impair endothelial function in rodent blood vessels, and this appeared to be mediated by the activity of the scavenger receptor Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) in uterine arteries. However, the mechanisms by which STBEVs may interact with the endothelium to impair vascular function, and the involvement of potential receptors (such as LOX-1), are unknown. In the current study, we assessed the uptake of STBEVs by human endothelial cells in order to study the potential mechanisms and receptors involved in the future.

Methodology: STBEVs were collected from a placenta of a normal pregnant woman by our collaborators at the University of Oxford. Umbilical cords were obtained from normal pregnant women at the Lois Hole Hospital for Women (n=4). Human Umbilical Vein Endothelial Cells (HUVECs) were isolated from the umbilical cords, and cultured until confluent. HUVECs were incubated with fluorescently dyed STBEVs (using carboxyfluorescein succinimidyl ester [CFSE], 10 µM) at increasing concentrations (0-80 µg protein/mL, for 1 hour) and times (0-6 h, at 40 µg protein/mL). Cells were fixed in paraformaldehyde (4%) and treated with phalloidin for staining of actin filaments. Images were obtained by confocal microscopy. Attachment and uptake of STBEVs (CFSE positive staining) was analyzed using the FIJI/ImageJ software. Data were analyzed using Kruskal-Wallis test with Dunn's multiple comparisons test; $p<0.05$ was considered significant.

Results: STBEVs attached to HUVECs after 15 min. of incubation, and their attachment increased progressively with time ($p=0.0033$; n=4) and with increasing STBEV concentration ($p=0.0208$; n=3). A Z-plane cross-section confirmed that STBEVs were located inside the endothelial cells after 1 hour of incubation.

Conclusions: We showed that STBEVs are internalized by HUVECs. Being able to confirm and quantify the uptake of STBEVs will allow us to study the mechanisms by which STBEVs may affect endothelial dysfunction in PE. Since previous studies have proposed that STBEVs and LOX-1 may play an important role in endothelial/vascular dysfunction in PE, our next step will be to evaluate the contribution of LOX-1 in the uptake of STBEVs.

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Abstract #: 18
Presenter: Richelle Waldner
Supervisor: Grimbly, Chelsey
Title: QTc Intervals in Gender Diverse Adolescents on Leuprolide Acetate

Authors: Richelle Waldner, Manpreet Doulla, Jospeh Atallah, Chelsey Grimbly
Theme: Children's health and well-being

Background:

Leuprolide acetate, or Lupron, is a gonadotropin releasing hormone agonist commonly used to achieve pubertal suppression in gender diverse adolescents. Lupron is a fully reversible treatment that can halt the permanent changes of puberty and may help relieve gender dysphoria. There are concerns that Lupron prolongs the rate-corrected QT (QTc) interval when used as androgen deprivation therapy in the management of prostate cancer; however, there is a paucity of literature regarding Lupron and QTc interval in gender diverse adolescents. Our study aimed to evaluate QTc intervals in this population.

Methods:

We retrospectively reviewed data for youth between 9-18 years who were managed at the Stollery Endocrinology Gender Clinic (Edmonton, Alberta, Canada) between July 1, 2018 to December 31, 2019. A total of thirty-three pubertal adolescents were on Lupron and had a 12-lead electrocardiogram (ECG) obtained while on treatment. QTc intervals were analyzed, with QTc prolongation considered to be greater than 460 milliseconds (ms). When available, ECGs obtained prior to Lupron initiation were reviewed and the interval change was assessed. Data on concomitant medications and gender affirming hormones were obtained from the medical record.

Results:

Our cohort had a mean (SD) age of 13.7 (2.1) years and 69.7% identified as male after being assigned female at birth. None of the adolescents on Lupron demonstrated QTc interval prolongation. The mean (SD) QTc interval was 415 (27) ms. There were 8 adolescents (24.2%) with a QTc between 440 ms and 460 ms, categorized as borderline prolongation. Of these 8 adolescents, 6 (75%) were on concomitant psychotropic medications and 3 (37.5%) were on gender affirming hormones; 2 on oral estrogen and 1 on intramuscular testosterone. Of the 19 patients who had both a baseline and post-Lupron ECG, the mean (SD) QTc interval change was -4.77 (26.5) ms and 1 adolescent had an interval change greater than 40 ms. This patient identified as male, was on gender affirming therapy (intramuscular testosterone), and had an interval QTc increase of 44ms with their follow-up QTc being 448 ms.

Conclusion:

To our knowledge, this is the first study to report on QTc intervals in gender diverse adolescents on Lupron for pubertal suppression. Reassuringly, none of our cohort had QTc prolongation, defined as a QTc value greater than 460ms, or significant increase in QTc upon initiation of therapy. Borderline QTc prolongation was observed in 24.2% of adolescents and 62.5% of these patients were on at least 1 concomitant psychotropic medication classified as having a conditional risk for torsades de pointes.

Funded By: WCHRI Resident/Clinical Fellow Trainee Research Grant

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Abstract #:	150
Presenter:	Joy Wang
Supervisor:	Goping, Ing Swie M
Title:	Unphosphorylated BAD prevents metastasis of breast tumors by promoting apoptosis and limiting proliferation
Authors:	Joy Wang, Namrata Patel, Heather Muranyi, John Maringa Githaka, Raven Kirschenman, and Ing Swie Goping
Theme:	Lifelong women's health

Breast cancer is the most frequently occurring type of cancer among Canadian women and cancer metastasis is almost always the cause of death for the patient. The Bcl-2 family protein BAD is a prognostic indicator for breast cancer patient survival. How BAD contributes to good clinical outcome is unknown and investigating this may uncover important new knowledge on breast cancer biology. At the cellular level, BAD can modulate apoptosis, proliferation, cell motility and mitochondrial metabolism. Thus, we hypothesized that BAD was prognostic for favourable clinical outcome because it increased breast cancer cell apoptosis and decreased proliferation and motility. To test this, we took advantage of the fact that BAD's diverse functions are modulated by its phosphorylation state, where non-phosphorylated BAD stimulates apoptosis, decreases motility and has an unclear role in proliferation. We generated a genetic breast cancer mouse model wherein the endogenous BAD could not be phosphorylated due to serine to alanine substitutions in 3 key phosphorylatable amino acid residues (PyMT-3SA). We then characterized the resultant primary and metastatic tumors to determine whether the phosphorylation state of BAD differentially affected tumor characteristics. We assessed apoptosis and proliferation of primary breast tumors using immunohistochemistry and determined that PyMT-3SA primary tumors had significantly increased apoptosis and decreased proliferation compared to the tumors from control PyMT animals that harbored the wild-type Bad allele. PyMT-3SA animals showed decreased area of lung metastatic tumors and the trend of decreased proliferation in PyMT-3SA tumors was also seen in metastatic tumors. PyMT metastatic tumors were twice as proliferative as PyMT primary tumors while PyMT-3SA metastatic tumors were five times as proliferative as PyMT-3SA primary tumors. Unlike primary tumors, there was no difference in apoptosis between PyMT and PyMT-3SA metastatic tumors. To determine whether decreased metastatic burden of PyMT-3SA animals is due to decreased motility of the primary tumor cells, we are currently performing cell motility assays on cell lines generated from PyMT and PyMT-3SA primary tumors. Our results suggest that non-phosphorylated BAD causes decreased proliferation in primary and metastatic tumors and increased apoptosis in primary tumors only. Metastatic tumors had much higher proliferation than primary tumors in both BAD phosphorylation states. Possibly highly proliferating primary tumor cells are responsible for seeding the lung metastases, or the cancer cells become highly proliferative after reaching the site of metastasis. In summary, our data suggests that unphosphorylated BAD may contribute to beneficial patient outcomes by limiting proliferation and increasing apoptosis of primary breast tumors that together limit metastatic spread.

Funded By: Research was supported by Canadian Institute of Health Research (CIHR) operating funds to ISG and Alberta Innovates Summer Research Studentship (SRS) to JW.

Abstract #:	60
Presenter:	Adrianne Watson
Supervisor:	Voronova, Anastassia
Title:	Engaging endogenous central nervous system precursor cells to promote healthy brain development
Authors:	A. Watson, Y. Li, M. de Almeida, N. Dittmann, T. Footz, A. Voronova
Theme:	Children's health and well-being

During brain development, neural stem and precursor cells (NPCs) generate diverse progeny, including neurons, astrocytes and oligodendrocytes. Oligodendrocytes are glial (non-neuronal) cell types that generate myelin, a fatty substance that coats and protects nerve projections. The ability to form healthy myelin, which comprises white matter, is critical for proper brain development and cognition; however, in children with neurodevelopmental disorders, white matter formation is abnormal. NPCs in the subventricular zone (SVZ) of mammalian brain have the ability to produce oligodendrocytes throughout life. If we can identify the signals that instruct NPCs to become oligodendrocytes, we may be able to utilize this information to engage endogenous precursor cells to regenerate oligodendrocytes and myelin for proper brain development and function. My project focuses on fractalkine (FKN), a chemokine that is secreted by neurons. Importantly, mutations in FKN receptor (CX3CR1) are present in patients with autism spectrum disorder and schizophrenia. While CX3CR1 is highly expressed in brain immune cells (microglia), recent reports suggest NPCs also express this receptor, although at a lower level (Watson et al. 2020 Neurosci Lett). However, the role of FKN-CX3CR1 signalling axis in postnatal and adult NPCs is not known. My hypothesis is that fractalkine regulates oligodendrocyte formation from postnatal NPCs.

We utilized RNA scope to detect Cx3cr1 mRNA expression in postnatal brain. We also injected FKN directly conjugated to fluorophore Alexa-647 (CX3CL1-647) into lateral ventricle of murine brain to identify which cell types bind FKN in vivo. We then infused FKN into the lateral ventricle of NPC lineage tracing mice (NestinCreERT2;RosaYFPSTOP/+) to assess the role of FKN signaling in de novo oligodendrocyte genesis. Oligodendrocytes develop via 2 steps: 1) NPC to OPC (oligodendrocyte precursor cell); and 2) OPC to oligodendrocyte differentiation. To test the direct effect of FKN on precursors, we generated microglia-free NPCs and OPCs from murine postnatal SVZ neural stem cells. These cultures were incubated in the presence of FKN or function blocking antibodies raised against FKN or CX3CR1 and analyzed for differences in proliferation, differentiation and survival.

We show that in addition to microglia, postnatal SVZ NPCs and OPCs express Cx3cr1 and bind FKN in vitro and in vivo. When FKN is added to NPC cultures, it 1) enhances NPC to OPC commitment; and 2) accelerates OPC to oligodendrocyte differentiation without affecting precursor proliferation or survival. Inhibition of FKN signalling with function-blocking antibodies inhibits oligodendrocyte differentiation from OPCs. Finally, infusion of FKN into lateral ventricle of NPC lineage tracing mice enhances OPC and oligodendrocyte genesis from SVZ NPCs in vivo.

We show FKN-CX3CR1 signalling is sufficient and necessary for oligodendroglial cell formation from neural stem cells. Our results also suggest that mutations in FKN-CX3CR1 signalling axis may lead to dysfunctional neural stem cells and aberrant brain development seen in autism and schizophrenia patients. Finally, our results identify FKN as a potential therapeutic target for oligodendrocyte genesis.

Funded By: WCHRI, 75th Anniversary, MSGPS and endMS scholarships to A.W. as well as NSERC and CIHR operating grants to A.V.

Abstract #: 41
Presenter: Jason Wong
Supervisor: Lou, Edmond HM
Title: Applying machine learning algorithms to measure Cobb angle semi-automatically on ultrasound images for children with adolescent idiopathic scoliosis - a feasibility study
Authors: Jason Wong, Marek Reformat, Edmond Lou
Theme: Children's health and well-being

Introduction

Scoliosis is a three-dimensional deformity, characterized by lateral curvature and axial vertebral rotation. The most common form of scoliosis is adolescent idiopathic scoliosis (AIS), affecting 1-3% of adolescents aged 10 to 16 years old. To assess the severity of AIS, the gold standard is to measure the Cobb angle on a posteroanterior radiograph. However, taking radiographs exposes children with AIS to ionizing radiation which may increase the risk of cancer, and so ultrasonography has been investigated and found to be comparable to radiography in terms of measurement accuracy and reliability. Since ultrasound imaging of the spine has only been applied for 6 years, it takes more time for a clinician to manually extract parameters from ultrasound than radiographic scans. It also requires a significant amount of training to accurately measure the Cobb angle on ultrasound images. Even an experienced rater of 3 years may take two minutes to measure all of the parameters. Consequently, automation of the Cobb angle measurement would not only free up clinicians' time to see more patients, but also minimize errors from human judgment. It also may encourage more scoliosis centers to consider using ultrasound for monitoring children with AIS. This study aimed to investigate the feasibility of using machine learning to semi-automate Cobb angle measurements on ultrasound spinal images.

Methods

A type of artificial intelligence model, called a convolutional neural network, was developed to segment and identify the laminae of each individual vertebra on ultrasound images. Prior to performing this pilot study, 50 images were labelled and used to train the model. The Cobb angle was calculated using the lines that joined the predicted laminae on each vertebra. To test the preliminary model, 7 ultrasound spinal images were selected from our database. Among these images, 12 curves were identified in total. The average manual measurement on these Cobb angles was 25.9±12.0°. The Pearson correlation and the mean absolute differences (MAD) between the manual and the semi-automatic method were calculated.

Results

The MAD between the manual and semi-automatic measurements was 2.3±2.2°, which is within the clinically accepted error (5°). Only one curve, which was in the lumbar region, had a difference of >5° (7°), as it is generally more difficult to measure this region on ultrasound images. The Pearson correlation coefficient between the manual and semi-automatic measurements was 0.966, indicating a strong correlation. Furthermore, the semi-automatic measurement took around 30 seconds, with the network generating a segmentation in less than one second.

Conclusions

This feasibility study demonstrated there is great potential to apply machine learning to semi-automatically measure the Cobb angle on children with AIS with accuracy similar to manual measurements. The semi-automatic method is faster and does not require accumulated experience to perform. A full clinical study will be conducted to completely validate the developed method. Future work will develop a fully automated method to further simplify the process so that ultrasound can be an alternative diagnostic imaging for children with AIS, thereby minimizing the risk of cancer in these children.

Funded By: The Women and Children's Health Research Institute, Natural Sciences and Engineering Research Council of Canada, Edmonton Orthopaedic Research Committee

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Abstract #:	30
Presenter:	Andrew Woodman
Supervisor:	Bourque, Stephane
Title:	Perinatal iron deficiency alters patterns of cellular senescence and apoptosis in the developing kidney in a sex-dependent manner
Authors:	Andrew Woodman, Richard Mah, Claudia Holody, Ronan Noble, Stephane Bourque
Theme:	Pregnancy and developmental trajectories

Introduction: Iron deficiency (ID) commonly occurs during pregnancy, resulting in decreased birthweight and an increased risk of offspring developing non-communicable chronic disease later in life. Previously, we have shown that male but not female offspring exposed to perinatal ID exhibit hypertension and altered renal structure and function in adulthood. However, the mechanisms through which renal structure is altered remain poorly understood. Here, we sought to assess how perinatal ID alters patterns of cellular senescence and apoptosis, which are both important developmental mechanisms dictating cellular proliferation and patterning within the developing kidney. Moreover, we assessed the role of oxidative stress and renal antioxidant defense due to their critical role in stress-induced senescence and apoptosis.

Methods: Six-week old Sprague Dawley dams were fed an iron-restricted (3-10 mg/kg) or iron-replete (37 mg/kg) diet two weeks prior to and throughout gestation. Offspring kidneys were collected within 24h of birth and were either flash frozen or cryo-sectioned. Apoptosis was assessed by TUNEL assay and Caspase 3 and 9 activity assays. Cellular senescence was assessed via senescence-associated β-galactosidase (SA-βGal) activity. RT-qPCR was used to assess expression of various antioxidant enzymes [catalase, superoxide dismutase (SOD)1 and 2, glutathione peroxidase, and glutathione reductase. Oxidant damage was assessed by the malondialdehyde assay for lipid peroxidation, and glutathione levels were measured using available kits.

Results: ID resulted in neonatal anemia and decreased birth weight ($P<0.05$). Renal caspase 3 activity and TUNEL staining were increased in male ($P=0.01$) but not female perinatal ID offspring, whereas caspase 9 activity was not affected in either sex. Perinatal ID reduced SA-βGal activity in kidneys of both sexes ($P<0.01$). Perinatal ID increased expression of sod1, sod2, and glutathione reductase in male but not female offspring (all $P<0.01$), whereas catalase and glutathione peroxidase expression were not altered. Perinatal ID altered lipid peroxidation in box sexes ($P=0.02$), and resulted in a reduction in total glutathione levels in male perinatal ID offspring ($P<0.01$) despite no alterations in the ratio of reduced to oxidized forms.

Conclusions: Perinatal ID reduces levels of renal developmental senescence in offspring of both sexes at birth. Interestingly, male but not female offspring exhibit renal oxidative stress and increased apoptosis due to perinatal ID. These data suggest increased apoptosis and oxidative stress coupled with decreased cellular senescence during development may underlie future renal dysfunction in male offspring.

Funded By: AW is supported by a Canadian Institutes of Health Research (CIHR) Vanier Scholarship and an Alberta Innovates Graduate Studentship. SB receives operating funding support from CIHR and the Women and Children's Health Research Institute.

Abstract #:	164
Presenter:	Amy Wooldridge
Supervisor:	Davidge, Sandra
Title:	Advanced maternal age impairs pregnancy adaptations in the rat main uterine artery
Authors:	Amy L. Wooldridge, Mazhar Pasha, Raven Kirschenman, Floor Spaans, Sandra T. Davidge, Christy-Lynn M. Cooke
Theme:	Pregnancy and developmental trajectories

Introduction: Women are increasingly having their first pregnancies at an older age. Advanced maternal age (>35 years) is a risk factor for pregnancy complications such as low birth weight and preeclampsia. Aging involves impaired vascular reactivity and increased vascular stiffness, however the impact of maternal age on uterine artery adaptations to pregnancy remains uncertain. Our lab previously showed that ex vivo vascular constriction responses to increasing intraluminal pressures (myogenic tone) was greater in uterine arteries from aged compared to young pregnant rats. We are further characterizing the mechanisms behind these effects, and studying the impact of age on uterine artery adaptations to pregnancy, by inclusion of young and aged non-pregnant animals. We aimed to determine if age-related vascular differences develop during, or exist prior to, pregnancy.

Methods: Pregnant young (~4 months) and aged (~9 months; ~35 years in humans) rats were studied on gestational day 20 (term=22 days) and compared to age-matched non-pregnant rats. Rats were euthanized and main uterine arteries were isolated and mounted in a pressure myograph system. The relationship between intraluminal pressure and vessel diameter was assessed under active (with calcium, and with preconstriction to 25% of initial lumen diameter using phenylephrine) and passive (calcium-free) conditions. Myogenic tone (n=2-7) and circumferential stress-strain properties (measures of elasticity and deformation whilst accommodating increases in pressure; n=8-23) were calculated and data were analyzed by Two-way ANOVA with Sidak post-hoc comparisons. Data are presented as mean area under the curve ± standard error of the mean.

Results: In young rats, pregnancy reduced uterine artery myogenic tone (non-pregnant: 55±5 vs. pregnant 13±1; p=0.002). This pregnancy adaptation was not observed in aged vessels, as myogenic tone was not different between the non-pregnant vs pregnant groups. Uterine artery circumferential stress was increased with pregnancy overall (non-pregnant 220±1 vs. pregnant 280±19; p<0.001) and maternal age reduced the circumferential stress of pregnant vessels (young pregnant 299±9 vs. aged pregnant 261±12; p=0.031). Circumferential strain was increased with pregnancy (non-pregnant 94±4 vs. pregnant 131±11; p<0.001) and the circumferential strain of pregnant vessels was reduced with age (young 143±7 vs. aged 120±4; p=0.019). Within non-pregnant rats, age did not affect circumferential stress or strain. The passive lumen diameters of aged pregnant vessels were smaller than those of young pregnant vessels, indicating a lower maximum capacity.

Conclusions: Our findings indicate that in young rats, the main uterine artery undergoes adaptations during pregnancy in circumferential stress-strain and myogenic tone that do not occur (or not to the same extent) in aged rats during pregnancy. Uterine arteries of aged pregnant rats are also more stiff and have a lower maximum volume capacity compared to young pregnant rats. These age-related reductions in both the pressure-dependent and maximum stretch capacity of the main uterine artery may impact uteroplacental blood supply, thus contributing to an increased risk of pregnancy complications in pregnancies at an advanced age.

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Abstract #:	114
Presenter:	Zhao Xin
Supervisor:	Kozyrskyj, Anita
Title:	Infant vitamin D supplementation is linked to fecal metabolites, glycerol and 1,2-propanediol
Authors:	Zhao X, Drall KM, Bridgman S, Mandal R, Azad MB, Becker AB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL
Theme:	Children's health and well-being

Background: Infant vitamin D liquid formulations often contain commercial stabilizers, glycerol or 1,2-propanediol (i.e. propylene glycol), which are available to gut microbiota due to their poor absorption. Certain gut microbiota are able to metabolize glycerol into 1,2-propanediol. Nothing is known about the impact of routine vitamin D supplementation of breastfed infants on intestinal levels of these stabilizers. This study aimed to investigate the effects of vitamin D supplementation on fecal levels of glycerol and 1,2-propanediol, and the correlation of these stabilizers with gut microbiota.

Method: Fecal samples were profiled, and vitamin D supplementation and breastfeeding status obtained at 3-month of age in 575 infants from the Canadian Healthy Infant Longitudinal Development (CHILD) Study. Fecal metabolites and microbiota were quantified using Nuclear Magnetic Resonance Spectroscopy and 16S rRNA sequencing, respectively. Linear and logistic regression were used to determine the association between vitamin D supplementation with fecal concentrations of glycerol and 1,2-propanediol, adjusting for covariates. Raw concentrations of fecal 1,2-propanediol and glycerol were dichotomized into above or below median concentrations in the logistic regression analysis. Spearman correlation was performed to evaluate the monotonic relationship between taxa and metabolites of interest with the fecal concentration of glycerol and 1,2-propanediol.

Results: 78% of infants of exclusively breastfed infant were supplemented with vitamin D drops (containing glycerol). High fecal 1,2-propanediol concentrations (above the median) were much more common (61.2% vs. 34%, $p < 0.001$) in infants with compared to those without vitamin D supplementation. High levels of glycerol and especially 1,2-propanediol, were both more common in exclusively-breastfed infants, compared to partially or not breastfed infants ($p<0.05$). Independent of breastfeeding status and infant age, vitamin D supplementation was associated with a 1.5-fold higher odds of high 1,2-propanediol levels (adjusted Odds Ratio [aOR]=1.46, 95% CI, 0.96, 2.22), but a 48% reduced odds of high fecal glycerol (aOR=0.63, 95% CI, 0.42, 0.91).

Fecal concentrations of 1,2-propanediol were positively correlated with the relative abundance of Lactobacillus spp. (rho=0.24, $p<0.05$), Enterobacteriaceae(rho=0.21, $p<0.05$), Haemophilus spp. (rho=0.28, $p<0.05$), and Bifidobacterium spp. (rho=0.18, $p<0.05$), but negatively correlated with the abundance of other gut microbiota, including Akkermansia (rho= -0.15, $p<0.05$), Veillonellaceae (rho= -0.19, $p<0.05$) and Lachnospiraceae (rho= -0.31, $p<0.05$). Accordingly, fecal concentrations of acetate and lactate were positively correlated with fecal 1,2-propanediol ($p<0.05$), whereas butyrate and propionate and their derivates were negatively correlated with fecal 1,2-propanediol ($p<0.05$). These correlations varied by breastfeeding status.

Conclusion: Infants supplemented with vitamin D were found to have higher fecal 1,2-propanediol levels. Several microbiota, notably bifidobacteria, metabolize glycerol to produce this metabolite. This study brings awareness to non-medicinal ingredients in infant vitamin D supplements and their potential metabolism by gut microbiota.

Funded By: Canadian Institutes of Health Research (CIHR), Microbiome Initiative; Allergy, Genes and Environment (AllerGen) Network of Centers of Excellence; University of Alberta Faculty of Agriculture and Life Sciences Graduate and Postdoctoral Vitamin Fund

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Abstract #:	151
Presenter:	Sidney Yap
Supervisor:	Le Melledo, Jean-Michel
Title:	Impact of perimenopausal status on glutamate levels in the medial prefrontal cortex
Authors:	Jean-Michel Le Melledo, Jessica Luki, Sidney Yap, Peter Seres, Chris Hanstock, Huaying Zhao, Alyna Lirette, Sarah Hanstock
Theme:	Lifelong women's health

Over their lifetime, women are at an increased risk of experiencing depression compared to men. This increased prevalence may be due in part to the increased risk of experiencing depression during the perimenopause, a period of changing female hormone concentrations. Women at particular risk of developing perimenopausal depression (PMD) are those with history of mood sensitivity to female hormone fluctuations i.e. women with a history of premenstrual dysphoric disorder and/or post-partum depression (PPD). Our previous research showed that glutamate (Glu) levels in the medial prefrontal cortex (MPFC) fluctuate during the menstrual cycle (MC) and were increased in women with PPD. Furthermore, the glutamatergic dysregulation hypothesis is a promising avenue of depression research, illustrated by the rapid onset of antidepressant effect of ketamine, a glutamatergic modulator. The MPFC is suspected to be a key brain area for this unique antidepressant activity. In this study we compared MPFC Glu levels in healthy reproductive women (R-HC, n=14) and healthy perimenopausal women (P-HC, n=14) to assess whether MPFC Glu was influenced by the specific hormonal environment of perimenopause. Absence of mental health illness history was confirmed by semi-structured interview (MINI). Participants were scanned during early follicular phase of the MC. A 3T magnet was used to perform a Magnetic Resonance Spectroscopy (MRS) scan of the MPFC. We found that P-HC had decreased mean Glu concentrations when compared to R-HC within the MPFC (P-HC: mGlu= 0.57±0.06; R-HC: mGlu = 0.63±0.06; p=0.01). Once corrected for differences in grey matter concentration due to aging, mean Glu concentrations were no longer significantly different (p=0.99). We now need to assess whether MPFC Glu levels differ in individuals with PMD compared to P-HC. Furthering this research could lead to more effective treatments for women experiencing PMD and potentially aid in increasing our understanding of other depressive syndromes that are tied to fluctuations in female hormone concentrations.

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Perimenopausal Depression Research Fund

Abstract #:	98
Presenter:	Kevin Yoon
Supervisor:	Waskiewicz, Andrew
Title:	Uncovering the genetic determinants of superior coloboma, a novel ocular congenital disorder
Authors:	Kevin H. Yoon, Melissa M. Wilson, Jennifer C. Hocking, Ordan J. Lehmann, Andrew J. Waskiewicz
Theme:	Children's health and well-being

Congenital ocular coloboma is a genetic disorder that is typically observed as a cleft in the inferior aspect of the eye due to failed choroid fissure closure. Recently, identification of individuals with coloboma in the superior aspect of the iris led to the discovery of a novel developmental structure, referred to as the superior ocular sulcus (SOS), that is transiently present on the dorsal aspect of the optic cup during early vertebrate eye development. Previous research in our lab demonstrated that manipulation of BMP signaling results in SOS closure delay. We aim to elucidate the role of a key dorsoventral (DV) eye axis patterning gene identified in patient #4 exome sequencing data, VAX2, a transcription factor regulated by Shh signaling that is expressed in the ventral eye. Using zebrafish, we created a vax2-null allele, and observe that resultant homozygous mutant embryos display SOS closure delay. Overexpression of wildtype VAX2 mRNA in zebrafish embryos leads to SOS closure delay and perturbed expression of DV-axis patterning genes. Analysis of the patient variant (p.Leu139Met) conclusively demonstrates decreased activity when compared to wildtype VAX2, indicating that the patient variant is likely to be hypomorphic. These findings suggest that SOS closure appears to require a tightly-regulated expression of vax2, wherein both loss and increase in vax2 expression can result in aberrant closure. In an effort to explain the rarity of superior coloboma, we are currently testing the hypothesis that multiple loci are mutated. We have recently identified a second variant in patient #4, predicted to strongly reduce the function of the planar cell polarity gene, SCRIBBLE. Preliminary zebrafish experiments demonstrate a key role for planar polarity in SOS closure. Thus, our results provide support for a model in which multiple pathways are essential for SOS closure, including both DV axis specification and planar cell polarity.

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women & children's health research institute

Abstract #:	91
Presenter:	Kennedi Young
Supervisor:	Alexander, R Todd
Title:	The knockout of claudin-2 and claudin-12 results in hypocalcemia and reduced bone mineralization due to reduced paracellular renal and intestinal calcium absorption
Authors:	Kennedi Young, Megan R. Beggs, Matthew Saurette, R. Todd Alexander
Theme:	Children's health and well-being

Calcium (Ca^{2+}) is an essential mineral obtained from the diet. Its concentration in plasma is tightly regulated and it is an essential component of bone. Bone mineralization occurs throughout childhood and a failure of this leads to adverse health outcomes later in life. Additionally, with aging there is a greater chance of developing osteoporosis, a disease characterized by low bone mass and deterioration of bone tissue that affects 1 in 3 women in Canada. As such, it is important to understand what may contribute to this disease process that disproportionately affects women. Throughout adulthood, however, it is unclear how the kidneys and intestines absorb calcium so as to maintain a normal calcium balance. The majority of Ca^{2+} absorption across intestinal and renal epithelial cells occurs paracellularly, i.e. between the cells through claudin proteins that make up the tight junction. Claudin-2 and claudin-12 confer Ca^{2+} permeability to the renal tubule and intestine. However, deletion of either gene individually does not cause hypocalcemia, or reduced bone mineralization, potentially due to compensation of one by the other. We, therefore, hypothesized that the knockout of both claudin-2 and claudin-12 would result in a phenotype of hypocalcemia and reduced bone mineralization. To test this hypothesis, we generated claudin-2 and claudin-12 double knockout (DKO) mice. They were placed in metabolic cages permitting the collection of urine and feces, after which they were euthanized and blood and tissue collected. DKO mice had hypocalcemia relative to wildtype (WT) mice (WT = 1.1 +/- 0.02mmol/L, DKO = 1.0 +/- 0.02mmol/L, P = 0.002). They also demonstrated increased urinary calcium excretion (WT = 0.4 +/- 0.3mg/24hr, DKO = 1.0 +/- 0.5mg/24hr, P = <0.0001) and reduced calcium bioavailability (WT = 34.0 +/- 8.8%, DKO = 23.3 +/- 11%, P = 0.0008). DKO mice had increased mRNA expression of S100g (P = 0.0002) and Trpv6 (P = 0.03) in the proximal colon and increased expression of Atp2b1 (P = 0.003) and Calb1 (P = 0.03) in the kidney, consistent with an upregulation of transcellular Ca^{2+} absorption and reabsorption pathways, which failed to completely compensate for the loss of claudin-2 and claudin-12. DKO mice did not have increased expression of Cyp24a1 or Cyp27b1 relative to WT, as well as no difference in urinary phosphate excretion between the two groups, suggesting that vitamin D is not compensating for the loss of claudin-2 and claudin-12. Micro-CT analysis of bone was therefore performed to assess the effect of the DKO on bone morphology. Preliminary analysis found decreased trabecular bone volume in the DKO relative to WT. These findings contribute to the understanding of bone mineralization, since the loss of these genes may contribute to suboptimal bone mineralization. These results suggest that claudin-2 and claudin-12 are essential for normal Ca^{2+} homeostasis and that the loss of both results in an inability to effectively maintain normal blood Ca^{2+} levels, potentially due to loss of compensation by one gene for the other.

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Abstract #:	20
Presenter:	Brenna Zatto
Supervisor:	Hoglund, Wendy
Title:	Depressive and anxious symptoms in early childhood: prediction by emotion self-regulation
Authors:	Brenna R. L. Zatto, Zoe Schuster, Abby MacLean, Krisytn Gannon, & Wendy L. G. Hoglund
Theme:	Children's health and well-being

Emotion self-regulation, or the ability to modify emotions, is a key developmental task of early childhood. Young children who show difficulty with emotion self-regulation are at greater risk of experiencing symptoms of depression (e.g., sadness, worthlessness) and anxiety (e.g., fearfulness, worries). Specific dimensions of emotion self-regulation may act as predictors of children's distinct experiences of depressive and anxious symptoms across early childhood. For instance, children's ability to self-regulate negative (e.g., sadness, anger) and exuberant (e.g., excitement) emotions, maintain positive emotions (e.g., happiness, content), and respond appropriately to disappointing events may influence and distinguish between typical and elevated or increasing depressive and anxious symptoms. The purpose of the current study was to examine: 1) distinct patterns of change in depressive and anxious symptoms in early childhood; and 2) whether dimensions of emotion self-regulation predict these patterns.

The study included 443 children assessed in the fall and spring of preschool and kindergarten, totaling four waves of assessment. Children's depressive and anxious symptoms were assessed at all waves by teacher-report. Dimensions of emotion self-regulation were assessed at the fall of preschool by teacher-report (positive emotion maintenance, negative and exuberant emotion self-regulation) and by a behavioral assessment that measured children's response to receiving a disappointing gift (positive and negative response to disappointment).

Growth mixture modeling identified two distinct patterns of depressive symptoms: high-stable and low-stable. Compared to children with a low-stable pattern of depressive symptoms, children with a high-stable pattern were more likely to show greater positive emotion maintenance and negative response to disappointment as well as less negative and exuberant emotion self-regulation at fall of preschool.

For anxious symptoms, three distinct patterns were identified: low-increasing, high-decreasing, and low-stable. Compared to children with a low-stable pattern of anxious symptoms, children with low-increasing or high-decreasing patterns were more likely to show less positive emotion maintenance and negative emotion self-regulation at fall of preschool. Children with a low-increasing pattern of anxious symptoms were also more likely to show less exuberant emotion self-regulation and greater positive and negative response to disappointment, while children with a high-decreasing pattern were more likely to show greater exuberant emotion self-regulation and less positive and negative response to disappointment.

The current study's findings suggest that distinct patterns of depressive and anxious symptoms are evident as early as preschool and that dimensions of emotion self-regulation can act as unique early predictors of typical versus elevated or increasing symptoms. Promotion of strategies to support children in self-regulating their negative and exuberant emotions, maintaining positive emotions, and responding appropriately to disappointing situations may help deter depressive and anxious symptoms as well as promote positive engagement in the early school context.

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