women & children's health research institute

10 years

2016 Research Day

Abstract Book

November 16, 2016 | Westin Hotel

The Power of Partnership

University of Alberta

Alberta Health Services

Stollery Children's Hospital Foundation

Lois Hole Hospital for Women

Acknowledgements

Thank you

The Women and Children's Health Research Institute (WCHRI) is a partnership between the University of Alberta and Alberta Health Services and is generously supported by the Stollery Children's Hospital Foundation and donors to the Lois Hole Hospital for Women. The Faculty of Medicine & Dentistry provides operating and in-kind support.

The University of Alberta and the Faculty of Medicine & Dentistry

The University of Alberta strives to create and promote an environment of research excellence across the university to fuel knowledge advancement, discovery and innovation; all of which provide significant contributions to society provincially, nationally and globally. The University of Alberta's Faculty of Medicine & Dentistry (FoMD) is home to many of WCHRI's core groups and entire administrative staff. Its continued and generous support makes possible the training of our future scientists and physicians. The FoMD also provides partial funding for WCHRI's operating expenses, without which WCHRI would not be able to manage its many grants programs and research support initiatives.

Alberta Health Services

Alberta Health Services (AHS) is a strong and active supporter of WCHRI. Their guidance has been invaluable in ensuring that women and children's health and AHS standards in the delivery of clinical care, wellness and prevention, remain a focus of WCHRI's mandate.

The Royal Alexandra Hospital Foundation and the Lois Hole Hospital for Women

The Royal Alexandra Hospital Foundation (RAHF) advances healthcare for all Albertans through support of the Royal Alexandra Hospital and its medical centres of excellence. This includes the Lois Hole Hospital for Women, where donor dollars provide advanced technologies, facility enhancements and exciting new opportunities for research in women's health. In 2016 the Royal Alexandra Hospital Foundation renewed its commitment to the Women and Children's Health Research Institute (WCHRI) for another ten years, extending their contributions into 2025. This funding will build upon the foundation's initial investment of $11 million by providing an additional $14.5 million to WCHRI in support of women's health research.

The Stollery Children's Hospital Foundation

The Stollery Children's Hospital Foundation raises funds to build the Stollery Children's Hospital into the best children's health-care delivery, research and teaching institution in the world. The Foundation recognizes the tremendous impact pediatric research has on disease prevention, treatment and improved health outcomes for children. In 2016, the Foundation committed $40 million over ten years – the largest donation in the University of Alberta's history – to support WCHRI, bringing its total committed support to $70 million since 2006.

List of presenters

Name	#	Time	Room
Abeysekera, Jayani	29	09:00-10:30	Leduc Room
Adam, Laura	97	10:30-12:00	Ballroom
Adria, Steffen	68	10:30-12:00	Ballroom
Agrawal, Ambika	167	15:15-16:45	Ballroom
Ahmed, Haroon	147	15:15-16:45	Ballroom
Alaee, Mahsa	175	15:15-16:45	Ballroom
Albrecht, Lauren	90	10:30-12:00	Ballroom
Ali, Noureen	70	10:30-12:00	Ballroom
Aljabri, Basma	66	10:30-12:00	Ballroom
Aljunaidy, Mais	47	13:45-15:15	Chairman Room
Allan, Chantal	131	15:15-16:45	Ballroom
Alsaif, Maha	113	10:30-12:00	Ballroom
Alvarez, Silvia	30	10:30-12:00	Ballroom
Ananthakrishnan, Gayathri	40	13:45-15:15	Chancellor
Andrishak, Sarah	165	15:15-16:45	Ballroom
Annamraju, SaiKrishna	78	10:30-12:00	Ballroom
Baddam, Pranidhi	50	13:45-15:15	Consulate Room
Bahari, Mohammed	127	15:15-16:45	Ballroom
Bahry, Ashley	7	09:00-10:30	Chancellor
Bain, Alexandra	121	10:30-12:00	Ballroom
Bedi, Prabhjot	51	13:45-15:15	Consulate Room
Beggs, Megan	150	15:15-16:45	Ballroom
Bilyk, Olena	42	13:45-15:15	Chancellor
Brennan, Lesley	141	15:15-16:45	Ballroom
Brosinsky, Larissa	71	10:30-12:00	Ballroom
Browne, Nadia	35	13:45-15:15	Turner Valley Room
Cantor, Arielle	43	13:45-15:15	Chancellor
Care, Alison	98	10:30-12:00	Ballroom
Carvalho, Julyana Gomes de Oliveira	146	15:15-16:45	Ballroom
Chan, Brandon	2	09:00-10:30	Turner Valley Room
Chan, Andrew	24	09:00-10:30	Consulate Room
Charchuk, Rhianna	74	10:30-12:00	Ballroom
Chen, Jerry	82	10:30-12:00	Ballroom
Cherak, Stephana	159	15:15-16:45	Ballroom
Chetan, Devin	132	15:15-16:45	Ballroom
Choi, Maria	149	15:15-16:45	Ballroom
Coatham, Mackenzie	38	13:45-15:15	Chancellor
Crawford, Jenna	73	10:30-12:00	Ballroom
Crosley, Powel	125	10:30-12:00	Ballroom
Crossman, Jacqueline	144	15:15-16:45	Ballroom
Dalmer, Tim	118	10:30-12:00	Ballroom
Danesh, Ghazal	114	10:30-12:00	Ballroom
De Jong, Kirstie	39	13:45-15:15	Chancellor
Do, Victor	6	09:00-10:30	Turner Valley Room
Dube, Nomathemba	13	09:00-10:30	Chairman Room
Dunsmore, Garett	5	09:00-10:30	Turner Valley Room
Echigoya, Yusuke	1	09:00-10:30	Turner Valley Room

Name	#	Time	Room
El Hassar, Btissam	15	09:00-10:30	Chairman Room
El-Kalla, Mohamed	57	13:45-15:15	Leduc Room
Ellestad, Kristofor	49	13:45-15:15	Chairman Room
Elloumi, Yesmine	170	15:15-16:45	Ballroom
Fagan, Kelly	79	10:30-12:00	Ballroom
Faught, Erin	163	15:15-16:45	Ballroom
Featherstone, Robin	86	10:30-12:00	Ballroom
Fung, Ryan	112	10:30-12:00	Ballroom
Fung, Daniel	164	15:15-16:45	Ballroom
Ganguly, Esha	101	10:30-12:00	Ballroom
Gates, Allison	89	10:30-12:00	Ballroom
Gazie, Hillary	36	13:45-15:15	Turner Valley Room
Gazzaz, Malak	52	13:45-15:15	Consulate Room
Gehring, Nicole	166	15:15-16:45	Ballroom
Ghaneei, Maliheh	69	10:30-12:00	Ballroom
Golfar, Atoosa	172	15:15-16:45	Ballroom
Greenwell, Amanda	20	09:00-10:30	Consulate Room
Gyenes, Dora	102	10:30-12:00	Ballroom
Haas, Justin	173	15:15-16:45	Ballroom
Hajar, Ali	133	15:15-16:45	Ballroom
Han, Xiaolu	180	15:15-16:45	Ballroom
Haynes, Kate	103	10:30-12:00	Ballroom
Heo, Giseon	119	10:30-12:00	Ballroom
Heydari, Emma	58	13:45-15:15	Leduc Room
Ho, Kim	64	10:30-12:00	Ballroom
Hosoki, Kana	83	10:30-12:00	Ballroom
Hou, Shangmei	41	13:45-15:15	Chancellor
Houshmandi, Mohammad Mehdi	100	10:30-12:00	Ballroom
Hui, Dorothea	138	15:15-16:45	Ballroom
Hunter, Stephen	67	10:30-12:00	Ballroom
Hyderi, Abbas	134	15:15-16:45	Ballroom
Isaac, Andre	171	15:15-16:45	Ballroom
Jafari, Nooshin	75	10:30-12:00	Ballroom
Johnson, Peter Anto	99	10:30-12:00	Ballroom
Jun, Shelly	155	15:15-16:45	Ballroom
Kamal, Muna	174	15:15-16:45	Ballroom
Kang, Liane	32	13:45-15:15	Turner Valley Room
Kapasi, Aamena	136	15:15-16:45	Ballroom
Kassam, Shehzad	126	10:30-12:00	Ballroom
Kebbe, Maryam	162	15:15-16:45	Ballroom
Khanpour Ardestani, Samaneh	110	10:30-12:00	Ballroom
Khoury, Michael	25	09:00-10:30	Leduc Room
Kim, Tiffany	3	09:00-10:30	Turner Valley Room
Klaver-Kibria, Justine	117	10:30-12:00	Ballroom
Kowal, Stephanie	153	15:15-16:45	Ballroom
Krysa, Jacqueline	46	13:45-15:15	Chairman Room

List of presenters

Name	#	Time	Room
Kumari, Manjeet	33	13:45-15:15	Turner Valley Room
Lavy, Rotem	137	15:15-16:45	Ballroom
Le, Andy	4	09:00-10:30	Turner Valley Room
Lee, HanHyung	9	09:00-10:30	Chancellor
Lee, Justin	85	10:30-12:00	Ballroom
Leimert, Kelycia	105	10:30-12:00	Ballroom
Luthra, Tania	106	10:30-12:00	Ballroom
MacDonald, Krista	115	10:30-12:00	Ballroom
Madsen, Mette	161	15:15-16:45	Ballroom
Mah, Kandice	31	10:30-12:00	Ballroom
Mah, Richard	94	10:30-12:00	Ballroom
Mamede, Fabiana	92	10:30-12:00	Ballroom
Mansukhani, Gitanjali	27	09:00-10:30	Leduc Room
Manz, Joren	135	15:15-16:45	Ballroom
Martin, Billie-Jean	44	13:45-15:15	Chairman Room
Maruyama, Rika	148	15:15-16:45	Ballroom
Masoud, Waleed	59	13:45-15:15	Leduc Room
Matenchuk, Brittany	96	10:30-12:00	Ballroom
McColl, Hunter	77	10:30-12:00	Ballroom
McCurdy, Ashley	183	15:15-16:45	Ballroom
McLavish, Meagan	160	15:15-16:45	Ballroom
Meenakshi Sundaram and Daniel Nisakar	122	10:30-12:00	Ballroom
Meherali, Salima	88	10:30-12:00	Ballroom
Miyagishima, Rebecca	177	15:15-16:45	Ballroom
Monteiro, Juliana Cristina dos Santos	93	10:30-12:00	Ballroom
Morris, Jill	91	10:30-12:00	Ballroom
Mugaba, Proscovia	128	15:15-16:45	Ballroom
Nesari, Maryam	156	15:15-16:45	Ballroom
Nguyen, Kim Cuong	145	15:15-16:45	Ballroom
Nielsen, Charlene	108	10:30-12:00	Ballroom
Norris, Allison	17	09:00-10:30	Chairman Room
Nosherwan, Asma	26	09:00-10:30	Leduc Room
Penner, Stephanie	72	10:30-12:00	Ballroom
Pitre, Nicole	176	15:15-16:45	Ballroom
Pollock, Michelle	14	09:00-10:30	Chairman Room
Powley Unrau, Stephanie	140	15:15-16:45	Ballroom
Purdy, Graeme	8	09:00-10:30	Chancellor
Rai, Usha	168	15:15-16:45	Ballroom
Rawat, Sonia	129	15:15-16:45	Ballroom
Raza, Sarah	21	09:00-10:30	Consulate Room
Reyes, Laura	65	10:30-12:00	Ballroom
Ricci, M. Florencia	28	09:00-10:30	Leduc Room
Roczkowsky, Andrej	130	15:15-16:45	Ballroom
Rosychuk, Rhonda	154	15:15-16:45	Ballroom
Rycroft, Jordan	116	10:30-12:00	Ballroom
Sabiri, Peter	84	10:30-12:00	Ballroom
Sacrey, Lori-Ann	19	09:00-10:30	Consulate Room
Saini, Jasmeen	53	13:45-15:15	Consulate Room
Schreiber, Sanja	23	09:00-10:30	Consulate Room
Semeniuk, Joel	56	13:45-15:15	Leduc Room
Shave, Kassi	151	15:15-16:45	Ballroom
Shulhan, Jocelyn	169	15:15-16:45	Ballroom
Shulman, Lisa	158	15:15-16:45	Ballroom
Sidhu, Anmol	45	13:45-15:15	Chairman Room
Sivananthajothy, Priatharsini (Tharsini)	18	09:00-10:30	Chairman Room
Sklar, Cameron	10	09:00-10:30	Chancellor
Skow, Rachel	54	13:45-15:15	Consulate Room
Smith, Allison	143	15:15-16:45	Ballroom
Sosniuk, Morgan	63	10:30-12:00	Ballroom
Spaans, Floor	11	09:00-10:30	Chancellor
St. Hilaire, Brianne	120	10:30-12:00	Ballroom
Stewart, Catherine	142	15:15-16:45	Ballroom
Sutton, Reed	87	10:30-12:00	Ballroom
Sydora, Beate	123	10:30-12:00	Ballroom
Tang, Xiaoyun	124	10:30-12:00	Ballroom
Thorpe, Marian	60	13:45-15:15	Leduc Room
Toosi, Amy	22	09:00-10:30	Consulate Room
Touznik, Aleksander	76	10:30-12:00	Ballroom
Tran, Uyen	139	15:15-16:45	Ballroom
Tran, Tho	178	15:15-16:45	Ballroom
Tun, Hein Min	109	10:30-12:00	Ballroom
Usman, Iram	62	10:30-12:00	Ballroom
Verstraeten, Barbara	95	10:30-12:00	Ballroom
Wadge, Emily	37	13:45-15:15	Turner Valley Room
Walton, Sarah	16	09:00-10:30	Chairman Room
Wang, Yiqun	48	13:45-15:15	Chairman Room
Waskiewicz, Andrew	81	10:30-12:00	Ballroom
Wee, Wallace	61	13:45-15:15	Leduc Room
Wijesuriya, Tishani Methsala	80	10:30-12:00	Ballroom
Wine, Osnat	157	15:15-16:45	Ballroom
Wollin, Daniel	55	13:45-15:15	Consulate Room
Woodman, Andrew	12	09:00-10:30	Chancellor
Wu, Jessica	111	10:30-12:00	Ballroom
Yang, Zelei	179	15:15-16:45	Ballroom
Yang, Samuel	181	15:15-16:45	Ballroom
Yoo, Jihee	107	10:30-12:00	Ballroom
Zaidi, Deenaz	34	13:45-15:15	Turner Valley Room
Zhou, Jiesi	182	15:15-16:45	Ballroom

Abstract #:	1
Presenter:	Yusuke Echigoya
Supervisor:	Toshifumi Yokota
Title:	Systemic multi-exon skipping with peptide-conjugated antisense morpholinos improves heart function of a dog model of Duchenne muscular dystrophy
Authors:	Yusuke Echigoya, Nhu Trieu, Dharminder Panesar, Joshua Lee, Kenji Rowel Lim, Toshifumi Yokota
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction: Duchenne muscular dystrophy (DMD) is an X-linked lethal genetic disorder that affects approximately 1 in every 5000 boys. Patients develop progressive muscle weakness and degeneration, and typically die around 20 – 30 years of age due to cardiac and/or respiratory failure. DMD is caused by mutations in the *dystrophin* (*DMD*) gene leading to an absence of the dystrophin that is an essential protein for maintaining muscle membrane integrity. Exon skipping via synthetic antisense phosphorodiamidate morpholino oligomers (PMOs) restores the reading frame and allows the production of short but functional dystrophin protein. Currently, PMO-mediated exon skipping represents one of the most promising therapeutic options. However, PMOs have shown very little efficacy in the cardiac muscle. To increase therapeutic potency and rescue cardiac muscle from degeneration, we tested the efficacy of arginine-rich cell-penetrating peptide-conjugated PMOs (PPMOs) in a dog model of DMD.

Methods: We examined the effects of PPMO-mediated multi-exon skipping in skeletal and cardiac muscles of a dystrophic dog model, the canine X-linked muscular dystrophy in Japan ($CXMD_J$). A 3-PPMO cocktail designed to skip *dystrophin* exons 6 and 8 was injected intracoronarily or intravenously into $CXMD_J$ dogs. Two weeks after the treatment, therapeutic efficacy was evaluated with rescued dystrophin levels, histological amelioration, electrocardiogram, and blood tests.

Results: A single intracoronary or intravenous PPMO injection restored dystrophin expression in the heart of $CXMD_J$ dogs. By extended treatment with four systemic PPMO administrations at 2-week intervals, dystrophin protein was rescued in working myocardium and cardiac Purkinje fibers, as well as skeletal muscles. Vacuole degeneration of cardiac Purkinje fibers, as seen in DMD patients, was ameliorated in $CXMD_J$ dogs treated with the 3-PPMO cocktail. Electrocardiogram abnormalities (increased Q amplitude and Q/R ratio) were improved in the $CXMD_J$ dogs after intracoronary or intravenous administration, while they were exacerbated over time in non-treated and unmodified PMO cocktail-treated dogs. Blood tests indicated no toxicity in $CXMD_J$ dogs after the treatment with four intravenous PPMO injections.

Conclusions: The present study first reports rescue of dystrophin expression and recovery of the conduction system in the heart of dystrophic dogs by PPMO-mediated multi-exon skipping. We demonstrate that rescued dystrophin expression in the Purkinje fibers leads the improvement/prevention of cardiac conduction abnormalities in the dystrophic heart.

Funded By: Innovation Grant

Abstract #:	2
Presenter:	Brandon Chan
Supervisor:	Richard Schulz
Title:	Doxorubicin induces de novo expression of N-terminal truncated MMP-2 which impairs calcium transients in neonatal cardiomyocytes
Authors:	Brandon Chan, Bryan Hughes, Andrej Roczkowsky, Mathieu Poirier, Ramses Ilarazza, Klaus Ballanyi, Richard Schulz
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Oncology

INTRODUCTION: Anthracyclines, such as doxorubicin (DXR), are effective anticancer agents prescribed in many chemotherapeutic regimens, including breast and pediatric cancers. However, their therapeutic utility is limited by severe cardiotoxicity. The mechanism of DXR cardiotoxicity is not fully understood, but is associated with increased oxidative stress and impaired calcium (Ca^{2+}) handling. In cardiomyocytes, oxidative stress activates a protease, matrix metalloproteinase-2 (MMP-2), which impairs cardiac contraction by cleaving sarcomeric proteins and putative Ca^{2+} regulatory proteins. We hypothesize that MMP-2 contributes to DXR cardiotoxicity by proteolyzing sarcomeric proteins and impairing Ca^{2+} transients.

METHODS: Neonatal rat ventricular myocytes (NRVM) were treated with 0.5 μM DXR in presence or absence of MMP inhibitors ARP-100 or ONO-4817 for up to 24 hr. MMP-2 activity and protein/mRNA expression was measured by gelatin zymography, immunoblot, and RT-qPCR, respectively. Ca^{2+} transients in NRVM, loaded with Fluo-8L, were visualized under basal and isoproterenol-stimulated conditions using live-cell confocal microscopy.

RESULTS: DXR increased MMP-2 activity in a time-dependent manner, up to maximum of 300% by 12 hr exposure. DXR upregulated both *Mmp2* and *NTT-Mmp2* mRNA levels by 680% and 560%, respectively. 90% of DXR-induced *Mmp2* expression consisted of N-terminal truncated MMP-2, an MMP-2 isoform that is exclusively expressed during oxidative stress. ARP-100 or ONO-4817 attenuated DXR-increased MMP-2 activity by 67%. 24 hr DXR reduced levels of a known MMP-2 target, troponin I, by 40% through a MMP-2-independent mechanism. 24 hr DXR decreased the amplitude of Ca^{2+} transients by 72% and 63% under basal and isoproterenol-stimulated conditions, respectively. DXR also reduced the frequency of both basal and stimulated Ca^{2+} transients by 87% and 97%, respectively. ARP-100 restored both the DXR-reduced amplitude and frequency of Ca^{2+} transients. In control cells, nifedipine (L-type Ca^{2+} channel blocker, 10 μM) blocked Ca^{2+} transients under both basal and isoproterenol-stimulated conditions, whereas thapsigargin (SERCA inhibitor, 10 μM) only prevented isoproterenol-stimulated Ca^{2+} transients. These results suggest voltage-gated Ca^{2+} channels and/or SERCA may be targeted by MMP-2 in DXR-treated NRVM. Studies investigating the effect of MMP-2 inhibitors against DXR cardiomyopathy on in vivo cardiac function are underway.

CONCLUSIONS: MMP-2 activation in early DXR cardiotoxicity, including de novo expression of NTT-MMP-2, contributes to impaired Ca^{2+} transients likely by targeting voltage-gated Ca^{2+} channels and/or SERCA.

Funded By: Graduate and Summer Studentship

Abstract #:	3
Presenter:	Tiffany Kim
Supervisor:	Simon Urschel
Title:	Lymphocyte alterations in heart-transplanted children in relation to development of allergic and autoimmune disorders
Authors:	Tiffany Kim, Nicholas Avdimiretz, Lavinia Ionescu, Ingrid Larsen, Bruce Motyka, Lori West, Simon Urschel
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction: Pediatric heart transplant (HTx) recipients are at higher risk for allergic and autoimmune disorders than non-transplanted children. We found young age at HTx and thymectomy (TE) to be associated factors. We hypothesized that TE and immunosuppression at an early age affect the development of T and B-cell subsets, especially regulatory T-cells (Tregs), which are key in maintaining peripheral tolerance. We investigated the impact of TE and lymphocyte-depleting induction on lymphocyte subtype proportions, and asthma and allergies in HTx patients.

Methods: Flow Cytometry phenotyping was used to determine proportions of lymphocyte subsets in peripheral blood samples from patients transplanted before age 18, detecting expression of specific surface markers. Clinical data were collected in standardized questionnaires on allergic and autoimmune disorders including asthma and eczema. Medical charts were reviewed for consolidation.

Results: Proportion of CD45RA+CD27+ naïve Treg cells within the Treg population (CD4+CD25+CD127low) was lower in thymectomized (n=8) than non-thymectomized (n=4) patients ($p<0.05$). 71% of thymectomized patients developed asthma or eczema post-transplant vs 15% of the general population and 41% of HTx children. Although Tregs were visibly fewer in patients with asthma and eczema, this did not reach significance. Memory CD4+ cell proportions were higher in thymectomized patients. Breg populations were lower in patients with few allergic disorders. Memory B-cell proportions were not different between groups.

Conclusions: Lower percentages of certain Treg subsets, following TE, may underlie increased risk of asthma and eczema in HTx children. Other lymphocyte subsets such as Bregs may also contribute to increased risk. A larger sample will allow us to elucidate a possible correlation between immune phenotype and clinical complications.

Funded By: AIHS

Abstract #: 4
Presenter: Andy Le
Supervisor: Joanna MacLean
Title: Impaired quality of life in children following extreme preterm birth: contribution of cardiorespiratory function and problem behaviour
Authors: Andy Le, Joanna MacLean
Affiliations: University of Alberta

Introduction

Children with a history of extremely preterm (EP) have more cardiorespiratory problems and lower quality of life (QoL) compared to term born children. What is not known is whether cardiorespiratory problems impact quality of life in the same children. In this cohort study, we examined the relationship between cardiorespiratory function and QoL in children born EP.

Methods

We recruited children 8-12 years of age who were born EP (≤28 weeks gestation) between 1997 and 2004. EP children were grouped as no/mild BPD (n=53) and moderate/severe (mod/sev) BPD (n=50) based on no or continued oxygen used at 36 weeks gestational age respectively. Age-matched controls (n=64) were born at term. All children attempted lung function and cardiorespiratory exercise testing, and completed a QoL questionnaire (PedsQL). Parents completed a parent version of the PedsQL and the Child Behavior Checklist (CBCL). Parents also completed a PedsQL Asthma questionnaire if they indicated that their child had asthma.

Results

PedsQL child self-report total score was lower in children with mod/sev BPD (72.6) compared to both no/mild BPD (84.3) and Control children (86.1, $p<0.05$). Scores from the PedsQL parent-report showed the same pattern. There was no significant difference in the PedsQL asthma score between the mod/sev BPD (75.5, n=14), no/mild BPD (82.1, n=14), and Control children (80.2, n=7) groups. CBCL total competence score indicated a higher frequency of combined subclinical and clinical problem behavior in children with mod/sev BPD (62.5%) compared to both no/mild BPD (25.0%) and Control children (15.8%, $p<0.05$). Multi-variate regression modeling showed that BPD status, VO_2 %predicted, 'shortness of breath' with activity, household smoke, and a history of asthma were significantly associated with QoL ($R^2=0.24$, $p<0.001$). Adding measures of problem behavior to the model improved the model ($R^2=0.30$, $p<0.001$) but removed cardiorespiratory variables as important predictors of QoL.

Conclusion

QoL following EP birth is impaired in children with a history of mod/sev BPD compared to no/mild BPD and control children. Cardiorespiratory impairments are associated with lower QoL in EP children; however, problem behavior has a stronger influence on QoL.

Funded By: Summer Studentship

Abstract #:	5
Presenter:	Garett Dunsmore
Supervisor:	Shokrollah Elahi
Title:	CD71+ erythroid precursor cells compromise neonatal host defense to Bordatella pertussis infection
Authors:	Garett Dunsmore, Cole Delyea, Najmeh Bozogmehr, Afshin Namdar, Shokrollah Elahi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology

Introduction: Contrary to previous belief, our recent findings have demonstrated that the immune system of an infant is not under developed, but instead it is actively suppressed. Consequentially, this immune suppression predisposes the infant to infectious diseases. We have demonstrated that this immune suppression in infants is associated with the abundance of CD71+ erythroid precursors. CD71+ erythroid precursors suppress innate immune responses by multiple mechanisms, for instance by production of Arginase-2. Here the role of CD71+ erythroid precursors in whooping cough, one of the most common infections in children, is investigated.

Methods: Newborn mice were intraperitoneally injected with either a rat IgG isotype control or an anti-CD71 antibody. Twenty-four hours post IP injection they were infected intranasally with *B. pertussis* (newborns with $1x10^6$ CFUs, and adults with $1x10^6$ or $1x10^8$ CFUs). Tissues were harvested at two, four, and six days following infection.

Results: Our data demonstrate that CD71+ erythroid precursors compromise host defense against *B. pertussis* as depletion of CD71+ erythroid precursors protects newborns against the infection. Our results show that depletion of CD71+ erythroid precursors is associated with increased IFN-g, and enhanced phagocytosis by CD11b+ cells, which results in lower bacterial load in their lungs.

Conclusions: Our data provides additional evidence that CD71+ erythroid precursor cells compromise neonatal innate host defense against infections.

Funded By: Innovation Grant

Abstract #:	6
Presenter:	Victor Do
Supervisor:	Lisa Hornberger
Title:	Fetal programming: Cardiovascular structure, function and aortic stiffness in fetuses, early and late infants of pre-gestational diabetic mothers
Authors:	Victor Do, Tina Ojala, Tim Colen, Silvia Goncalvez-Alvarez, Sandra Davidge, Najlaa Al-Rajaa, Jesus Serrano-Lomelin
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction: Adults whose mothers had diabetes mellitus (DM) during pregnancy have increased risk of cardiovascular disease (CVD). While it is well-recognized that infants of diabetic mothers (IDMs) develop transient left ventricular (LV) hypertrophy and mild diastolic pathology before birth, whether these changes persist and contribute to adult CVD long-term has not been explored. The aims of this study were to determine 1) if myocardial hypertrophy and diastolic dysfunction observed in the fetus and early IDM persist into later infancy, 2) if IDM's have increased aortic stiffness early in life that contributes to LV hypertrophy, and 3) if altered cardiovascular structure and function in the offspring of DM is associated with worse glycemic control in pregnancy.

Methods: We prospectively and longitudinally investigated myocardial and vascularstructure and function by echocardiography in the offspring of pregnancies complicated by pregestational DM, from fetal stages (3 each, midtrimester to term) through infancy (4-6 weeks/6-12 months). We compared LV (LVPWd) and septal (IVS) wall thickness, systolic and diastolic function parameters (pre and postnatal), and aortic stiffness (postnatal) between IDM and pre and postnatal age-matched, controls.

Results: Compared to controls, increased LVPWd and IVS ($p < 0.001$) was present in DM fetuses beginning in late second and in the third trimester, and this was accompanied by an increase in the LV Tei index, in the third trimester only. In both early and late infancy, we observed a significant increase in LVPWd and IVS thickness ($p < 0.001$ for both ages) in IDM compared to controls. Although subtle differences in diastolic function were observed in early infancy, by late infancy there were no LV functional differences between IDM and controls. Pulse wave velocity (PWV), a measure of aortic stiffness, was significantly increased in late infancy IDMs (3.7 +/- 1.2 vs 2.2 +/-0.47m/s, $p <0.01$) and correlated with both LVPWd and IVS thickness (R^2 0.82 and 0.87, respectively, $p<0.05$). PWV in late infancy linearly correlated with maternal HbA1c in the 3rd trimester ($R^2 = 0.83$, $p<0.05$).

Conclusion: IDMs display ventricular hypertrophy from mid-gestation that is not resolved by late infancy. Aortic stiffness is increased IDMs in late infancy which may relate to maternal glycemic control in pregnancy. Further studies are underway to better define the relationship between myocardial hypertrophy and aortic stiffness in IDMs, and to explore the evolution of cardiovascular health in early childhood in this cohort.

Funded By: Summer Studentship

Abstract #: 7
Presenter: Ashley Bahry
Supervisor: Jerome Yager
Title: Alterations in brain connectivity in a model of placental insufficiency and the effects of broccoli sprout supplementation
Authors: Ashley Bahry, Edward Armstrong, Jerome Yager
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Neuro-cognitive Development

Introduction: Current evidence shows that 70-90% of cerebral palsy (CP) cases result from insults during gestation, such as placental insufficiency (PI). Unfortunately, no treatments are available to target these *in utero* insults. To address the majority of infants with no therapeutic options, and explore a prophylactic approach to CP, we are investigating broccoli sprouts (BrSp). Previously our data has shown BrSp to prevent developmental delays in intrauterine growth restricted (IUGR) offspring resulting from PI. Although abnormalities in both cognition and motor functioning are evident in these IUGR offspring, no long-term overt pathology is present. It is suggested that alterations in neuronal morphology in these offspring may be the underlying mechanism for the persistent aberrant behavior.

Objectives: Determine if IUGR causes detrimental effects on neuronal morphology, and if BrSp supplementation remediates these aberrant alterations.

Methods: Timed pregnant Long-Evans rat dams were randomly selected to undergo either bilateral uterine artery ligation or sham surgery on day (E)20 of a 23-day gestation and to receive dietary BrSp supplementation (200mg/day), from E15 to postnatal day (P)21. On P35 offspring were euthanized and brain tissue was processed using Golgi-Cox staining. Neurons were traced and underwent two methods of analysis, 1) Sholl analysis for dendritic length (DL), and 2) Branch order analysis for dendritic complexity (BPs). A three-way ANOVA was performed.

Results: No significant three-way interactions were found for any of the outcome variables in the CA1 region of the hippocampus. A significant two-way interaction was found between IUGR and sex for the apical BPs ($F(1, 36)=5.12$, $p=0.30$), apical DL ($F(1, 36)= 7.65$, $p=0.009$), and basilar DL ($F(1, 36)= 5.97$, $p=0.02$). A significant two way interaction was found between BrSp and IUGR in both the basilar BPs ($F(1, 36)= 4.58$, $p=0.039$) and DL ($F(1, 36)= 12.06$, $p=0.001$). Follow-up analysis showed a significant difference between: SHAM and IUGR in the basilar BPs ($p=0.049$), SHAM and IUGR in the basilar DL ($p=0.001$), and IUGR and IUGR+BrSp in the basilar DL ($p=0.016$).

Conclusions: These findings show that IUGR offspring following PI have alterations in neuronal morphology in the CA1 region, which may contribute to the behavioral changes seen in this model. Moreover, these findings provide further evidence that BrSp as a dietary supplement during pregnancy may prevent CP, by obviating the alterations in dendritic morphology. Further research is needed to further refine our understanding of these mechanisms and the preventive capacity of BrSp.

Funded By: Start-up or Retention Funding, Innovation Grant, Partnership resources

Abstract #: 8
Presenter: Graeme Purdy
Supervisor: Craig Steinback
Title: There and back again: Cardiovascular adaptations to exercise in pregnancy
Authors: Graeme Purdy, Marina James, Paige Wakefield, Rachel Skow, Christina MacKay, Margie Davenport, Craig Steinback
Affiliations: University of Alberta
Research Activity: Cardiovascular Health

Introduction

The underlying mechanisms of blood pressure regulation during pregnancy are not well understood. Autonomic control of heart rate plays an important role in blood pressure regulation. Heart rate variability (HRV) is a measure that provides insight into this control, and has been shown to decrease in pregnancy. The cardiovagal baroreflex is a mechanism that responds to acute drops or rises in blood pressure with beat-by-beat changes in heart rate to maintain arterial blood pressure. Cardiovagal baroreflex gain (BRG) is decreased during exercise in other populations and may also be reduced during pregnancy. However, it is unclear how these mechanisms operate during pregnancy, particularly as it pertains to exercise. We examined how these regulatory reflexes are controlled during and following prenatal exercise.

Methods

Forty-three pregnant (n=10 first trimester [TM1], n=17 second trimester [TM2]; n=16 third trimester [TM3]) and 20 non-pregnant women without contraindication to exercise underwent an incremental exercise test to volitional fatigue (peak exercise). Beat by beat blood pressure was derived using photoplethysmography (Finometer) and heart rate via 3-lead ECG. Spontaneous BRG was calculated as the slope of the relationship between fluctuations in systolic blood pressure (SBP) and R-R interval (RRI) HRV was calculated as the standard deviation of consecutive RRI (SDRR). BRG and HRV were assessed at rest, during steady-state exercise (25W; PRE), and following peak exercise (25W; POST).

Results

Participants were 30.3±5.0 years with a pre-pregnant BMI of 23.4±2.8 kg/m2. As pregnancy progressed, BRG was increasingly blunted and was significantly lower in TM3 compared to NP (17.9±6.9 vs 24.8±7.4 ms/mmHg, p=0.017). Exercise blunted BRG during PRE and was not altered by pregnancy (delta rest to PRE for NP: -12.0±8.4 ms/mmHg, TM1: -11.5±9.7ms/mmHg, TM2: -14.4±12.0 ms/mmHg, TM3: -10.2±6.5 ms/mmHg). Overall, there was significantly less blunting from PRE to POST in TM3 than NP (-3.1±4.2 vs -8.8±8.7, p=0.026). In conjunction with an increasingly blunted BRG as pregnancy progressed, resting HRV (SDRR) was lower in all pregnant groups (TM1: 44±16 ms, TM2: 44±13 ms, TM3: 44±20 ms) than NP (61±19 ms, p=0.027, p=0.013, p=0.012, respectively).

Conclusions

At rest, the TM3 group had reduced ability to respond to changes in blood pressure and a less responsive autonomic nervous system, but during exercise they demonstrated baroreflex and autonomic control comparable to the non-pregnant group.

Funded By: Summer Studentship

Abstract #: 9
Presenter: HanHyung Lee
Supervisor: David Olson
Title: Leukocyte migration into the uterine tissues is upregulated prior to spontaneous birth
Authors: HanHyung Lee, Xin Fang, David Olson
Affiliations: University of Alberta
Research Activity: Maternal Research : Pre-term Birth

Introduction. Each year, fifteen million babies are born preterm. They have the highest risk of perinatal mortality and morbidity because there are no effective means to diagnose and predict who is at risk for preterm birth. To meet this clinical need, the Olson laboratory has been developing a diagnostic test based on the principle that leukocyte invasion of the uterine tissues is a reliable, timely marker of pending labour whether term or preterm. We hypothesized that this phenomenon is characterized by a higher sensitivity of the peripheral leukocytes to migrate in response to labour-specific chemotactic factors, as well as a greater presence of these factors in the uterus and fetal membranes.

Methods. Peripheral blood was collected from pregnant women at multiple points from 24 weeks of gestational age to term and in spontaneous labour (STL). In a modified Boyden chamber, leukocytes were migrated across a selective filter (3 μm pores) in response to chemotactic factors from the fetal membranes of women at STL or at term but not in labour (TNL) (pooled samples, n = 6). STL leukocytes were also migrated in response to chemotactic factors from the mouse lower uterus at multiple gestational points leading up to STL (pooled samples, n = 6). Chemotactic factors were isolated via tissue homogenization and density centrifugation. Flow cytometry was used to characterize the number and phenotype of chemoattracted leukocytes. Multiplex analysis was used to quantitate the expression of known cytokines in the mouse uterus. Statistical analysis was performed with one-way ANOVA.

Results. Granulocytes exhibited greater migratory activity with increasing gestational maturity and upon stimulation with chemoattractant extracts of later gestational age ($n = 6$, $r = 0.36$, $P < 0.05$). Increased expression of neutrophil chemoattractants (MIP-2, KC, G-CSF) and pro-inflammatory mediators (IL-1β, IL-6) were detected in laboring as compared to gestational day 15 samples of the mouse lower uterus.

Conclusion. Leukocyte invasion of the uterus is upregulated by the priming of peripheral granulocytes for migration and by the secretion of local chemoattractants into the uterine tissues. Increased expression of the neutrophil chemoattractants and inflammatory mediators offer direction for studying the underlying mechanisms of leukocyte invasion. Harnessing this information may ultimately allow us to discover new diagnostic and therapeutic measures for preterm birth.

Funded By: Innovation Grant

Abstract #:	10
Presenter:	Cameron Sklar
Supervisor:	Kentia Naud
Title:	Accuracy of prenatal ultrasound in detecting growth abnormalities in triplets: a retrospective cohort study
Authors:	Cameron Sklar, Maryna Yaskina, Sue Ross, Kentia Naud
Affiliations:	University of Alberta
Research Activity:	Maternal Fetal Medicine

Introduction: Triplet pregnancies are high risk to both mother and fetuses, and have increased in number over the last 30 years due to assisted reproductive techniques. Significant management decisions in these pregnancies are made based mainly on ultrasound measurements of fetal growth, although there is a paucity of data examining the accuracy of fetal weight measurements in these gestations. The purpose of this study was to evaluate accuracy of prenatal ultrasound to diagnose growth abnormalities (intrauterine growth restriction, severe growth discordance,) in triplet pregnancies.

Methods: A retrospective cohort study of 78 triplet pregnancies (234 fetuses) delivered at a single tertiary hospital from January 2004 to May 2015 was performed. Growth percentiles from the last ultrasound were derived from estimated fetal weight using Hadlock's formula for each triplet. Definition of intra-uterine growth restriction was estimated fetal weight or birth weight <10th percentile for gestational age on population-based singleton growth curves. Growth discordance was calculated for each triplet set using the formula {(estimated fetal weight largest triplet-estimated fetal weight smallest)/estimated fetal weight largest}. These estimations were compared to birth weights.

Results: Mean gestational age at delivery was 31.1 ± 3.7 weeks. Sensitivity of ultrasound to predict ≥1 growth restricted fetus in a triplet set was 55.6% (95% CI 35.3 – 74.5%); specificity was 100% (95% CI 93.0 – 100%); PPV 100% (95% CI 74.7 – 100%); NPV 81.0% (95% CI 73.2 – 85.7%). Sensitivity of ultrasound to detect fetal growth discordance >25% in a triplet set was 80.0% (95% CI 44.4 – 97.5%), specificity 94.1% (95% CI 85.6 – 98.4%); PPV 66.7% (95% CI 42.4 – 84.5%); NPV 97.0% (95% CI 90.2 – 99.1%).

Conclusions: Prenatal ultrasound currently remains the most reliable tool to screen for growth anomalies in triplet pregnancies; however, it appears to have less than ideal sensitivity, missing a number of cases of intra-uterine growth restriction and significant growth discordance. Increasing the sensitivity of prenatal ultrasound for growth anomalies using new modalities (3-Dimensioanal ultrasound, new estimated fetal weight formulae, etc.) could potentially improve perinatal outcomes for these high-risk gestations.

Funded By: Trainee Travel Grant and Partnership resources

Abstract #: 11
Presenter: Floor Spaans
Supervisor: Sandra Davidge
Title: Syncytiotrophoblast extracellular vesicles alter angiotensin II induced vasoconstriction in mouse uterine artery
Authors: Floor Spaans, Jude Morton, Dionne Tannetta, Ian Sargent, Sandra Davidge
Affiliations: University of Alberta
Research Activity: Maternal Research : Preeclampsia

Introduction

The development of hypertension and proteinuria in preeclampsia (PE) is thought to be due to the release of placental factors, one of which is syncytiotrophoblast extracellular vesicles (STBEVs), leading to maternal endothelial dysfunction. The lectin-like oxidized LDL receptor-1 (LOX-1) is a multi-ligand scavenger receptor and both STBEVs and LOX-1 expression are increased in women with PE. We have recently shown that STBEVs impair endothelium-dependent vasodilation of rat uterine arteries and this was prevented using a LOX-1 blocking antibody. However, the role of LOX-1 in contributing to vascular maladaptations to pregnancy is not known. Thus, to further investigate a role for LOX-1 in pathological pregnancies, we propose to use genetically modified mice. Our aim was to further investigate the role of STBEVs and the LOX-1 receptor in vascular dysfunction using LOX-1 deficient (knock-out; KO) mice. We hypothesized that STBEVs activate LOX-1 and contribute to vascular dysfunction in mouse uterine arteries, and that this effect will not be evident in LOX-1 KO mice.

Methods

Uterine arteries were obtained from late pregnant (gestational day 18; term = day 19) C57BL/6 mice (WT) and LOX-1-KO mice (C57BL/6 background). Isolated vessels were incubated for 24hrs in the absence or presence of STBEVs (200 µg/ml). Using wire myography, endothelium-dependent (methylcholine; MCh) and -independent (sodium nitroprusside; SNP) vasodilation, and phenylephrine (PE), angiotensin II (Ang II) and high potassium physiological salt solution (KPSS) mediated vasoconstriction were measured.

Results

Our preliminary results showed that responsiveness to Ang II was increased after incubation with STBEVs as compared with the controls, i.e. a prolonged response to Ang II was observed (AUC: 3.3±0.9 controls vs. 4.9±0.9 STBEVs; $p<0.03$). Increased responsiveness to Ang II following STBEV incubation was observed in arteries obtained from WT mice but not in arteries from LOX-1 KO mice. STBEV incubation did not alter vascular responses to PE, KPSS, SNP or MCh in the arteries of either WT or LOX-1 KO mice.

Conclusion

STBEVs induced hyper-responsiveness to Ang II which was LOX-1 dependent. Further studies are required to determine the mechanisms: i.e. whether AT-1 receptor expression is altered by STBEV activation of LOX-1. Interestingly, this is in accordance with a recent report showing that LOX-1 activation is associated with AT-1 receptor activation. These data indicate that elevated levels of circulating STBEVs in pregnancy could contribute to the development of uterine artery vascular dysfunction via the LOX-1 receptor.

Funded By: AIHS, CIHR and WCHRI

Abstract #:	12
Presenter:	Andrew Woodman
Supervisor:	Stephane Bourque
Title:	Sex dependent cytochrome c oxidase upregulation in iron deficient fetal rat kidneys: A potential protective mechanism
Authors:	Andrew Woodman, Hélène Lemieux, Stephane Bourque
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease

Introduction
Iron deficiency (ID) is the most prevalent nutritional deficiency worldwide, and affects populations across the socioeconomic spectrum. The incidence of ID anemia in pregnant women is of chief concern, with rates estimated to be 50-80 % in developing countries, and 30% in western countries (23 % in Canada). Prenatal ID has been shown to cause intrauterine growth restriction in the offspring, although precise mechanisms underlying these altered growth and developmental trajectories are unknown. We have previously shown persistent kidney and vascular dysfunction in adult ID offspring, which is more prominent in male than female offspring, which may stem from stress occurring *in utero*. We hypothesize maternal ID causes fetal hypoxia, kidney mitochondrial dysfunction and cell death within offspring kidneys, which are expected to be more pronounced in male fetuses.

Methods
Six and 12-week old female rats (severe and moderate ID groups, respectively) were fed either a low iron (3 mg/kg diet) or iron-replete (35 mg/kg diet) diet throughout pregnancy. Dams were treated with pimonidazole on gestational day (GD)20 to assess tissue hypoxia. Pregnant dams and fetuses were euthanized on GD21, at which time maternal plasma ferritin, transferrin, and Hb, as well as fetal Hb levels were measured. TUNEL was performed on fetal kidneys to assess apoptosis. High-resolution respirometry was used to assess integrated mitochondrial function in fetal kidney homogenates.

Results
Maternal iron restriction resulted in 17% ($P<0.01$) and 48% reduction ($P<0.001$) in maternal Hb in the moderate (M-ID) and severe (S-ID) groups on GD21, respectively. While maternal plasma transferrin and ferritin levels were not altered in M-ID, S-ID maternal plasma ferritin decreased 75% ($P<0.01$) and plasma transferrin increased 25% ($P<0.05$). Accordingly, M- and S-ID resulted in 39% and 65% decreases in fetal Hb (both $P<0.001$), which was accompanied by asymmetric fetal growth restriction, an effect more pronounced in the S-ID group. Evidence of hypoxia was present in kidneys of both M- and S-ID fetuses (both $P<0.01$). Interestingly, S-ID male kidneys exhibited elevated apoptosis ($P=0.001$) while females did not ($P=0.86$); these results coincided with cytochrome *c* oxidase upregulation in female, but not male, mitochondria ($P<0.05$).

Conclusions
Fetal anemia and hypoxia occur in both moderate and severe maternal ID. Upregulation of cytochrome *c* oxidase in female fetal kidneys may represent a protective mechanism that mitigates apoptosis within the kidneys. Experiments are ongoing to study the role of cytochrome *c* oxidase in attenuating ID-induced kidney damage.

Funded By: Innovation Grant

Abstract #:	13
Presenter:	Nomathemba Dube
Supervisor:	Paul Veugelers
Title:	Does access to and use of TVs, computers, tablets, video games and cellphones before bedtime affect sleep and body weight of children?
Authors:	Nomathemba Dube, Kaviul Khan, Sarah Loehr, Yen Chu, Paul Veugelers
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction: The use of electronic entertainment and communication devices (EECDs) (TVs, computers, tablets, video games, cellphones) has been demonstrated to affect sleep. Poor sleep quality and short sleep duration, in turn, have been proven to increase the risk for obesity. Understanding the impact that the use of EECDs versus reading a book has on sleep and body weight is essential to promote good sleep and prevent childhood obesity. We sought to determine how sleep quality, sleep duration and weight status are influenced by (i) access to EECDs in children's bedrooms, (ii) use of EECDs during the hour before sleep, and (iii) calming activities like reading during the hour before sleep.

Methods: A population-based survey amongst 2,334 grade 5 students and parents was conducted in randomly selected elementary schools in Alberta, Canada. Multivariable mixed effect linear and logistic regression models were used to analyse the data.

Results: Compared to no access and no use, bedroom access to and use of a computer, tablet, video game or cell phone decreased good sleep quality particularly by 33% amongst users of cell phones (OR=0.67, 95% CI: 0.61-0.74) and by 24% amongst users of computers (OR=0.76, 95% CI: 0.69-0.83) during the hour before sleep. Sleep duration was shorter by 10.2 minutes (computer), 9.0 minutes (cell phone), and 6.6 minutes (TV) for those with bedroom access to and used these EECDs during the hour before sleep. Odds of obesity were doubled by bedroom access to and use of a cell phone during the hour before sleep compared to no access and no use. Frequently reading in the bedroom during the hour before sleep with no EECD access (i) improved sleep quality (29%) and duration (10.8 minutes) when compared to rarely reading with EECD access, and (ii) reduced obesity odds (85%) when compared to rarely reading without EECD access.

Conclusions: Our findings suggest that childhood sleep quality, sleep duration and weight status can be improved by both removing EECDs from the bedroom and reading a book during the hour before sleep as opposed to using EECDs during that period. These findings will inform health promotion messages and may give rise to national policies regarding EECD use.

Funded By: Graduate Studentship

Abstract #:	14
Presenter:	Michelle Pollock
Supervisor:	Lisa Hartling
Title:	Guidance for conducting overviews of reviews: Results from a scoping review and qualitative metasummary
Authors:	Michelle Pollock, Ricardo M Fernandes, Lorne A Becker, Robin Featherstone, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Knowledge synthesis methods

Introduction: Systematic reviews (SRs) combine the results of multiple similar primary studies to answer a specific clinical question, whereas overviews of reviews (overviews) compile data from multiple similar SRs. Given their objective to synthesize extensive data in a user-friendly format, overviews have been gaining momentum as a valuable knowledge synthesis product. Despite their increasing popularity, there is limited methodological guidance available for researchers wishing to conduct overviews. This scoping review aimed to identify and collate all published and unpublished guidance documents for conducting overviews of healthcare interventions. Our objectives were to: provide a map of existing guidance documents; identify similarities, differences, and gaps in guidance; and identify common challenges involved in conducting overviews.

Methods: We conducted a comprehensive search that involved reference tracking, handsearching of websites and conference proceedings, and contacting producers of overviews, supplemented with traditional database and web searches of Medline, EMBASE, DARE, Scopus, Cochrane Methods Studies Database, and Google Scholar. Guidance statements and challenges encountered were extracted, edited, grouped, abstracted, and presented using a qualitative metasummary approach.

Results: We identified 52 guidance documents produced by 19 author groups. Consistent guidance was available for the first stages of the overview process (deciding when/why to conduct an overview, specifying the scope, and searching for and including SRs). In contrast, there was limited or conflicting guidance for the latter stages of the overview process (quality assessment of SRs and their primary studies, collecting and analyzing data, and grading the quality of evidence), and many of the challenges identified also related to these stages. An additional, overarching challenge identified was that overviews are limited by the methods and reporting of their included SRs.

Conclusion: This compilation of methodological guidance for conducting overviews of healthcare interventions will facilitate the production of future overviews and can help authors address key challenges they are likely to encounter. This research has been recognized by the international Cochrane Collaboration, which is widely recognized as producing high-quality SRs of health evidence. Accordingly, we are currently using the results of this project to update the chapter on overviews for the next edition of *The Cochrane Handbook for Systematic Reviews of Interventions*.

Funded By: Trainee Travel Grant

Abstract #:	15
Presenter:	Btissam El Hassar
Supervisor:	Rebecca Gokiert
Title:	Using stakeholder engagement to develop an evaluation capacity building instrument: Improving use by interweaving science and participation
Authors:	Btissam El Hassar, Rebecca Gokiert, Bethan Kingsley , Cheryl Poth
Affiliations:	University of Alberta
Research Activity:	Research and Evaluation for Improving Women and Children's Programs

Introduction: The Evaluation Capacity Network (ECN) is an emerging provincial multidisciplinary and intersectoral partnership of government, community, funding, and academic stakeholders focused on creating evaluation-based capacity and aligning evaluative thinking in the field of early childhood development (ECD). Gathering contextual and measurable evidence is important to understand the effectiveness of ECD programs, services, and policies. However, engaging in evaluative processes requires certain individual and organizational capacities that many ECD organizations lack (Alberta Government, 2013).

Building such capacity requires an empirical and contextual understanding of existing capacity, the gaps, and ways to address them. In this presentation, the development of an instrument for measuring individual and organizational evaluation capacity building (ECB) that is contextually relevant will be described. The lessons learned, and benefits of engaging diverse stakeholders (core research team and steering committee) in the development will be shared.

Methods: The ECB instrument was developed using a participatory approach through a multistage process. First, a review of the ECB literature (including existing ECB frameworks and measures) was conducted. Constructs that were common across the frameworks and measures were presented to ECN stakeholders, eight diverse content experts, and a facilitated discussion revealed the most relevant constructs for the ECD field. Once the ECB instrument was created, stakeholders were reconvened to review items and scales with a focus on the quality of the items, and appropriateness to the ECD context. Stakeholders also recommended participants and recruitment strategies. The instrument was pilot-tested in two stages, in four regional events, and to a broad sample of employees working in ECD organizations. The data gathered is used for its validation.

Results: The engagement process resulted in the development of a relevant instrument that meets the needs of the stakeholders. As a result, the instrument is grounded in theory and context. This has improved stakeholder buy-in and instrument usefulness. This buy-in is reflected in the high response rate of 102 and 230, respectively during the two pilot administrations. Engaging diverse stakeholders in the development process resulted in clearer items and scales, in combination with psychometric analysis will contribute to the validation of the instrument.

Conclusions: This study was received with enthusiasm from our stakeholders given their need to improve the services they provide and to respond to their funder's accountability. The study will inform potential ECB strategies that meet the needs of the ECD stakeholders. This will ultimately improve the services provided to children and their families.

Funded By: Graduate Studentship

Abstract #: 16
Presenter: Sarah Walton
Supervisor: Shannon Scott
Title: Usability evaluation of knowledge translation tools for parents with acutely ill children
Authors: Sarah Walton, Lauren Albrecht, Rachel Flynn, Shannon Scott
Affiliations: University of Alberta
Research Activity: Knowledge Translation; Peadiatric Emergency Care

Introduction

Traditional modes for communicating health information (ie. standardized written instruction sheets) are ineffective at reaching a diverse audience with varying literacy and language skills. Digital arts-based knowledge translation (KT) tools bridge this gap by actively engaging families with consumer friendly information. We have created three digital arts-based KT tool prototypes: a Gastroenteritis eBook, Gastroenteritis Whiteboard video, and Croup Whiteboard video with the purpose of better equipping parents and caregivers with knowledge to make informed decisions about their children's health. This usability evaluation is necessary to determine these tools' capacity to be used easily, efficiently, and satisfactorily by these parents/caregivers. Furthermore, the parent population is difficult to access for research studies. As such, there is also a need to evaluate whether or not the emergency department (ED) waiting room is a viable setting to access them for future research.

Methods

Using a mixed methods research design, qualitative and quantitative data from parents and caregivers was collected in a paediatric ED waiting room. A sample of 61 parents and caregivers participated in our study. After being randomly selected to view one of the three prototypes, the participants completed an electronic usability survey on an ipad. The survey included nine Likert-styled quantitative survey questions and three open-ended qualitative survey questions.

Results

Quantitative analysis using a Kruskal-Wallis test was used to compare the median scores on all Likert-scaled questions. The eBook, compared to the two Whiteboards, was found to have significantly lower scores ($p<0.05$) in four areas: simplicity of use, overall satisfaction, future use, and recommendation to a friend (Whiteboard median=5; eBook median=4). Qualitative thematic analysis further supported the above findings as the eBook received more negative feedback than the Whiteboards (ie. It was too long and unclear who target audience was- parents or children?) Regarding the research experience of parents and caregivers: data revealed that the use of ipads to conduct the survey was both "interactive" and "easy to use." Furthermore, approaching parents in the ED waiting room was reported as a "good use of parents' time."

Conclusion/Discussion

Although all of the KT digital tools were reported as effective in communicating health information to parents and caregivers, the Whiteboards were more positively received than the eBook. Also, by utilizing the time when parents and caregivers are sitting in ED waiting rooms, researchers are able to gain valuable research information from a population that is often very challenging to access.

Funded By: Summer Studentship

Abstract #: 17
Presenter: Allison Norris
Supervisor: Shannon Scott
Title: The experiences of parents who have children with chronic pain: A qualitative descriptive study
Authors: Allison Norris, Kathy Reid, Samina Ali, Lisa Hartling, Shannon Scott
Affiliations: University of Alberta
Research Activity: Pediatric Chronic Pain

Introduction

A health care issue being increasingly recognized as a significant clinical problem is pediatric chronic pain. Studies indicate that pediatric chronic pain affects between 11- 38% of children, and that the incidence of chronic pain increases with a child's age and affects more girls than boys. Chronic pain can result in substantial disability for the child, including missed school and loss of friendships. Research has demonstrated that parents are also affected by their child's chronic pain, due to financial burdens, and feelings of frustration and helplessness. The purpose of this study was to gain insight from parents' experiences of having a child with chronic pain.

Methods:

Qualitative descriptive methodology was used to understand parents' experiences of having a child with chronic pain. Following ethics approval, participants were recruited from the Stollery Hospital, Edmonton, Canada. Participant recruitment lasted from January 2015 until December 2015. Inclusion criteria were that participants had to: 1) speak English, and 2) have a child (younger than 18) with chronic pain. A total of 13 semi-structured interviews (12 moms, 1 dad) were conducted with parents. All interviews were audio-recorded, and transcriptions were anonymized and checked for data accuracy. Data was analyzed using content analysis, and coded in NVivo 10.

Results:

A total of 13 themes emerged from the data: defining chronic pain, information seeking and information needs, effects on the family, expenses of chronic pain, social support, perceived lack of understanding, parenting role, emotional experiences, dealing with disbelief, watching one's child endure chronic pain, experiences with the chronic pain clinic, relationships with health professionals, and parent suggestions.

Conclusions:

The semi-structured interviews revealed a large amount of rich data. This study demonstrates several common experiences for parents who have children with chronic pain, such as how chronic pain affects the family, how parents perceive their parenting role while caring for a child who has a child with chronic pain, and the positive and negative emotions that parents feel. Results also reveal the specific health needs and health services that parents and families need, as well as parents' suggestions about what families and health professionals need to learn about having a child with chronic pain.

Funded By: Innovation Grant

Abstract #:	18
Presenter:	Priatharsini (Tharsini) Sivananthajothy
Supervisor:	Zubia Mumtaz
Title:	Who holds the power? Exploring obstetrical decision-making within the experiences of Canadian and newcomer women in Edmonton, Alberta
Authors:	Priatharsini (Tharsini) Sivananthajothy, Zubia Mumtaz
Affiliations:	University of Alberta
Research Activity:	Obstetrical Decision-Making

Introduction:

Caesarean section (C-section) deliveries are conducted when there is a failure to progress in labor, or compromised fetal status. However, they place women at higher risk for immediate complications compared to vaginal deliveries. Mumtaz et al. (2014) showed that newcomer women in the prairie provinces experienced significantly higher C-section delivery rates compared to Canadian-born women, even though rates of recommendations by healthcare providers was equal. This study aims to understand this trend, and explore how decisions regarding C-section deliveries are made within the experiences of newcomer and Canadian-born women.

Methods:

A focused ethnography was conducted at a university-affiliated hospital in Edmonton, Alberta for an 8-month period in 2015. The study population comprised: 1) newcomer women who immigrated to Canada after 2004 (N=25) and 2) Canadian-born women (N=20). All women included in the study had a higher risk of undergoing a C-section. Data collection strategies included participant observation of prenatal appointments, labour and delivery and in-depth interviews with the women. Written informed consent was obtained from all participants and ethics approval was received from the University of Alberta.

Results:

Our findings showed that power differentials existed between healthcare providers and patients, and these power differentials affected obstetrical decision-making. Power differentials manifested in two forms: 1) the perception participants held towards their healthcare providers, including unquestionable trust, which resulted in discomfort in expressing their personal preferences, and 2) the subtle acts of persuasion and power carried out by healthcare providers when interacting with patients. However, both Canadian-born women and newcomer women of higher socio-economic status were able to demonstrate their power as patients and actively express their preferences during decision-making, including demanding or denying treatment. This was often due to knowing what interventions were available and knowing that they could be requested.

Conclusion:

This discrepancy in the role of patients in decision-making between Canadian-born and newcomer mothers of higher socioeconomic status, compared to other newcomer mothers warrants further attention, to ensure all patients play an active, informed role in decision-making processes.

Funded By: Graduate Studentship and Trainee Travel Grant

Abstract #:	19
Presenter:	Lori Sacrey
Supervisor:	Lonnie Zwaigenbaum
Title:	The Autism Parent Screen for Infants (APSI): A novel parent report questionnaire of early behavioral signs of autism spectrum disorder (ASD) between 6
Authors:	Lori Sacrey, Sysan Bryson, Lonnie Zwaigenbaum, Jessica Brian, Isabel M Smith, Wendy Roberts, Peter Szatmari, Tracy Vaillancourt, Caroline Roncadin, Nancy Garon
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development

Introduction: Identifying early impairments in children who will subsequently be diagnosed with Autism Spectrum Disorder (ASD) is crucial to ensure that they gain timely access to interventions that will improve functional outcomes. Parent reports may provide valuable information for development, as parents are familiar with their infant's naturally occurring behaviors across varied contexts. The objective of this study was to examine whether parent report on a novel screening tool, the Autism Parent Screen for Infants (APSI), distinguishes high-risk infants ('HR'; older sibling with ASD) who were diagnosed with ASD at 36 months from other HR and low-risk infants('LR'; no family history of ASD) on repeat assessments from ages 6 to 24 months.

Methods: *Participants*: (1) HR siblings who did not receive an ASD diagnosis at 36 months (HR-N; n = 138), (2) HR siblings who did receive a diagnosis of ASD at 36 months (HR-ASD; n = 66), and (3) LR infants without ASD (LR; n = 79). *Parent Report Questionnaire*: The APSI is a 26-item questionnaire modeled in content from the AOSI (Bryson et al., 2008), thus including items inquiring about atypical patterns of eye contact, visual tracking, responding to name, imitation, language, social development, joint attention, visual examination of objects, and emotional regulation. Parents completed the APSI at 6, 9, 12, 15, 18 and 24 months. *Statistical Analyses*: Performance on the APSI was compared using linear mixed modeling with Group (HR-ASD, HR-N, LR) and Age as independent measures and total score on the APSI as the dependent measure. Group by age interactions were explored using Benjamini & Hochberg (1995) corrections.

Results: Total score on the APSI differentiated the HR-ASD group from HR-N and LR beginning at 6 months of age and at each subsequent age ($q \leq .036$). Estimates of sensitivity (range 0.58 to 0.67), specificity (range 0.72 to 0.87), and positive (range 47.4 to 78.6) and negative (range 75.8 to 82.6) predictive validity indicate the APSI's ability to distinguish between HR infants who will and will not be diagnosed with ASD across all ages assessed.

Conclusions: The APSI shows promise as a simple, low-cost parent-report monitoring system, which can lead to earlier identification of symptoms and access to interventions to remediate atypical development in children at risk for ASD.

Funded By: CIHR, AIHS, NeuroDevNet

Abstract #:	20
Presenter:	Amanda Greenwell
Supervisor:	Lawrence Richer
Title:	Derivation of a clinical prediction model of medically important causes of pediatric 'brain attack'
Authors:	Amanda Greenwell, Samiha Rahman, Meghan Linsdell, Jerome Yager, Lawrence Richer
Affiliations:	University of Alberta
Research Activity:	Child and Youth - Emergency medicine

Introduction: There are many causes of acute focal brain dysfunction ('brain attack') in children and adolescents presenting to the Emergency Department (ED) ranging from benign conditions like migraine to life threatening conditions like stroke. Differentiating benign from non-benign conditions can be very challenging as presenting signs and symptoms often overlap. Knowledge of the most predictive clinical indicators of non-benign etiologies like stroke will support timely diagnosis and management.

Methods: A retrospective cohort of children or adolescents presenting to the Stollery Children's Hospital ED between Feb 2014 and Jan 2015 was created by International Classification of Disease encoded discharge diagnoses. Any cause of acute focal brain dysfunction was included. Head trauma within 7 days of presentation was excluded.

Results: A total of 909 presentations met inclusion criteria and medical charts were abstracted using a standardized form. Fifty-nine non-benign cases were identified including meningo-encephalitis (n=31), neoplasm (n=13), intracerebral hemorrhage (n=7), stroke (n=4), hydrocephalus (n=4), demyelinating disorder (n=3), vascular malformation (n=2), and inborn error of metabolism (n=1). A model was developed for the most predictive clinical indicators using a stepwise linear regression procedure. The most significant predictors for medically important causes included cranial nerve abnormality (OR 14.78, 95% CI 2.29 to 95.47), ataxia or gait disturbance (OR 3.38, 95% CI 1.17 to 9.73), focal weakness (OR 3.98, 95% CI 1.33 to 11.96), fever (OR 2.74, 95% CI 1.21 to 6.20), and vomiting (OR 2.81, 95% CI 1.42 to 5.55).

Conclusions: Timely recognition of these clinical predictors may help ED physicians identify children most at risk of a non-benign etiology for acute focal brain dysfunction and guide diagnostic approaches. Future research will validate the derived model in a validation cohort.

Funded By: Seed and Start-up or Retention Funding

Abstract #:	21
Presenter:	Sarah Raza
Supervisor:	Lonnie Zwaigenbaum
Title:	The Infant-Toddler Social and Emotional Assessment (ITSEA) for early risk detection of Autism Spectrum Disorder
Authors:	Sarah Raza, Lori-Ann Sacrey, Lonnie Zwaigenbaum, Susan Bryson, Jessica Brian, Isabel Smith, Wendy Roberts, Peter Szatmari, Tracy Vaillancourt, Caroline Roncadin
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development

Background: Understanding the atypical development of children diagnosed with Autism Spectrum Disorder (ASD) in the first few years of life is crucial in order to identify early risk markers. Currently, evidence is growing that early social-emotional difficulties may predict later ASD symptomology and developmental problems, highlighting the need for early screening of these concerns in infants at-risk for ASD. One method of identifying early social-emotional atypicalities is the parent-report tool, Infant-Toddler Social Emotional Assessment (ITSEA). To date, few studies have utilized the ITSEA as an early detection tool for high-risk ASD populations. This study prospectively examined the ability of the ITSEA to predict ASD symptomology and diagnostic outcomes at 36 months in a cohort of infants at high-risk (HR) of developing ASD.

Method: Three groups of infants were examined: (1) HR siblings who received an ASD diagnosis at 36 months (HR-ASD; *n*=93), (2) HR siblings who did not receive an ASD diagnosis at 36 months (HR-N; *n*=238), (3) low-risk infants with no family history of ASD (LR; *n*=133). Parents completed the ITSEA at 18 months to identify social-emotional atypicalities and competencies in their child. At 36 months, a diagnostic ASD assessment was conducted for all infants using the ADI-R and the ADOS. With respect to statistical analyses, performance on the ITSEA was compared using a series of one-way ANOVAs with Group (HR-ASD, HR-N, LR) as the independent measure and domain scores (Externalizing, Internalizing, Dysregulation, and Competency domains) and indices (Maladaptive, Social Relatedness, and Atypical indices) as the dependent measures. Predictive ability of the ITSEA was assessed using correlations between domain scores and indices at 18 months and ADI-R and ADOS scores at 36 months.

Results: HR-ASD infants reported higher scores on the ITSEA Internalizing and Dysregulation domains and Maladaptive and Atypical indices, and lower scores on the Competency domain and Social Relatedness index at 18 months relative to the HR-N and LR infants – indicating more impaired social-emotional functioning. With the exception of the Externalizing domain, all ITSEA domain and indices predicted ASD symptom severity in the HR-ASD group on the ADI-R, but not on the ADOS at 36 months.

Conclusion: Parent-report using the ITSEA can facilitate earlier detection of social-emotional symptoms characteristic of ASD in HR infants and may be useful in predicting later diagnostic outcomes on the ADI-R.

Funded By: Partnership resources

Abstract #:	22
Presenter:	Amy Toosi
Supervisor:	Solina Richter
Title:	Early childhood development in children of immigrant families: A cohort study
Authors:	Amy Toosi, Sheila McDonald , Dawn Kingston, Solina Richter
Affiliations:	University of Alberta
Research Activity:	Early Childhood Development

Introduction: Mounting evidence indicates that early childhood experiences have lifetime consequences for adult functioning and therefore the wellbeing of societies. Early childhood life is also considered the most effective and cost-efficient time for preventing inequalities in human life. Despite the large numbers of international migrants and their children worldwide, as well as the growing interest in understanding and supporting optimal child development, there is little understanding about the early development of children in immigrant families and the factors that influence their development.

Purpose: The aim of this research was two-fold. The first aim was to compare indices of early childhood development across key developmental domains (fine and gross motor, communication, problem solving, personal-social, social-emotional and behavioural problems and competencies) between children at two years of age who were born to foreign-born parents and their counterparts who were born to Canadian-born parents. The second aim was to identify and compare factors associated with communication and social-emotional behavioural problems and competencies of early childhood development at two years of age for children who were born to foreign-born parents and their counterparts who were born to Canadian-born parents.

Methods: This study used data from a prospective longitudinal pregnancy cohort study, the All Our Babies (AOB) study (n=3200) in Alberta, to answer the research questions. We classified all mother-infant dyads who participated in the two year follow-up (n=1597) into two groups based on the parents' country of birth: 1) children who were born to Canadian-born parents (n=1129, 73%) and 2) children who were born to families with at least one foreign-born parent (n=429, 27%).

Results: Children with foreign-born parents were more likely to need further assessment in communication (17%), as compared to those with Canadian-born parents (12.4%). They were more likely to be at risk for social-emotional and behavioural problems (20.9%) and delay in social-emotional and behavioural competencies (18.9%) as compared to those with Canadian-born parents (12.6% and 11.1% respectively).

Conclusion: Our findings suggest that the quality of stimulating activities in families with foreign-born parents differs from that of families with Canadian-born parents, which can influence the communication and emotional-social development of these children. Foreign-born parents may benefit from parenting supports to improve the quality of parenting practices. History of mental health issues was a universal risk factor for social-emotional delays in both groups. Addressing maternal mental health as a modifiable risk factor is warranted.

Funded By: Graduate Studentship

Abstract #:	23
Presenter:	Sanja Schreiber
Supervisor:	Eric Parent
Title:	Schroth Physiotherapeutic Scoliosis-specific exercises improve Cobb Angles in adolescents with Idiopathic Scoliosis – a randomized controlled trial
Authors:	Sanja Schreiber, Eric Parent, Elham Khodayari Moez, Douglas Hedden, Doug Hill, Marc Moreau, Edmond Lou, Elise Watkins, Sarah Southon
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Spinal Disorders

Introduction

In North America the non-surgical standard of care for adolescent idiopathic scoliosis (AIS) includes observation and bracing, but not physiotherapy. The objective was to determine the effect of a six-month Schroth physiotherapeutic scoliosis-specific exercises added to standard of care (Experimental group) on the Cobb angle compared to standard of care alone (Control group) in patients with AIS.

Methods

Fifty patients with AIS aged 10 -18 years, with curves of 10°- 45° and Risser grade 0 -5 recruited from a pediatric scoliosis clinic were randomized to the Experimental or Control group. The outcomes included the change in Largest Curve and Sum of Curves from baseline to 6 months. The intervention consisted of a 30 - 45 minute daily home program and weekly 1h-long supervised sessions. Exercises, adapted to the curve types were taught over 5 individual sessions, and adjusted weekly according to an algorithm. Cobb angles were measured on digital radiographs using a semi-automated method with high reliability. Intention-to-treat (ITT) and per protocol linear mixed effects model analyses are reported.

Results

The mean Largest Curve and Sum of Curves were 28.5° (SD=8.8°) and 51.2° (SD=22.3°). Risser sign was 1.60 (SD=1.73). Schroth curve types were balanced between groups including: 3c (n=7), 3cp (n=15), 4c (n=5) and 4cp (n=23). Six/50 (12%) dropped out (4 in the Schroth and 2 in the Control group). Using ITT principle 76% of visits and 73% of the prescribed home exercises were completed.

After six months the ITT showed that Schroth group had significantly smaller Largest Curve than controls (-3.5°, 95%CI -1.1° to -5.9°, p=0.006). Likewise, the difference in the square root of the Sum of Curves was -0.40°, (95%CI -0.03° to -0.8°, p=0.046), suggesting that an average patient with a 51.2° at baseline, will have a 49.3° Sum of Curves at six months in the Schroth group, and 55.1° in the control group with the difference between groups increasing with severity. Per protocol analyses produced even larger differences.

Assuming that the patients with missing values had curve progression, more patients were successfully treated (improved + stable) in the Schroth than in the control group (88% vs. 60%, Chi^2 p=0.024).

Conclusions

Schroth exercises added to the standard of care were superior compared to standard of care alone in reducing the curve severity in patients with AIS. Schroth exercises alone or in combination with brace management present an enhanced alternative to conservative standard of care in patients with curves <45°.

Funded By: Trainee Travel Grant

Abstract #: 24
Presenter: Andrew Chan
Supervisor: Edmond Lou
Title: Accuracy and precision of motion capture cameras for adolescent idiopathic scoliosis image guidance system
Authors: Andrew Chan, Janelle Aguillon, Doug Hill, Edmond Lou
Affiliations: University of Alberta

Introduction: Adolescent idiopathic scoliosis is a 3-dimensional spinal deformity involving lateral curvature and axial rotation of the spine. Severe cases require spinal fusion surgery involving insertion of pedicle screws into the spine after surgical correction. Insertion of screws requires high accuracy to prevent damage to the spinal cord and blood vessels. Errors of less than 1mm and 5^{o} of rotation have been suggested as minimum accuracies for screw insertion. Motion capture can be used to track surgical tools to provide image guidance. The objective of this study is to determine the precision and accuracy of the Optitrack motion capture system for usage in spinal fusion surgery.

Methods: A motion capture setup with three to four Optitrack Prime 13W was tested in a mock operating room set-up. Three phases of testing included static, translational and rotational phases. A static rigid body was recorded to determine the precision of the system over six hours. Translational accuracy and repeatability was tested by moving the rigid body pre-determined distances as well as placement of cameras in multiple positions and orientations. The effect of size and position of markers on the rigid body on accuracy was evaluated as well. Rotational accuracy was tested comparing small angle rotations with large angle rotations.

Result: Six hours of static testing showed a precision of 0.01-0.12mm, improving to 0.005-0.01mm when a 1-hour pre-heat was completed. Rotational precision was unchanged regardless of preheating at <0.02^{o}. Translational accuracy was 0.06mm for <2cm translations and 0.08mm for <8cm translations and 0.11mm for 15cm translations. Accuracy from different camera positions ranged from 0.04-0.11mm with overlapping confidence intervals across all positions. Small 6.4mm markers had similar accuracies as 7.9mm markers at 0.07mm vs 0.09mm, while a linear rigid body had significantly poorer accuracy at 0.24mm. Accuracy of small rotations between 5-10^{o} were 1.4-1.9^{o}. Rotations of 60-65 ^{o} had accuracies of 3.6^{o}-4.7^{o} while even larger rotations of 70-75^{o} had accuracies of 6.2-8.6^{o}.

Conclusion: The precision of the motion capture system is excellent after a one-hour warm-up time. The translational and rotational accuracy are adequate for any translations and for rotations less than 70^{o} from the reference point. Future work will involve integrating motion capture with ultrasound to reproduce 3D images of the spine for image guidance.

Funded By: NSERC, AITF

Abstract #:	25
Presenter:	Michael Khoury
Supervisor:	Nee Khoo
Title:	Cardiac rehabilitation in the pediatric Fontan population: Developing an interval training program using a novel telemedicine gaming exercise platform
Authors:	Michael Khoury, Peter Woods, Jennifer Conway, Gwen Rempel, Devin Phillips, Pierre Boulanger, Michael Stickland, Andrew Mackie, Nee Khoo
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction

The Fontan surgery has contributed significantly to the increased survival seen in recent decades of children with single ventricle physiology. With improved short-term survival, attention has shifted towards optimizing physical function and reducing long-term morbidities in this population. Children with Fontan physiology are less physically active and have lower exercise tolerance than the general paediatric population. This may contribute towards the development of cardiovascular risk factors and disease including obesity, dyslipidemia, hypertension, and premature atherosclerosis in this already fragile population. Encouraging and facilitating exercise may therefore improve quality of life and reduce future morbidity. While standard aerobic exercise has not been shown to improve exercise tolerance in the Fontan population, interval-training regimens have not been assessed to date. Therefore, we intend to develop and implement an interval training cardiac rehabilitation program through the use of a novel video game-linked exercise platform.

Methods

This study involves the use of a custom pediatric remote bike ergometer called the MedBike. The technology is linked to a video game platform and, through telehealth, provides a medical supervisor with a live-feed of patient video/audio, electrocardiograph, blood pressure, and blood oximetery signals while allowing for determination of patient work. To calibrate the MedBike, 10 healthy subjects underwent a standard cardiopulmonary exercise test (CPET) followed by a MedBike assessment. Following calibration, 15 subjects with Fontan circulation, age 10-18yo, will be recruited. They will initially undergo a CPET to assess exercise capacity. From this data, a high-intensity interval-training program will be designed for each subject, occurring 3 times per week over 8 weeks. All data will be reported as median with ranges. Comparison between pre and post exercise training data (including peak oxygen consumption (VO2), heart rate recovery, and CPET duration) will be tested using paired Wilcoxon signed rank sum. Surveys will assess key demographic features, enjoyment and ease of use of the platform, and quality of life measures.

Results

N=10 healthy adults subjects participated in the MedBike calibration. Using ANOVA, there was no significant difference between the Medbike and CPET regarding measured VO2 at given power outputs. Recruitment of pediatric Fontan subjects is currently underway for the next phase of the study.

Conclusions

The MedBike is a novel exercise ergometer that may potentially provide the pediatric Fontan population with a safe, appealing, and supervised approach to exercise. An interval training program performed using this device may potentially improve exercise tolerance in this population.

Funded By: Seed Grant

Abstract #: 26
Presenter: Asma Nosherwan
Supervisor: Georg Schmolzer
Title: MRSOPA-Drills to improve mask ventilation in the delivery room
Authors: Asma Nosherwan , Po- Yin Cheung, Megan O' Reilly, Sylvia Van Os, Georg Schmolzer
Affiliations: University of Alberta
Research Activity: Prematurity Delivery room resuscitation

Introduction: Effective positive pressure ventilation (PPV) via facemask is dependent on adequate mask ventilation technique. Mask leak and airway obstruction can affect effective PPV. The Neonatal Resuscitation Program (NRP) emphasise that during PPV corrective steps “MR SOPA”should be performed to ensure effective mask PPV. However, skills taught during a NRP-course generally decline shortly afterwards and often do not result in proficiency during mask PPV. We hypothesised that daily simulation drills to teach the MRSOPA corrective steps will improve mask ventilation performance in preterm infants <33 weeks requiring PPV at birth.

Methods: After a 3-month observation period (baseline), we randomly assigned 58 healthcare members from the local neonatal resuscitation team to either daily MRSOPA drills (intervention) or self-directed revision of the 2015 NRP algorithm (control) over a period of 3 months (intervention phase). This was followed by a 3-momth post-observation phase (post-training phase). During baseline and post-training phase resuscitations of infants <33weeks gestation were recorded using our unique recording system (incl. respiratory function monitoringand video recordings). Mask ventilation performance and use of MRSOPA were compared between pre and post training phase.

Results: Overall, there was a significant increase in efficiently and correctly applying MRSOPA during PPV for the MRSOPA drill group. The rate of delivery room intubation decreased by 15% post intervention. There was no difference on days of respiratory support following admission to NICU or neonatal death at discharge.

Conclusion: Healthcare provider receiving daily MRSOPA drills had improved mask ventilation technique and performance compared to self-directed NRP learning.

Funded By: NRP Research Grant

Abstract #:	27
Presenter:	Gitanjali Mansukhani
Supervisor:	Paul Kantor
Title:	Outcomes of pediatric heart failure-related hospitalizations in Canada: 2004-2013
Authors:	Gitanjali Mansukhani, Sunjidatul Islam, Andrew Mackie, Padma Kaul, Paul Kantor
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Background: Heart failure (HF) is an important cause of morbidity and mortality in children with frequent hospitalizations. Recent data have described this problem in the United States. However, there are currently very limited data describing pediatric heart failure hospitalizations (HFH) in Canada. We sought to describe the prevalence, causes and outcomes of HFH in Canada during a contemporary 10-year time frame.

Methods: The Discharge Abstract Database (DAD) of the Canadian Institute of Health information (CIHI) was used to identify all HFH with heart failure as a primary or secondary diagnosis in patients <18 years of age between 2004 and 2013, in all provinces except Quebec and the Territories.

Results: A total of 4,693 HFH occurred among 3,523 children. Of these, 73.6% (3,457) occurred in children aged <1yr. The annual number of HFH ranged from 435 to 559 (7 to 10 HFH/ 100,000 children per year). Congenital heart disease (CHD) and cardiomyopathy were associated with 76.1% and 10.5% of HFH respectively. Ventricular septal defect was the most common CHD lesion (33%). Acquired heart diseases (infective and rheumatic) were present in 4.2% of HFH. Median length of stay (LOS) for all HFH was 10.7 days (IQR 4.1 – 28.7) and was highest in the 0-30 day age group at 21.7 days (IQR 8.1 – 46.6). The In-hospital mortality rate was 8.8%, with the majority of deaths occurring during the index hospitalization. Extra-corporeal life support (ECLS) was recorded in 2.4% of HFH, with ventricular assist-device implantation in only 0.7% and cardiac transplantation occurred in 1.9%. 68.5% hospitalizations were not associated with any intervention and cardiac surgery occurred in 23.4%. The remaining had surgery and/or cardiac catheterization. The overall annualized hospitalization rate per 100,000 population declined by 3% per year during the study period (rate ratio 0.97, 95% CI 0.96 to 0.98, p<0.001). For patients discharged alive, the cumulative 30-day readmission rate was 12.5%.

Conclusions: Pediatric HFHs in Canada are a high-risk event, occurring mainly in infants. There is a significant risk for death and early readmission after discharge. The rates of HFH are lower in Canada as compared to the United States (7-10 v/s 14.5-17.9 per 100,000 children) with higher crude mortality rate (8.8% v/s 7%). Over the ten-year study period, the annual hospitalization rate declined significantly in Canada by 3% per year, which differs from the United States, where the numbers remained constant.

Abstract #:	28
Presenter:	M. Florencia Ricci
Supervisor:	Charlene M.T. Robertson
Title:	The relationship between deterioration of functional abilities and stroke in children surviving the Fontan procedure
Authors:	M. Florencia Ricci, Billie-Jean Martin, Ari R. Joffe, Gonzalo Garcia Guerra, Charlene M.T. Robertson
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development

Introduction: Children surviving complex cardiac surgery are at high risk for neurodevelopmental delays. Deficits in functional abilities significantly impact the ability of a child to participate at home, school and in the community. This study evaluates the changes in functional abilities children have after the Fontan procedure. We hypothesized deterioration of functional abilities (DFA) is not uncommon after the Fontan procedure, and that stroke is often the event leading DFA. Objectives: To determine 1) the frequency of DFA post-Fontan, and 2) the frequency of post-Fontan stroke among those with and without DFA.

Methods: This retrospective chart review is part of The Western Canadian Complex Pediatric Therapies Follow-up Project (CPTFP), a prospective inception cohort follow-up study. From 1996-2016, 186 children registered in the CPTFP underwent a Fontan operation at Stollery Children's Hospital. At age 4.5 years, surviving children received multidisciplinary assessment. The Adaptive Behavior Assessment System-II general adaptive composite (GAC)(population mean: 100-SD:15) was determined for each child. DFA was defined as a 1 SD decrease in GAC in comparison to pre-Fontan scores. Post-Fontan stroke diagnosis was determined through chart review. Frequency of DFA and stroke are presented as percentage of assessed survivors. T-tests and chi-square tests were used to compare groups.

Results: Preliminary results are obtained for 154 (64% male, 51.3% classic hypoplastic left heart syndrome) of the 180 survivors. Post-Fontan, DFA occurred in 34/154 (22.1%), stroke occurred in 15/154 (9.7%)(7 with DFA and 8 without). Mean post-Fontan GAC in all children with stroke was 76.3(22.6) vs. 89.7(18.5) in those without stroke (p=0.01). Evidence of post-Fontan stroke was found in 7/34 (20.6%) of children with DFA, and in 8/120 (6.7%) of children without DFA (p=0.002). Mean GAC decline among children with DFA was greater in those with stroke (25.9, SD 10.3) than in those without (19.2, SD 5.1), though the difference was not statistically significant (p=0.14).

Conclusion: A significant proportion of children surviving the Fontan procedure show DFA, which has major implications for their functioning in life. Evidence of post-Fontan stroke is more commonly found among those with DFA; however stroke is not the only event leading to DFA as a high proportion of children deteriorate without evidence of stroke. Finally, stroke among those with DFA does not result in a larger decline in functional abilities. The next step in this study is to explore potentially modifiable predictors of post-Fontan DFA that may suggest strategies to prevent this adverse outcome.

Funded By: Support services

Abstract #:	29
Presenter:	Jayani Abeysekera
Supervisor:	Lisa Hornberger
Title:	Umbilical blood flow in the 3rd trimester and its association with clinical and neurodevelopmental outcomes in children with congenital heart disease
Authors:	Jayani Abeysekera, Charlene Robertson, Gwen Bond, Winnie Savard, Dianne Creighton, Joseph Atallah, Lisa Hornberger
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction Children with congenital heart disease (CHD) are at increased risk of adverse long-term neurodevelopmental outcomes (ND) which is believed for some lesions to be due in part to a prenatal insult. Altered ND outcomes have been reported in pediatric patients with critical neonatal CHD such as hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (d-TGA) and those with more complex CHD that necessitate early postnatal intervention. Fetuses with CHD, especially HLHS, often demonstrate altered middle cerebral artery (MCA) blood flow in utero, usually with a low pulsatility index (PI). This “brain sparing” phenomenon is believed to represent compensatory optimization of blood flow to the brain, especially in the context of placental insufficiency. CHD has also been found to be associated with increased placental pathology and altered function with reduced oxygen delivery. An increased umbilical artery (UA) PI is associated with placental insufficiency. In this study, we evaluated the effect of an altered fetal/placental circulation (MCA and UA flow patterns) in fetal TGA and HLHS on growth and 2-year ND outcomes. We hypothesized that increased MCA PI and increased UA PI would be associated with worse growth and ND outcomes at 2 years.

Methods We identified children with TGA and HLHS followed in the Western Canadian Complex Pediatric Therapies Follow-Up Program who had a 3rd trimester fetal echocardiogram between October 2004 and August 2014 with the University of Alberta Fetal &Neonatal Cardiology program. Participants with inadequate fetal Doppler data or death prior to the 2-year follow-up were excluded. PI measurements were obtained via offline analysis of 3rd trimester fetal echocardiograms. Growth and 2 year Bayley Scales of Infant and Toddler Development III were reported. Statistical analysis was performed using Pearson correlation coefficients.

Results Fifty-seven children with d-TGA (n=24) and HLHS (n=33) were included. MCA PI did not correlate with 2-year ND outcomes. UA-PI correlated inversely with birth head circumference, 2-year length, weight, and cognitive, language and motor scores ($p<0.05$).

ConclusionsA higher UA-PI in fetal HLHS and d-TGA is associated with worse 2-year ND outcomes. This suggests placental insufficiency could represent an additional insult that contributes to long-term outcome in CHD. Understanding these risk factors allows for early identification and intervention to ultimately improve outcomes and decrease disease burden, especially as more children with critical CHD are surviving into adulthood.

Abstract #: 30
Presenter: Silvia Alvarez
Supervisor: Nee Khoo
Title: Speckle tracking echocardiography and magnetic resonance imaging derived circumferential strain rate are closely associated in the single RV
Authors: Silvia Alvarez, Michelle Noga, Kumaradevan Punithakumar, Lily Lin, Benjamin Goot, Edythe Tham, Timothy Colen, Nee Khoo
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Cardiology

Background: Previous studies suggest right ventricular (RV) circumferential strain and strain rate from speckle tracking echocardiography (STE) is useful to assess function, despite imaging limitations of RV short axis and tracking algorithms designed for left ventricles. This study compares STE strain and strain rate in patients with single RV to magnetic resonance imaging (MRI) derived strain and strain rate, using proprietary MRI deformation software with published validation in hypoplastic left heart syndrome. Strain and strain rate relationships to MRI derived volumes and function is explored.

Methods: Single RVs patients (n=25) with STE and MRI performed with an interval up to 35 days, prior to stage 2 palliation (median age 3.9, range 0.9 - 6 months) were compared. STE (GE EchoPAC) and MRI derived longitudinal and circumferential strain and strain rate were analyzed offline. MRI RV end-diastolic (iEDV), end-systolic (iESV) volumes indexed to body surface area and ejection fraction were measured. Bland-Altman plot assessed agreement between the STE and MRI derived deformation measures. Correlations between variables were computed.

Results: STE and MRI strain rate had the best agreement between methods, longitudinal strain rate (bias -0.04 %; SD 0.26) and circumferential strain rate (bias 0.16 %; SD 0.20) while STE and MRI strain had minimal bias and an acceptable limits of agreement, longitudinal strain (bias 0.4 %; SD 3.2) and circumferential strain (bias -1.7 %; SD 4.4). Greater STE and MRI derived strain and strain rate is associated with smaller iEDV, iESV and greater ejection fraction (see table). MRI circumferential strain and strain rate has a greater correlation with volumes and ejection fraction than MRI longitudinal strain and strain rate. STE circumferential strain rate was best correlated MRI derived volumes and ejection fraction.

Conclusion: In single RV, STE and MRI derived strain and strain rate showed good agreement, with strain rate having the best equivalency. Furthermore, STE an MRI circumferential strain rate was the most consistently related to MRI derived RV size and function. This study reaffirms the performance of commercially available STE software in single RV and further emphasizes the importance of including circumferential deformation in routine evaluation.

Table 1. Correlations Between MRI and STE Deformation measures and MRI size measures and EF

Variables	MRI iRVEDV r (p-value)	MRI iRVESV r (p-value)	MRI RVEF r (p-value)
MRI Circumferential Strain	0.49 (p < 0.01)	0.67 (p < 0.01)	-0.67 (p < 0.01)
MRI Circumferential Strain Rate	0.71 (p < 0.001)	0.74 (p < 0.001)	-0.66 (p < 0.001)
MRI Longitudinal Strain	0.44 (p < 0.02)	0.42 (p < 0.02)	-0.41 (p < 0.03)
MRI Longitudinal Strain Rate	0.48 (p < 0.02)	0.47 (p < 0.02)	-0.46 (p < 0.02)
STE Circumferential Strain	0.40 (p < 0.02)	0.38 (p < 0.03)	NS
STE Circumferential Strain Rate	0.50 (p < 0.01)	0.65 (p < 0.001)	-0.58 (p < 0.003)
STE Longitudinal Strain	0.56 (p < 0.002)	0.54 (p < 0.003)	-0.46 (p < 0.02)
STE Longitudinal Strain Rate	NS	0.48 (p < 0.01)	-0.54 (p < 0.005)

MRI = magnetic resonance imaging; iRVEDV = indexed right ventricle end-diastolic volume; iRVESV = indexed right ventricle end-systolic volume; RVEF = right ventricle ejection fraction; STE =speckle tracking echocardiography.

Funded By: Trainee Travel Grant

Abstract #:	31
Presenter:	Kandice Mah
Supervisor:	Nee Khoo
Title:	Right ventricular remodelling in Hypoplastic Left Heart Syndrome: Impact of the Norwood and hybrid procedures
Authors:	Kandice Mah, Jesus Serrano Lomelin, Luke Eckersley, Lily Lin, Timothy Colen, Edythe Tham, Herald Becher, Luc Mertens, Nee Khoo
Affiliations:	University of Alberta

Background: Right ventricular (RV) remodeling in hypoplastic left heart syndrome (HLHS) begins prenatally and continues through staged palliations. The impact of the timing of cardiopulmonary bypass (CPB) on HLHS RV remodeling, early in Norwood-Sano vs. later in Hybrid palliation, is unclear.

Methods: Echocardiograms of HLHS undergoing Norwood and Hybrid procedures were retrospectively reviewed (Jan 2007 - Dec 2011)over five time points: Pre and Post-stage 1, Pre and Post-Glenn, and Pre-Fontan. We assessed RV end-diastolic area (RVEDAi) indexed to body surface area, RV fractional area change (FAC) and velocity vector imaging for longitudinal and derived circumferential deformation (peak radial displacement/end-diastolic diameter) and deformation ratio (longitudinal/circumferential). Generalized Estimation Equations was used to analyze changes over time for each group and to compare the two interventions for each parameter. Independent T-test assessed outcomes.

Results: Hybrid (n=20) and Norwood (n=27) patients had similar age, clinical status and echo parameters Pre-stage 1. No change in FAC in Norwood group throughout, while Hybrid group had transient reduction pre-Glenn ($p = 0.03$) before returning to baseline by Pre-Fontan ($p = 0.002$). Post-stage 1 hybrids RV size is increased and post-Glenn both groups RVEDAi decreased. Norwoods, with early CPB, post-stage 1 showed increase in circumferential deformation and decrease longitudinal strain, hence decrease deformation ratio ($p<0.05$). Hybrids post-stage 1, without bypass, had similar changes post-stage 1 but circumferential deformation return to baseline at pre-Glenn while reduced longitudinal strain rate persist ($p<0.0001$). Norwoods, at Glenn, showed further increase in circumferential deformation ($P <0.05$). Hybrids, with 1st CPB at Glenn, had reduced circumferential and longitudinal deformation ($p<0.05$). Comparisons between interventions, at post-stage 1 and pre-Glenn, Norwoods had greater circumferential deformation ($p<0.05$) and similar longitudinal deformation. No further difference was found between interventions post-Glenn. Outcomes were no different.

Conclusions: HLHS withHybrid procedure had similar change in RV contraction pattern (decreased longitudinal and increased circumferential) to Norwoods post stage-1 intervention, suggest an inherent RV remodeling process during early adaptation to single ventricle physiology. Early CPB does appear to further modify this process by increasing reliance of circumferential contraction in Norwood patients to maintain RV function.

Funded By: Resident/Clinical Fellow Trainee Research Grant

Abstract #:	32
Presenter:	Liane Kang
Supervisor:	Anita Kozyrskyj
Title:	Maternal pre and postnatal depression is associated with reduced 4-month gut immunoglobulin A levels in Canadian infants
Authors:	Liane Kang, Petya Koleva, Catherine Field, Allan Becker, Piushkumar Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, James Scott, Anita Kozyrskyj
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease

INTRODUCTION

Secretory immunoglobulin A (sIgA) has a critical role in early life gut mucosal immunity and is a marker of immune maturation. Delayed IgA production is associated with increased risk of allergic diseases. Animal studies of stressful events before birth and during infancy show changes in the vaginal microbiome, as well as changes in intestinal microbial composition and lower sIgA concentrations in offspring. A first report in humans found infants born to mothers with greater stress during pregnancy more likely have gut dysbiosis, but there is a paucity of literature on stress-microbiome-immunity pathways in humans. This study investigated differences in infant fecal sIgA levels at 4 months according to the depression/stress status of the mother during or after pregnancy.

METHODS

Data were obtained from a sub-sample of 403 term infants from the Vancouver, Edmonton and Winnipeg sites of the general cohort in the Canadian Healthy Infant Longitudinal Development (CHILD) Study. Mothers of the infants were enrolled during pregnancy and were asked to report stress and depressive symptoms through scored-scales administered to the general CHILD cohort at several time points throughout pregnancy and postpartum. Center for Epidemiologic Studies Depression (CES-D) Scale ascertained depressive symptoms, and Perceived Stress Scale (PSS) determined perceived stress. Infant stool samples were collected at a mean age of 3.8 months, and fecal sIgA levels were measured using the Immundiagnostik sIgA ELISA kit. Mann-Whitney U-tests detected differences in IgA levels according to maternal depression status using IBM SPSS version 23.

RESULTS

About 12% of women had prenatal depressive symptoms, 9% had symptoms postpartum and 9% had symptoms both pre and postnatally. Mothers with any depressive symptoms had infants with significantly lower sIgA compared to mothers without symptoms (p=0.004). Median sIgA levels are 6.3 (IQR=3.6 – 12.4)mg/g feces, 5.2 (IQR = 2.0 – 9.8)mg/g feces, 5.7 (IQR = 2.6 – 8.6)mg/g feces, 4.4 (IQR = 2.4 -8.0)mg/g feces for exposure to no symptoms, prenatal, postnatal, both pre and postnatal symptoms respectively. The risk of low fecal sIgA was 2.2 times higher when the mother had prenatal symptoms (p=0.037), and 2.4 times higher when the mother had both pre and postnatal symptoms (p=0.035) compared to no symptoms, after controlling for breastfeeding.

CONCLUSIONS

Infants born to mothers with depressive symptoms appear to have lower 4-month fecal sIgA levels independent of breastfeeding status. Due to the association with lower sIgA, maternal depression may put infants at higher risk of later development of allergic diseases.

Funded By: CIHR and AllerGen NCE

Abstract #:	33
Presenter:	Manjeet Kumari
Supervisor:	Anita Kozyrskyj
Title:	Cesarean section affects gut microbial metabolites that regulate human physiology
Authors:	Manjeet Kumari, Hein Tun, Tedd Konya, David Wishart, David Guttman, Allen Becker, Piushkumar Mandhane, Stuart Turvey, Padmaja Subbarao, Malcome Sears and James Scott
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease

Introduction: The unprecedented rise in cesarean section (CS) rates has resulted in every fifth infant being delivered by CS. Additionally, these CS delivered infants are often less likely to be breastfed as ~30-40% mothers have breastfeeding difficulties after CS and are more likely to discontinue breastfeeding before 12 weeks postpartum. Thus, dysbiosis of gut microbiota, as previously been implicated in infants born by CS could in part be attributed to breastfeeding. Gut microbiota produce large quantities of key metabolites known as short-chain fatty acids (SCFA), some of which have been associated with child asthma and overweight. We present here the first report of differential abundance of gut metabolites in infants delivered by CS than those delivered by vaginal birth.

Methods: Fecal samples from 235 infants at a mean age of 3.8 months were accessed from the Edmonton, Vancouver and Winnipeg sites of the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. The16s rRNA sequencing was conducted to determine composition of microbiota, and nuclear magnetic resonance spectroscopy was run to determine concentrations of microbial metabolites, including SCFA. Data on birth mode and infant breastfeeding status at time of fecal sample collection were obtained in the hospital birth chart and maternal self-report. Statistically significant associations between infant fecal microbiota composition, SCFA levels, breast feeding status, and mode of delivery were tested in SPSS version 24.

Results: In our study sample, 69 infants (~30%) were delivered by CS (18% emergency CS, 11% elective CS). Of all CS delivered infants, ~ 25% (13% emergency CS, 12% elective CS) were exclusively fed on formula. Consistent with previously reported reductions in Bacteroidetes after CS, we observed that CS (both elective and emergency) lowers gut microbial abundance of Bacteroidetes irrespective of breastfeeding; however, statistical significance was observed only among infants who were breastfed. Also, we report here that CS modifies the abundance of the fecal SCFA in 3 months old infants as compared to those born vaginally. In particular, significantly higher fecal levels of isobutyrate, lactate and pyruvate were detected within formula-fed infants delivered by elective CS than those delivered vaginally. Whereas, breastfed infants showed a higher abundance of valerate after emergency CS.

Conclusions: This study identified that CS modifies gut microbiota and metabolites in infants. These findings suggest that CS can have a major early life impact on infant's gut homeostasis and hence, may influence long-term health outcomes.

Funded By: Innovation Grant

Abstract #:	34
Presenter:	Deenaz Zaidi
Supervisor:	Eytan Wine
Title:	Dysregulation of TNFAIP3 (A20) is associated with inflammation in pediatric Crohn disease
Authors:	Deenaz Zaidi, Hien Huynh, Matthew Carroll, Shairz Baksh, Eytan Wine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology

INTRODUCTION: Inflammatory bowel diseases (IBD), including Crohn disease (CD) and ulcerative colitis (UC) are debilitating pediatric intestinal disorders. A20, also known as, tumor necrosis factor α-induced protein 3 (TNFAIP3), is a cytoplasmic protein that inhibits NF-κβ-induced inflammation. A20 interacts with ABIN-1 and TAX1BP-1 to attenuate inflammation. IKKβ phosphorylates A20, and stabilizes it. A20 expression is low in adult CD patients. We hypothesized that dysregulation of A20 leads to uncontrolled inflammation in IBD and that this is mediated by associated factors, as well as by microbes. We aimed to define the role of A20 in pediatric IBD by analyzing A20 expression and protein levels in the terminal ileum (TI) of IBD and non-IBD patients, characterize the expression of genes that interact with A20, and assess the effects of bacteria.

METHODS:

A total of 39 patients were included in the study (14 non-IBD controls, 15 CD, and 10 UC patients). The gene expression of A20, IKKβ, ABIN-1, TAX1BP, A20 protein, and cytokine levels in the TI of IBD and non-IBD patients were analyzed. Gene expression profiles and A20 protein levels in T-84 cells and *ex-vivo* biopsies of patients after treating with *Escherichia coli* strains LF-82 and HB101 and TNF-α were analyzed.

RESULTS:

In the TI of pediatric CD patients, the gene expression of A20 was significantly elevated, but A20 protein levels were low as compared to non-IBD and UC patients. ABIN-1 expression was low, IKKβ was unchanged, but TAX1BP1expression was high in CD patients. Levels of TNF-α in biopsies were significantly higher in the TI of CD patients as compared to non-IBD and UC patients. A20 expression positively correlated with biopsy TNF-α levels, serum C-reactive protein, and erythrocyte sedimentation rates in CD patients. Infection with *E.coli* strain LF82 triggered A20 expression in CD patients and T84 cells, but did not cause an increase in A20 protein levels.

CONCLUSIONS:

A unique signature profile in pediatric CD patients exists: high A20 and TAX1BP1 expression, low ABIN-1, and low A20 protein levels. The discrepancy between A20 gene expression and protein levels could be explained by lower expression of ABIN-1 and IKKβ, which could affect the function and stability of A20. *E.coli* strain LF82 could potentially impair the capacity of A20 to inhibit inflammation. Our study signifies that A20 expression is initially increased in pediatric CD patients due to NF-κβ-mediated inflammation, but factors affecting A20 protein are decreased, which prevents A20 from suppressing inflammation.

Funded By: Graduate Studentship

Abstract #:	35
Presenter:	Nadia Browne
Supervisor:	Geoff Ball
Title:	Can a novel eHealth tool nudge parents to discuss children's weight status with their pediatrician?
Authors:	Nadia Browne, Jillian Avis, Andrew Cave, Andrea Haqq, Nicholas Holt, Patricia Martz, Raj Padwall, T. Cameron Wild, Katerina Maximova, Geoff Ball
Affiliations:	University of Alberta
Research Activity:	Children's Health: Pediatric Obesity

Introduction: Open communication about children's weight status between parents and pediatricians is important to help prevent childhood obesity. Our objectives were to determine if *(i)* a newly-developed eHealth tool influenced parents' intentions to discuss children's weight status with their pediatrician and *(ii)* parents' self-reported communication with their pediatrician following their appointment.

Methods: From July – October 2015, our eHealth (a screening, brief intervention and referral to treatment [SBIRT]) tool was pilot tested with parents of 5–17 year olds while they waited for an appointment with their pediatrician in an Edmonton-area primary care clinic. Children's measured height (cm) and weight (kg) data were used to calculate body mass index (BMI) percentiles and weight status (*underweight, healthy weight, overweight, obese*). Following completion of the SBIRT using a tablet, parents reported their intention to discuss children's weight at their upcoming pediatrician appointment on a 5-point Likert scale (from 0 [*strongly disagree*]to4 [*strongly agree*]). At 1-month post-SBIRT, we followed-up with parents to determine if they discussed their children's weight during their pediatrician appointment. One-way ANOVA and Chi-square analyses were used to examine group differences.

Results: Parents (n=226) of children (9.9±3.4 years) were primarily biological mothers (n=198; 87.6%) and Caucasian (n=159; 70.4%); most children were classified as *healthy weight* (n=152; 67.3%). Upon completion of the SBIRT, 29.6% (n=67) of parents *agreed* or *strongly agreed* that they intended to discuss their children's weight at their upcoming appointment, with higher intention among parents of children categorized as *overweight* (2.1±1.4) and *obese* (2.8±1.6) compared to parents of children who were *healthy weight* (1.1±1.4; F=16.1; both p<0.001). Of the 136 parents who provided follow-up data at 1-month, 52.2% (n=71) reported discussing their children's weight with the pediatrician; in this sub-group, more parents of children classified as *overweight* (n=18/23 [78.3%]) and *obese* (n=11/13 [84.6%]) discussed weight compared to those with *healthy weight* children (n=35/90, [38.9%]; X^2=20.5; p<0.001).

Conclusions: Parents of children who were classified as overweight or obese reported stronger intentions to discuss and actual discussion about their children's weight with their pediatrician. This newly developed eHealth tool appeared to encourage parents' communication about preventing childhood obesity with their pediatrician.

Funded By: Trainee Travel Grant

Abstract #: 36
Presenter: Hillary Gazie
Supervisor: Hien Huynh
Title: Risk stratification in pediatric Crohn's disease
Authors: Hillary Gazie, Kassi Shave, Meghan Sebastianski, Hien Huynh
Affiliations: University of Alberta
Research Activity: Pediatric Gastroenterology

Introduction: Physicians risk stratify each patient in order to choose a treatment that will have the highest chance of efficacy, while avoiding an unnecessarily aggressive treatment. In pediatric Crohn's disease, many factors such as disease extent, disease activity, and disease behavior may be used to risk stratify patients, but there exists no summary of how these factors affect patient outcomes.

Aim: To summarize the evidence on the predictors of disease relapse, surgery, disease recurrence after surgery, hospitalization, and poor height in the pediatric Crohn's disease population.

Methods: A rapid review based on Cochrane methodology of the literature was performed using Ovid MEDLINE (2006 to present). Title and abstract screening was followed by secondary full text screening with verification by a second reviewer at each stage. Study quality was assessed using the Newcastle-Ottawa Scale.

Results: From 101 included studies, the strongest predictors of disease relapse, surgery, disease recurrence after surgery, hospitalization, and poor height were the presence and a larger variety of seropositive markers such as ASCA, and a poor response to exclusive enteral nutrition. Moderately effective predictors included stricturing disease behavior, and factors such as disease severity measures (ie. PCDAI), standard serological measures, and perianal disease were minimally important.

Conclusion: In pediatric Crohn's disease, the presence of seropositive markers and response to exclusive enteral nutrition should be used for risk stratification, while disease severity, serological measures, and perianal disease should be used with caution.

Funded By: CIDsCaNN, The Canadian Children Inflammatory Bowel Disease Network

Abstract #: 37
Presenter: Emily Wadge
Supervisor: Catherine Field
Title: The effect of maternal diet on breast milk medium chain fatty acid composition in the Alberta Pregnancy Outcomes and Nutrition (APrON) study
Authors: Emily Wadge, Fatheema Begum Subhan, Nour Wattar, Catherine J Field
Affiliations: University of Alberta

Introduction: Breast fed infants obtain approximately 60% of their energy from fat. Breast milk fat content has been reported to be independent of diet, while composition has not. Medium chain fatty acids (MCFAs) are synthesized endogenously in the mammary gland and secreted into breast milk. It is hypothesized that the reported variation in MCFAs between and within populations is due to the influence of maternal macronutrient intake. MCFAs are absorbed independently of bile and oxidized rapidly, but the importance to the infant has not been established. The objectives of this summer project were to: 1) describe MCFA content in the breast milk of Albertan women and 2) determine the relationship between maternal diet and the MCFA content in breast milk.

Methods: We extracted, methylated and determined the fatty acid composition of a spot sample of breast milk (n=413 women) collected at 3 months postpartum from the Alberta Pregnancy Outcomes and Nutrition (APrON) study using gas liquid chromatography. Dietary intake was compiled from previously analyzed 24-hour recalls.

Results: The average MCFA content of breast milk was 11.3 ± 3.7% (4.3-28.7%) of total fat. Lauric acid (C12:0) (R^2=0.96, P<0.001) and myristic acid (C14:0) (R^2=0.93, P<0.001) correlated strongly with total MCFA content, while capric acid (C10:0) did not (R^2=0.39, P<0.001). The maternal carbohydrate intake showed a weak association (R^2=0.11, P=0.04) with MCFA content. Neither total caloric intake nor fat:carbohydrate ratio were associated with MCFA content. Age and gravidity did not significantly affect the content of MCFAs in breast milk. MCFAs showed an inverse relationship with socioeconomic status (SES), with women of a higher SES producing breast milk with a lower MCFA content as compared to women of a lower SES (P=0.02). Women with a dietary fat intake in the highest quartile had an average MCFA content of 10.8% of total fat, whereas women in the lowest quartile of fat intake had a significantly higher average breast milk MCFA content of 12.2% (P=0.04).

Conclusion: These results suggest an influence of maternal dietary fat intake and SES on breast milk MCFA composition. As MCFAs are metabolized and absorbed differently from other fatty acids in breast milk, the effect of MCFAs on infant growth and health should be elucidated in future studies to identify dietary fat recommendations for women during lactation.

Funded By: Summer Studentship

Abstract #:	38
Presenter:	Mackenzie Coatham
Supervisor:	Lynne Postovit
Title:	Inactivation of SWI/SNF chromatin remodelling complex proteins in clinically aggressive dedifferentiated endometrial carcinoma
Authors:	Mackenzie Coatham, Xiaodong Li, Bo Meng, Martin Koebel, Cheng-Han Lee, Lynne Postovit
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology

Introduction:

In Canada, 1 in 36 women will develop uterine cancer, making it one of the most common gynecological malignancies. Dedifferentiated endometrial carcinoma (DDEC) is a subtype of uterine cancer where an undifferentiated carcinoma arises abruptly from a well-differentiated endometrioid adenocarcinoma. It is a highly aggressive disease with about 50% of patients succumbing to the disease within a year of diagnosis. It is also the more aggressive component, constituting the majority of extrauterine spread and is typically resistant to chemotherapy. We recently identified mutually exclusive inactivating mutations involving several key subunits of the SWI/SNF chromatin-remodeling complex that resulted in the loss of protein expression in the undifferentiated component of DDEC. These included BRG1 inactivation, ARID1A and ARID1B co-inactivation and INI1 inactivation, and such inactivation occurred preferentially in a highly microsatellite instable (MSI-H) molecular context. Understanding how inactivation of the different chromatin-remodeling proteins maintains undifferentiated gene expression programs in DDEC will provide valuable insights into how arrested differentiation accelerates tumor progression and likely unveil novel therapeutic approaches.

Methods:

Targeted sequencing together with immunohistochemistry was utilized to detect mutations and loss of BRG1, INI1, ARID1A and ARID1B in clinical cases of DDEC. Established human endometrial cancer cell lines were characterized for their level of BRG1 and ARID1A/ARID1B expression by pairing immunofluorescence and immunohistochemical studies with Western blot analysis. The expression of EMT and stem cell-related genes in these cells lines was determined using qRT-PCR. *In vitro* disease models of DDEC are currently being generated from select endometrial cell lines using both shRNA and CRISPR technology.

Results:

Close to 80% of clinical cases of DDEC show a loss of BRG1, INI1 or ARID1A and ARID1B with the majority having developed in a mismatch repair protein-deficient molecular context. Gene expression profiling analysis comparing the SWI/SNF CRC protein-deficient undifferentiated component to the well differentiated component of DDEC showed increases in the level of expression of markers of stemness and epithelial to mesenchymal transition (EMT).

Conclusions:

A subset of endometrial cancer cell lines appear to represent ideal models for generating BRG1-deficient or ARID1A/1B co-deficient cell line models for further *in vitro* and *in vivo* (xenograft) characterization. Direct comparison between the *in vitro* derived human DDEC models and patient derived xenograft (PDX) models from clinical DDEC cases will be critical to our understanding of the role of SWI/SNF CRC subunits in cellular dedifferentiation at the genetic, epigenetic and molecular level.

Funded By: Graduate Studentship

Abstract #:	39
Presenter:	Kirstie De Jong
Supervisor:	Sean McGee
Title:	Women with Polycystic Ovary Syndrome exhibit an increased risk of left ventricular hypertrophy
Authors:	Kirstie De Jong, Alan Appelbe , Mark Kotowicz, Kimberly Cukier, Sean McGee
Affiliations:	Deakin University, Australia
Research Activity:	Women's Health : Urology/Gynecology

Introduction: It remains unclear as to whether polycystic ovary syndrome (PCOS) is an additional risk factor in the development of left ventricular hypertrophy (LVH) in obese women. This is largely due to the asymptomatic nature of LVH and the way in which risk is monitored in obese women with and without PCOS. In the current study, we provide clarity on this issue by rigorously analysing patient left ventricular geometry beyond the basic clinical measures currently used. Importantly, the sample contained only those patients that would normally be deemed low risk with no further action required (normotensive, asymptomatic).

Methods: This cross section study comprised a total of 21 women with PCOS and 23 control women (age and BMI matched). Transthoracic echocardiography was used to evaluate left ventricular structure and function as per the American Society of Echocardiography (ASE) guidelines. Basic clinical and metabolic data were collected for each participant consisting of age, BMI, blood pressure, fasting glucose, LDL-C, HLD-C, cholesterol and triglyceride levels (after overnight, 8 hour minimum fast). Exclusion criteria included; BMI < 30 g/m^2, type 2 diabetes, history of hypertension or use of anti-hypertensive medication and history of cardiac disease.

Results: Both groups exhibited remodelling of the left ventricular posterior wall at a prevalence of >30%, this associated with the presence of grade 1 diastolic dysfunction ($p<0.05$). Estimated left ventricular mass/$height^{2.7}$ was increased in obese patients with PCOS (46 ± 2.3 vs 38 ± 1.8 vs, $p<0.01$). With 33% of PCOS patients exhibiting LV mass/$height^{2.7}$ above ASE guidelines, compared to 8% in patients without PCOS ($p<0.05$). These increases in LV mass however did not associate with diastolic dysfunction.

Conclusions: The results from the current study suggest that obese women with PCOS are at greater risk of LVH than obese only women, however this may not associate with a decline in diastolic function.

Funded By: Australian Government, Department of Education and Training

Abstract #: 40
Presenter: Gayathri Ananthakrishnan
Supervisor: Donna Vine
Title: Androgens modulate lipid metabolism in a rodent model of Poly Cystic Ovary Syndrome
Authors: Gayathri Ananthakrishnan, Spencer Proctor, Mahua Ghosh, Rene Jacobs, Donna Vine
Affiliations: University of Alberta
Research Activity: PCOS and dyslipidemia

Background: In Polycystic Ovary Syndrome (PCOS) a high plasma level of testosterone (T) has been correlated with an adverse plasma lipid profile and exacerbated CVD risk. The metabolic syndrome is highly prevalent in PCOS and is also associated with impaired intestinal lipid and apoB-lipoprotein metabolism. Impairments in fasted and postprandial triglycerides (TG) and apoB-lipoprotein remnants have been associated with elevated CVD risk and end-stage ischemic events. At present we do not know the direct action of androgens on the physiological or mechanistic pathways that regulate intestinal lipid and apoB-lipoprotein metabolism under control and hyperandrogenemia-PCOS conditions. The aim of this study was to determine the effects of testosterone and dihydrotestosterone (DHT) on intestinal lipid absorption and synthesis in control and PCOS-MetS rodents.

Methods: Control and PCOS-MetS rodents were administered vehicle, testosterone propionate (T) or DHT (non-aromatizeable) for 7 days. Following treatment animals underwent a mesenteric lymphatic cannulation procedure to determine bolus lipid absorption, and intestinal secretion of lipids and chylomicrons (apoB48-lipoproteins).

Results: T and DHT treatment did not alter fasted plasma TG, however both treatments increased plasma LDL-C and decreased apoB48 in PCOS-MetS animals. T and DHT increased plasma apoB100-lipoproteins in control animals only. Intestinal secretion of TG in the fed state was increased in T and DHT treated animals, and T increased apoB48 secretion in PCOS-MetS animals. Whereas DHT reduced intestinal apoB48 secretion in both control and PCOS-MetS animals, suggesting different modes of action of androgen isoforms. These findings were also associated with T-dependant increases in fatty acid and cholesterol absorption in PCOS-MetS animals. The differential effects of T and DHT were further associated with changes in intestinal and hepatic lipidogenic (SREBP-2, ACC, MTP) and steroidogenic gene (AR, ER and SRDA51) expression.

Conclusion: These results show androgens upregulate intestinal lipidogenic pathways in the absorption and secretion of lipids, and differentially impact chylomicron-apoB48 secretion in control and PCOS-MetS conditions. The significance of these findings is androgens appear to cause or exacerbate lipid absorption and lipoprotein metabolism in PCOS. Further studies are needed to determine specific targets and safe treatments to improve lipid metabolism associated with hyperandrogenism and the MetS in PCOS.

Funded By: AITF, NSERC

Abstract #:	41
Presenter:	Shangmei Hou
Supervisor:	Tom Hobman
Title:	Zika virus inhibits the induction and downstream signaling of host interferon system
Authors:	Shangmei Hou, Anil Kumar, Adriana Ario, Daniel Limonta, Valeria Mancinell, William Branton, Christopher Power, Tom Hobman
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology

Introduction: Zika virus (ZIKV) is an emerging mosquito-borne viral pathogen that is associated with Guillain–Barré syndrome in adults and microcephaly and other neurological defects in newborns. Despite the health burden it poses on our global community, particularly for expecting mothers and newborns, little is known about ZIKV pathogenesis. Currently, there are no vaccines or treatments available for this virus. To better understand ZIKV biology and to identify novel antiviral targets, my research is focused on determining how this pathogen evades host cell antiviral systems, particularly, the interferon response.

Methods: To determine the effect of ZIKV infection and viral proteins on the induction and downstream signaling of type-I interferons, quantitative real-time PCR and luciferase reporter assays were performed and comparisons were made between control samples and experimental groups. To demonstrate that ZIKV infection or expression of viral NS5 induced loss of STAT2, indirect immunofluorescence microscopy as well as immuno-blotting was used to measure the steady state level of endogenous STAT2. Finally, to reveal a physical interaction between NS5 and STAT2, co-immunoprecipitation was performed in cells expressing a wildtype NS5 or mutants of NS5.

Results: Initially, we observed that ZIKV infection was impervious to interferon treatment, which usually stimulates the host cell to generate an antiviral state against pathogens. This suggests that ZIKV deploys effective countermeasures to host cell defences. We confirmed this hypothesis by demonstrating that ZIKV infection impaired induction of both type-I interferon and interferon-stimulated genes, which are antiviral proteins that limit viral replication and spread. Furthermore, to suppress downstream interferon signaling, ZIKV induces degradation of STAT2, a critical signaling molecule in the interferon system. We then identified the NS5 of ZIKV as the viral component that binds STAT2 and targets it for proteasomal degradation.

Conclusion: Our findings revealed that ZIKV employs multiple mechanisms to subvert the host interferon system. Such antagonism includes inhibition of interferon production as well as blocking downstream antiviral signaling. We believe that our discovery is important for understanding the pathogenesis of ZIKV and identifying novel targets for antiviral therapies.

Funded By: Graduate Studentship

Abstract #: 42
Presenter: Olena Bilyk
Supervisor: Lynne-Marie Postovit
Title: Nodal promotes cell plasticity and therapy resistance in ovarian cancer cells
Authors: Olena Bilyk, Jiahui Liu, Scott Findlay, Lynne-Marie Postovit
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology

Introduction. Following chemotherapy residual cancer cells could employ embryonic stem cell signaling pathways to sustain plasticity and resistance to therapy. Nodal is a potent embryonic morphogen which has been found to sustain stem cell pluripotency and cellular plasticity. However, Nodal expression re-emerges in cancer promoting cancer stem cell renewal, tumor growth and metastasis. We hypothesize that Nodal signaling drives plasticity in OC cells and that disease progression and therapy resistance will be mitigated when Nodal is inhibited.

Methods. We applied *in vitro* assays designed to assess growth (MTT and clonogenic assays), stem cell like phenotypes (sphere limiting diluting assays) and chemoresistance (surviving fraction assays and a human cancer drug resistance PCR array) in OC cells (A2780s) wherein Nodal was added with rhNodal or a Nodal expression construct, or knocked down/out with shRNA or CRISP/Cas9 genome editing.

Results. We found that Nodal is significantly up-regulated in OC cells (A2780s) in response to platinum drug treatment. When Nodal was ectopically expressed in OC cells, it promoted partial epithelial-to-mesenchymal transition (cellular plasticity) and increased resistance to carboplatin while Nodal knockdown sensitized cells to drug. Moreover, Applying of rhNodal prevented cell cycle arrest in OC cells after treatment with platinum. Drug resistance gene expression array identified the up-regulation of 21 genes in Nodal expressing cells as compared to controls. ERBB4 was the most upregulated.

Conclusion: These data demonstrate that Nodal is likely driving cancer cell plasticity and resistance chemotherapy in OC cells by promoting cancer stem cell-like phenotype and by upregulating target genes involved in multi-drug resistance, and may hold promise as a therapeutic target to prevent OC recurrence.

Funded By: AIHS

Abstract #: 43
Presenter: Arielle Cantor
Supervisor: Cathy Flood
Title: Do patients understand the role of resident physicians in the operating room? A survey of gynecology patients
Authors: Arielle Cantor , Cathy Flood , Savanna Boutin , Shauna Regan , Sue Ross
Affiliations: University of Alberta
Research Activity: Patient Education

Introduction

Strong physician-patient relationships are vital to achieving confidence in our patients. Nonetheless, confusion exists at the basic level of this interaction. Studies, mainly in emergency departments, have shown that although most patients believe it is important to know the level of training of their doctor, the majority have little knowledge about the responsibilities of physicians-in-training. Studies of this kind are lacking in the gynecological population.

In Edmonton recently a gynecological surgeon was sued because a patient alleged she was not fully informed about the role of a resident in her surgery. The goal of this research is to explore what gynecological surgery patients understand about the role of resident doctors.

Methods

A short answer questionnaire (based on those used in emergency department research) was distributed to English-speaking female patients in pre-admission clinics awaiting gynecological surgery in Edmonton. Surveys included knowledge and opinion-based questions about resident duties and their roles compared to staff physicians. The necessary sample size was estimated as 100 completed questionnaires. Anonymous responses were collected and managed using a REDCap database. Descriptive statistics were used to characterize the results.

Results

The mean age of the 108 participants was 53 years, with 60% having an education level greater than secondary school. Eighty-eight percent of participants had a previous surgical procedure. Fifty-nine percent of women believed a resident completed medical school. Although most (83%) understood that residents had a higher level of training than a medical student, 40% of patients were unsure or did not consider residents to be medical doctors. Almost half of patients (43%) were uncertain if residents required supervision in patient care, including when performing surgery (20%).

The majority of patients (92%) felt it was important to know their physician's level of training, yet only 63% reported actually knowing this information. Only half of participants described feeling comfortable with resident doctors operating on them under supervision. A considerable number of patients (56%) wanted to learn more about residents' training.

Conclusions

Patients do not fully understand the role of residents, despite believing it is important to know their level of training. Many were also not comfortable with residents operating on them under supervision. Considering the dominant role that residents play in patient care, educating patients about their providers is essential to improve their satisfaction, comfort and the overall consent process.

This research was facilitated by WCHRI through generous supporters of the Lois Hole Hospital for Women.

Abstract #:	44
Presenter:	Billie-Jean Martin
Supervisor:	Ivan M. Rebeyka
Title:	Regionalized surgical care: Lack of association between on site surgical program and post-operative outcomes in children undergoing Fontan Palliation
Authors:	Billie-Jean Martin, David B. Ross, Mohammed Al Aklabi, Joyce Harder, John Dyck, Ivan M. Rebeyka
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction Evidence suggests that outcomes in pediatric cardiac surgery are improved by consolidating care into high volume centers of excellence. In Western Canada, pediatric cardiac surgical services from several sites were relocated to Stollery Children's Hospital 20 years ago, with some patients and their families travelling long distances to receive care. Our objective was to determine if outcomes are equivalent in Fontan patients across a large regional referral base, or if patients from centers without on site surgery are at a disadvantage.

Methods Since 1996, all pediatric cardiac surgery has been offered at a one of two centers within the region assessed, with the majority being performed at Stollery Children's Hospital. All patients who underwent a Fontan operation between 1996 and 2015 were included. Baseline data including cardiac diagnosis, previous operations, age, sex, home center, and hemodynamic data were collected from the Western Canadian Children's Heart Network database and through chart review. Follow-up data including length of stay (LOS), repeat surgical interventions and transplant-free survival were acquired for each patient. The association between post-operative outcomes and home center (surgical site versus other site) were assessed using Kaplan-Meier survival analysis and Cox proportional Hazards models, adjusted for all appropriate covariables.

Results 292 children (median age 3.3 years, IQR 2.8 – 4.1; 127 (43.5%) female) were included; 109 (37.3%) had the surgical center as their home center. Cardiac anatomy was hypoplastic left heart syndrome in 108 (37.0%) subjects. Median LOS was 10 days (IQR, 7-16), and there were 2 early deaths. There were 16 deaths and 11 transplants over the full course of follow-up. Five-year transplant-free survival was 92.7%. There was no difference in hospital re-intervention, late re-intervention or survival by home center (all $p>0.05$). In multivariable analysis, home center was not predictive of either LOS (R^2=-0.53, $p=0.75$) or transplant-free survival (1.90, 95% CI 0.78, 4.61).

Conclusions In children with complex congenital heart disease, a regionalized care model achieves good outcomes, which do not differ according to a patient's home base. Our findings offer evidence to support the fact that a regionalized care model may be an acceptable way to offer complex congenital cardiac surgical care to large geographical regions with low population densities.

Abstract #: 45
Presenter: Anmol Sidhu
Supervisor: Timothy Colen
Title: Progressive reduction of leaflet coaptation with time is associated with increased tricuspid valve regurgitation in hypoplastic left heart syndrome
Authors: Anmol Sidhu, Kandice Mah, Nee Khoo, Timothy Colen
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Congenital Abnormalities

Introduction: Hypoplastic left heart syndrome (HLHS) is a congenital heart defect characterized by a hypoplastic left ventricle and aorta, requiring 3 staged, surgical procedures. Despite advances in management, outcomes remain poor, with 30% mortality in the first year of life. Tricuspid regurgitation (TR) is caused by abnormalities of the tricuspid valve (TV) and right ventricle (RV), and is associated with increased mortality. We aimed to describe changes in TV and RV size and functional parameters across the surgical period.

Methods: We examined echocardiographic data in 54 patients with HLHS, at 4 time-points (prior to each of 3 surgical stages, and 2 years after final surgery). Echocardiographic measures included TV annulus and leaflet size, leaflet coaptation length, leaflet prolapse and tethering, and RV size and fractional area change (FAC). Measurements were indexed to body surface area. TR was evaluated by vena contracta (VC) size and qualitative grading.

Results: Rate of significant TR (³moderate) increased for the first 3 time-points then remained stable (9%, 17%, 35%, 22%: P=0.002). Similarly, there was a rise in VC (indexed to TV annulus) from time 1 to 2 (0.07, 0.09; P=0.005) and then remained unchanged. Annulus size decreased across all 4 time-points (7.1cm/m^2, 6.3cm/m^2, 4.5cm/m^2, 3.9cm/m^2; P<0.001), and leaflet size decreased across all time-points (10.9cm/m^2, 9.6cm/m^2, 6.8cm/m^2, 5.8cm/m^2; P<0.001). Coaptation length decreased from time 1 to 2 to 3 then remained stable (3.7cm/m^2, 3.0cm/m^2, 2.1cm/m^2, 2.0cm/m^2; P<0.001). Leaflet tethering increased from time 1 to 2 (6.7mm^2/m^2, 9.6mm^2/m^2; P=0.007) and then decreased from time 2 to 3 to 4 (9.6mm^2/m^2, 6.3mm^2/m^2, 4.2mm^2/m^2; P<0.001. Prolapse area increased from time 2 to 3 (2.0mm^2/m^2 vs 8.4mm^2/m^2; P=0.03), but did not change from time 1 to 2 or time 3 to 4. RV size increased from time 1 to 2 (26cm^2/m^2, 29cm^2/m^2; P=0.002), but decreased in size from time 2 onwards (29cm^2/m^2, 24cm^2/m^2, 22cm^2/m^2; P<0.001). There was no significant change in RV function (FAC) over time.

Conclusion: Increased rate of TR with time is likely related to progressive changes in TV parameters, although the specific cause may vary at each time-point. Coaptation length, a measure of leaflet tissue involved in coaptation, progressively decreases, suggesting it is an important contributor to TR at all time-points.

Funded By: Start-up or Retention Funding

Abstract #:	46
Presenter:	Jacqueline Krysa
Supervisor:	Spencer Proctor
Title:	The relationship of remnant cholesterol to sub-clinical cardiovascular risk in youth
Authors:	Jacqueline Krysa, Donna Vine, Lawrence Beilin, Sally Burrows, Rae-Chi Huang, Trevor Mori, Spencer Proctor
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction (Purpose): Cardiovascular disease (CVD) remains the leading cause of death in Canada. While adverse cardiovascular events typically occur in adulthood, there is strong evidence to suggest that heart and vascular diseases are initiated in childhood. Traditional blood lipids (low density lipoprotein cholesterol (LDL-C) and total cholesterol (TC)), which are measured to assess CVD risk in children, often do not have the power to detect subclinical CVD risk at this age. This forces us to investigate novel lipid markers to identify youth at early periods of risk. Remnant cholesterol has recently emerged as a significant CVD risk factor in adults. Elevated remnant cholesterol contributes to the build up of lipids in the arteries and is an independent predictor of CVD risk. We can measure remnant cholesterol in the plasma directly by quantifying fasting plasma apoB48 - the functional protein of intestinal remnant cholesterol. We have previously demonstrated that fasting apoB48 is elevated two-fold in obese pre-pubertal children and tracks with early changes in central adiposity. However, it is unclear if remnant cholesterol metabolism is influenced during puberty and/or if it remains elevated in conditions of cardiometabolic risk in adolescent boys and girls.

Objectives: To verify and validate the strength of fasting apoB48 as a marker of subclinical CVD risk and its relationship with other cardiometabolic risk parameters in a large adolescent population.

Methods: Fasting apoB48, anthropometry and biochemistry were assessed in a cross-sectional analysis of participants from the Western Australian Pregnancy Cohort (Raine) study aged 17 (n=1045). Fasting apoB48 was measured using a validated enzyme linked immunosorbent assay (ELISA). Multiple regression analysis examined the relationship between apoB48 and cardiometabolic risk factors.

Results: Fasting apoB48 was significantly higher in males than females and significantly elevated in individuals that fell into a “high risk” group with features of the metabolic syndrome. In regression analysis, there was a positive association between fasted apoB48 and triglycerides, total cholesterol, insulin, HOMA-IR, leptin, waist circumference, and abdominal and subscapular skinfold thickness. ApoB48 levels were inversely associated with HDL-C, adiponectin, and C-reactive protein.

Conclusions: Fasting apoB48 associates with measures of adiposity and features of the metabolic syndrome in adolescents and appears to be more elevated in “high risk” males. These findings suggest that fasting apoB48 may be an important biomarker to detect subclinical CVD in youth.

Funded By: Heart & Stroke Foundation, Queen Elizabeth Scholars

Abstract #:	47
Presenter:	Mais Aljunaidy
Supervisor:	Sandra T. Davidge
Title:	Effect of maternal antioxidant MitoQ treatment on offspring cardiovascular function in a rat model of intrauterine growth restriction (IUGR)
Authors:	Mais M. Aljunaidy, Jude S. Morton, Raven Kirschenman, Patrick Case, Christy-Lynn M. Cooke, Sandra T. Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease

Introduction: A suboptimal environment in fetal life is linked to cardiovascular disease in adult life. Maternal hypoxia can lead to placental oxidative stress, which is associated with abnormal cardiovascular function in the offspring. We hypothesize that maternal treatment with MitoQ, a mitochondrial antioxidant, may prevent placental oxidative stress and the development of cardiovascular disease in adult offspring.

Methods: Pregnant rats were randomly divided into two groups, and injected with either MitoQ loaded nanoparticles (125 μM) or saline via tail vein on gestational day (GD) 15 (nanoparticles prevent MitoQ from crossing to the fetus). Rats were further subdivided into two groups exposed to either hypoxia (11% O_2) or normoxia (21% O_2) from GD 15-21 (term; 22 days). At 7 months of age, cardiac function (echocardiography) and vascular function (wire myography) were assessed in both male and female offspring. A 2-way ANOVA or Student's t-test was used for statistical analyses.

Results: Prenatal hypoxia led to later-life diastolic dysfunction and to a reduction in the pulmonary artery peak velocity (PV Peak Vel) in male, but not female offspring and MitoQ treatment prevented PV Peak Vel reduction (hypoxia: 620±28 mmHg vs. hypoxia+MitoQ: 781±53 mmHg, $P<0.05$). In male offspring, the nitric oxide synthesis inhibitor (L-NAME) increased mesenteric artery sensitivity to phenylephrine (PE), and this effect was absent in the prenatal hypoxia group (PE: 5.79±0.02 vs. PE+L-NAME: 5.89±0.05, $P=0.22$) and restored when maternal MitoQ was provided. In female offspring, however, sensitivity to PE was similarly increased by L-NAME in normoxic and hypoxic group. In contrast in females, MitoQ treatment diminished this increase in prenatal hypoxia exposed group(PE: 5.55±0.03 vs. PE+L-NAME: 5.68±0.06, $P=0.12$). Further, L-NAME increased vasoconstriction responses to big endothelin-1 in all groups compared to control in male, but not female, offspring; an effect which was unaltered by hypoxia or treatment.

Conclusion: In males, MitoQ treatment rescued pulmonary artery function and ameliorated the abnormal vasoconstriction responses which were caused by hypoxia. In females, vascular function was not affected by hypoxia *in utero*, however, maternal treatment with MitoQ led to a decreased nitric oxide involvement in hypoxic exposed animals. Further studies are required to further assess the effect of MitoQ on the cardiovascular function of adult offspring.

Funded By: Graduate Studentship

Abstract #:	48
Presenter:	Yiqun Wang
Supervisor:	Lori West
Title:	Blood group A-antigen-specific tolerance following infant A-antigen exposure in a mouse model of ABO-incompatible heart transplantation
Authors:	Yiqun Wang, Brendon Lamarche, Ibrahim Adam, Jean Pearcey, Kesheng Tao, Chris Cairo, Bruce Motyka, Lori West
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant

Purpose: ABO-incompatible transplantation (ABOi HTx) can be performed safely in infants due to absent-low levels of anti-A/B antibodies (Ab), in contrast to adults. Tolerance develops to donor blood group A/B-antigen(s) following ABOi HTx by mechanisms not well understood. Using an A-transgenic (A-Tg, C57BL/6) mouse model, we showed A-antigen specific tolerance following HTx in young, wild type B6 (WT) mice. Herein, we sought to explore induction of A-antigen-specific tolerance in a form other than a graft. A-antigen is present at high levels in A-Tg blood cells. We hypothesized that A-antigen-specific tolerance would be induced following treatment of infant WT mice (≤3 weeks of age) with A-Tg erythrocytes (RBCs).

Methods: WT mice at 7, 14, and 21 days of age were injected intraperitoneally (i.p.) with: 1) *intact* A-Tg RBCs (n=12); 2) A-Tg RBC *membranes* (n=4); 3) human A RBC membranes (hA-RBCs) (n=6); or 4) left untreated (n=9). As adults (7 weeks), all mice were injected i.p. with hA-RBCs ('A-sensitized') in an attempt to elicit anti-A Ab production. Serum anti-A and 3rd-party Ab were assessed by hemagglutination assay and ELISA. Intact A-Tg RBC treated (n=3) and untreated (n=4) groups received heterotopic HTx from A-Tg donors. Grafts were monitored for function and antibody-mediated rejection (AMR) at 14 days post-Tx or when beating ceased.

Results: Following A-sensitization, high levels of anti-A Ab developed in mice untreated as infants (median titre 1:1024, mean IgG 47 ng/mL, IgM 198 ng/mL), treated with hA-RBCs (median titre 1:2048, mean IgG 991 ng/mL, IgM 7622 ng/mL) or ATg RBC *membrane* (median titre 1:256, undetectable IgG, IgM 277 ng/mL). In contrast, anti-A Ab remained undetectable-low in A-sensitized mice treated with *intact* ATg RBC (median titre ≤1:2, mean IgG 6.5 ng/mL, IgM 89 ng/mL); 3rd-party Ab levels were high (median titre 1:64). All grafts survived until the 14-day endpoint. Morphologic AMR features are currently being assessed.

Conclusions: The ability to elicit 3rd-party but not A-antigen-specific Ab in A-sensitized mice treated as infants with *intact* A-Tg RBCs suggests the development of robust A-antigen-specific tolerance.

Funded By: Summer Studentship

Abstract #:	49
Presenter:	Kristofor Ellestad
Supervisor:	Colin Anderson
Title:	PD-1-/- newly generated CD4+ T cells drive autoimmunity in lymphopenia independent of Fas and perforin-dependent killing
Authors:	Kristofor Ellestad, Colin Anderson
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology

Introduction:

While developing T cells undergo thymic selection processes that eliminate the majority of strongly self-reactive T cells, some potentially "dangerous" T cells escape into the periphery and must be controlled via peripheral tolerance mechanisms. In a normal adult, recent thymic emigrants (RTE) comprise a small proportion of total peripheral T cells. However, in conditions of lymphopenia such as occur in neonatal life, they will necessarily comprise a much larger proportion of peripheral T cells and thus control of these RTE is critical to avoid host autoimmune pathology. Inhibitors of T cell signaling such as programmed death-1 (PD-1) are important for this control.

Reconstitution of the lymphoid compartment of lymphopenic adult Rag1$^{-/-}$ mice via transplant of PD-1$^{-/-}$ hematopoietic stem cells (HSC) leads to severe and lethal systemic autoimmunity. In contrast, established peripheral T cells from adult PD-1$^{-/-}$ mice do not cause disease, suggesting that 1) RTE have heightened autoimmune potential compared to established T cells, and 2) PD-1 is critical for control of RTE. However, whether RTE in a normal host maintain heightened autoimmune-generating potential for a period of time in the periphery, or if they become tolerized rapidly upon contact with a lymphoreplete periphery is unknown. Furthermore, which subsets (CD4+ or CD8+) of PD-1$^{-/-}$ RTE drive autoimmunity in lymphopenic hosts and the mechanisms by which they do so (i.e. Fas or perforin mediated killing) are unclear.

Methods:

Purified RTE from adult Rag2pGFP x PD-1$^{-/-}$ transgenic mice were tested for their ability to drive autoimmunity upon transfer to lymphopenic recipients. We also transferred PD-1$^{-/-}$ HSC or Perforin$^{-/-}$ x PD-1$^{-/-}$ thymocytes to lymphopenic hosts deficient in MHC-II or Fas and monitored for disease.

Results:

RTE purified from the periphery of lymphoreplete animals had heightened autoimmune-generating potential in lymphopenic recipients. MHC-II deficient hosts were resistant to disease. Neither perforin in the T cells nor functional Fas in the host were required for the induction of autoimmunity.

Conclusions:

These data suggest that RTE in normal hosts maintain heightened autoimmune potential for a period of time in the periphery, and these cells may be important for "sowing the seeds" of autoimmunity in circumstances associated with lymphopenia such as in early life. CD4+ T cells appear critical for driving autoimmunity in our lymphopenia-driven autoimmunity model, and this does not depend on Perforin- or Fas-dependent killing mechanisms. This may suggest that PD-1$^{-/-}$ RTE-driven systemic autoimmunity in lymphopenia is primarily mediated by a cytokine storm.

Funded By: Start-up or Retention Funding

Abstract #:	50
Presenter:	Pranidhi Baddam
Supervisor:	Daniel Graf
Title:	Loss of neural crest-derived Bmp7 causes craniofacial malformations leading to Obstructive Sleep Apnea
Authors:	Pranidhi Baddam, Sahand Eslaamizaad, Christopher Percival, Benedikt Hallgrimsson, Daniel Graf
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction

Craniofacial tissues are affected in three out of four human congenital birth defects. Obstructive Sleep Apnea (OSA) may result as a consequence. The etiology and physiological consequences of OSA are still poorly understood, which negatively affects our ability to provide optimal patient treatment. BMP7, crucial osteogenic signaling molecule, regulates development of various oral and facial structures. Complete loss of Bmp7 leads to cleft palate and perinatal death precluding analysis of Bmp7 function in postnatal craniofacial growth. Mice carrying a deletion of Bmp7 in neural crest cells *(Bmp7$^{fl/fl}$:Wnt1Cre)* are viable and present with an obvious mid-facial hypoplasia. Here we identify and characterize the aetiology of this and other craniofacial abnormalities in these mice using morphometric and molecular analysis.

Methods

Bmp7$^{fl/fl}$:Wnt1Cre (mutant) mice were obtained by crossing a conditional Bmp7 allele to Wnt1-Cre mice. Microcomputed Tomography (μCT) datasets were analyzed for morphometric changes using Amira software. For this, landmarks were placed using geometric locations and Cartesian coordinates on the skulls of mice at various ages. Bone mineral density was determined from μCT datasets using BoneJ. Skeletal preparations of E15.5, E17.5 embryos and P0 pups were made using Alizarin red and Alzian blue.

Results

Bmp7- mutant mice display multiple craniofacial abnormalities including shorter mandible, depressed maxilla outgrowth, submucosal cleft palate, mild to severe airway blockage, and abnormal eyes. The compressed nasal and pharyngeal airways became particularly apparent after 2-3 weeks of age. More than 50% of mutant mice would die between 4-6 weeks, presumably due to OSA. Mice also present with ossification phenotypes such as incomplete closure of the fontanelle and reduced ossification of the frontal and sagittal sutures. Skeletal preparations of E17.5 embryos and newborn pups revealed prominent changes to the cranial base with underdeveloped wings at the sphenoid bone and pterygoid plate, Turbinates and shorter mandibles, which could cause lack of mid-facial growth. Molecular analysis revealed that Bmp7 regulates many extracellular matrix genes, amongst them collagen II (*Col2a1*), IX(*Col9a1/a2/a3*), XI(*Col11a2*), genes when mutated cause Stickler syndrome characterized by a flattened facial appearance due to underdeveloped bones in the middle of the face. Obstructive sleep apnea is often observed in children with Stickler syndrome.

Conclusions

This mouse model allows us to study the etiology of craniofacial alterations leading to OSA as well as systemic consequences of the resulting hypoxia, such as altered bone development and growth. In conclusion, better understanding of OSA could lead to effective treatment approaches.

Funded By: Innovation Grant

Abstract #:	51
Presenter:	Prabhjot Bedi
Supervisor:	Joanna MacLean
Title:	Infants represent a distinct group within the pediatric non-invasive ventilation population in Alberta
Authors:	Prabhjot Bedi, Kristie DeHaan, Maria Castro-Codesal, Joanna E MacLean
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction: The use of non-invasive ventilation (NIV), a method of providing positive pressure breathing support from the upper airway, has increased in infants and children over the past decade. Despite this increase, little data exists on the use of this respiratory support in the infant population. Given that infants have a unique sleep architecture and breathing pattern compared to older children, the approach to long-term NIV therapy in infants may need to differ from that in older children. The aim of this study is to determine whether infants represent a distinct group with respect to the approach to long-term NIV within the pediatric population.

Methods: This study is a 10 year retrospective chart review of all children receiving long-term NIV across Alberta. Data was collected from medical charts and sleep study records. To establish a comparison group, infants (age <2 years) were matched 1:1 to older children (age 2-18 years) of the same sex and closest date of NIV initiation.

Results: We identified 628 children who started NIV, of which 123 (20%) were infants. The mean age of NIV initiation in infants and older children was 10.5 +/- 7.0 months and 9.1 +/- 4.4 years respectively. While the most common underlying disease category for both infants and older children was upper airway disorders (44.7% vs. 59.3%), infants had more central nervous system disorders (19.5% vs. 11.4%) and pulmonary disease (12.2% vs. 2.4%) than older children ($p<0.05$). Infants required more additional technology (oxygen and gastrostomy tube) than older children (72.4% vs. 27.6%, $p<0.05$). Adherence to NIV, defined as % days of NIV use >4 hours, was similar for both groups (58.7% vs. 59.6%, p=ns). Discontinuation rates were higher in infants (61.0% and 47.9%, $p<0.05$). Reasons for discontinuation differed between the two groups, with infants most commonly stopping because of improvement in the underlying condition (36.1%) and older children stopping because of patient/family declining to continue (40.4%, $p<0.01$).

Conclusions: Infants using NIV exhibit a great dispersion with respect to conditions leading to NIV. Increased use of additional technology in infants, along with a higher rate of improvement in the underlying condition, support the idea that infants represent a distinct group within the pediatric NIV population and may require a separate treatment strategy. Somewhat surprisingly, adherence rates for NIV use are similar in infants and older children suggesting that parents/caregivers, rather than children, impact adherence across the pediatric NIV population.

Funded By: Support services

Abstract #:	52
Presenter:	Malak Gazzaz
Supervisor:	Hamdy El-Hakim
Title:	Does drug-induced sleep endoscopy change the surgical decision in children with snoring/sleep disordered breathing? A retrospective cohort study
Authors:	Malak Gazzaz, Andre Isaac, Scott Anderson, Noura Alsufyani, Yaser Alrajhi , Hamdy El-Hakim
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction

Adenotonsillectomy is the most commonly performed operation for pediatric snoring/sleep disordered breathing (S/SDB). However, 20-40% of patients will fail to improve. Drug-induced sleep endoscopy (DISE) may provide a more individualized surgical plan and limit unsuccessful surgeries. The aim of this study was to assess the impact of DISE on surgical decision-making in surgically naïve children with S/SDB.

Methods

A retrospective observational cohort study was undertaken at the Stollery Children's Hospital. Patients 3-17 years of age who underwent DISE-directed surgery for S/SDB between January 2009 and December 2015 were eligible. We excluded other indications for tonsillectomy and syndromic children. The primary outcome was the level of agreement between a DISE-based surgical decision and the reference standard based on the American Academy of Pediatrics (AAP) guidelines via un-weighted Cohen's kappa. Secondary outcomes included the frequency and type of alternate surgical targets identified by DISE. The agreement on tonsil size between in-office physical assessment and DISE was also calculated.

Results

558 patients were included. DISE changed the surgical plan in 35% of patients. Agreement between DISE-based and AAP clinical practice guidelines-based management was low (κ=0.354 +/- 0.021 [95% CI 0.312-0.395]). An alternate diagnosis or surgical target was identified by DISE in 54% of patients. There was moderate agreement on tonsil size (κ=0.44 [0.33-0.55]) between DISE and in-office clinical assessment.

Conclusions

DISE affects decision-making in surgically naïve children with S/SDB in up to 35% of patients. It has utility in individualizing first stage surgical treatments as well as identifying alternate targets for further surgical or medical therapy, while potentially limiting unsuccessful surgeries.

Abstract #: 53
Presenter: Jasmeen Saini
Supervisor: Silvia Pagliardini
Title: Expiratory modulated abdominal muscle recruitment in neonatal and adult rats across sleep states
Authors: Jasmeen Saini, Colin Andrews
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Sleep and Breathing Disorders

Introduction:

Breathing is an essential physiological process that is known to be fragile during sleep, particularly during rapid eye movement sleep (REM) in both humans and rodents. The brainstem contains the main neuronal networks responsible for generating the rhythms and patterns of respiration. The ventral surface of the medulla is therefore the central controller for respiration and works together with signals from sensors (chemoreceptors and stretch receptors) and to the respiratory muscles. The respiratory muscles thus play a crucial role in facilitating ventilation, specifically the movement of air into and out of the lungs.

Although a generally robust process, breathing is prone to instabilities like apneas and hypoventilation during the perinatal period. In rats, similar to humans, sleep is characterized by period of REM and nonREM, alternatively defined as active sleep (AS) and quiet sleep (QS). We hypothesize that in perinatal rats, expiratory muscle activity is recruited during sleep when respiration is irregular and this is associated with an increase in respiratory stability. Results from adult rats, in the Pagliardini lab indicate that recruitment of expiratory abdominal activity during REM sleep improved respiratory stability and increased the tidal volume and minute ventilation.

Methods:

Using P1, P3 and P7 rats in whole body plethysmography and EMG implantation, recording sessions will be obtained, with neck, intercostal and abdominal EMG's, as well as airflow as the rat pups cycle between their natural sleep cycles. A video recorder will be set up, to record overt behaviours that will assist in differentiating between sleep states along with the nuchal EMG. The intercostal and abdominal EMG will correspond to inspiratory and expiratory activity respectively.

Results:

Little is known about the expiratory abdominal activity in perinatal rats, specifically across sleep states and how this contributes to ventilation. Research in our lab suggests that that expiratory activity may be critical in the neonatal period, when respiratory activity is more likely to fail, to prevent breathing irregularities and to strengthen inspiratory activity. Compared to adults, neonatal rats have more frequent abdominal muscle recruitment events, which occur in both AS and QS. Our results also indicate that respiratory rate was less variable at the onset of abdominal muscle recruitment in AS, similar to adults.

Conclusions:

We conclude that expiratory modulated abdominal muscle activity is associated with stabilization in ventilation during sleep.

Funded By: Start-up or Retention Funding

Abstract #:	54
Presenter:	Rachel Skow
Supervisor:	Margie Davenport
Title:	Potential differences in sympathetic respiratory modulation in pregnant and non-pregnant women
Authors:	Rachel Skow, Stephanie Bladon, Charlotte Usselman, Michael Stickland, Rshmi Khurana, Rhada Chari, Colleen Julian, Sandra Davidge, Margie Davenport, Craig Steinback
Affiliations:	University of Alberta
Research Activity:	Maternal- cardiovascular/ respiratory

Introduction: Sympathetic nervous system activity (SNA) is coupled with respiration. As both ventilation and SNA increase with normal pregnancy, we sought to determine whether respiratory modulation of SNA is altered. We hypothesized that pregnancy would have a greater respiratory modulation.

Methods: Ten pregnant (33±4 weeks) and ten non-pregnant control women were assessed for blood pressure (beat-by-beat; photoplethysmography), ventilation (spirometer), and SNA (microneurography; peroneal nerve) during at least five minutes of rest. Respiratory modulation of SNA was defined as the average change in SNA across the duration of a complete respiratory cycle and was normalized for changes in the respiratory rate and tidal volume.

Results: Tidal volume (0.61±0.2L vs 0.360±0.2L; p=0.0006), but not respiratory rate (16.3±4.1 vs 15.3±2.9 breaths/minute; p=0.27) was higher during pregnancy. SNA burst frequency (38.3±19 vs 21.2±3.2 bursts/minute; p=0.006), burst occurrence (47.9±14 vs 33.8±4.6 bursts/100 heart beats; p=0.004) and total SNA (2122±987 vs 1110±202 a.u.; p=0.003) were also elevated during pregnancy. Pregnant women had 38% of burst occurring during expiration, while non-pregnant women had 55% of bursts occurring during expiration. Further, the timing of the bursts occurring across the respiratory cycle was different between pregnant and non-pregnant women (main effect, p=0.001); this difference disappeared when normalized for tidal volume (p=0.667).

Conclusion: These data indicate respiratory modulation of SNA is increased with pregnancy as a result of elevated tidal volume.

Funded By: Innovation Grant and Graduate Studentship

Abstract #:	55
Presenter:	Daniel Wollin
Supervisor:	Joanna MacLean
Title:	Unmasking a disorder: The characterization of treatment emergent central sleep apnea in children
Authors:	Daniel Wollin, Kristie DeHaan, Prabhjot Bedi, Maria Castro Codesal, Joanna MacLean
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction: Treatment Emergent Central Sleep Apnea (TECSA) is a sleep disorder in which central sleep apnea events occur once treatment has been applied to resolve obstructive sleep apnea events. This disorder has not been extensively studied in children and requires characterization in order to understand how it compares to TECSA in adults. The purpose of this study is to characterize a cohort of children who meet the adult criteria for TECSA and compare these characteristics with non-TECSA children also treated with long-term non-invasive ventilation.

Methods: This retrospective study included children aged 0-18 who were treated with long term non-invasive ventilation from 2002 to 2014 at the Stollery Children's Hospital. All children underwent diagnostic sleep studies prior to starting non-invasive ventilation. The criteria for TECSA included: an Obstructive Apnea-Hypopnea Index (OAHI) ≥5 during the diagnostic study, the OAHI improving during the treatment study, a Central Apnea Index (CAI) ≥5 during the treatment study, the CAI being ≥50% of the Total Apnea Index (AHI) during the treatment study, and the CAI remaining the same or worsening from diagnostic to treatment study. Each child with TECSA was matched to three children of similar age and sleep study date to construct a comparison group. Data collection included clinical characteristics in addition to the diagnostic, first and subsequent treatment studies.

Results: Out of our population of 146 children, 13 were identified as having TECSA for a prevalence of 8.9%. During diagnostic sleep studies, TECSA children had significantly higher OAHI and AHI than matched controls (OAHI: 29.5±25.1 events/h vs 16.0±15.0 events/h, $p<0.05$; AHI: 33.4±24.7 events/h vs 19.6±17.3 events/h, $p<0.05$). During titration sleep studies, CAI and AHI were significantly higher in TECSA children than matched controls (CAI: 22.6±32.1 events/h vs 2.0±3.7 events/h , $p<0.001$; AHI: 29.6±10.0 events/h vs 7.7±9.4 events/h ,$p<0.001$). Positive airway pressures being administered during titration studies were not significantly different between TECSA children and matched controls (6.9±1.8 mmHg vs 6.5±1.8 mmHg, p=ns). Six TECSA children had follow-up treatment studies; in 4 children (67%) criteria for TECSA was not met at follow-up.

Conclusions: The prevalence of TECSA in children is similar to what is reported in adults. Higher obstructive indices during diagnostic sleep studies may provide an early indicator for TECSA risk. TECSA may be a transient phenomenon as the majority of TECSA children did not meet the criteria for the disorder at follow-up. A prospective study would be helpful to further explore this finding.

Funded By: RHSCN Summer Studentship Award

Abstract #: 56
Presenter: Joel Semeniuk
Supervisor: Andrew Dixon
Title: How do Canadian pediatric emergency physicians repair fingernail injuries?
Authors: Joel Semeniuk, Andrew Dixon
Affiliations: University of Alberta
Research Activity: Emergency Medicine

Introduction

Children are explorers, and their hands are the primary method of exploring the world. This puts hands at high risk of injury, and fingernail injuries are a common presentation to emergency departments. The fingertip is the primary touch sensory unit, and it is supported by the fingernail which helps touch, protect the finger, pick up small objects, and make the finger appear natural. Because of this, it is important that fingernails are satisfactorily repaired to ensure good functional and cosmetic outcomes.

A review of current literature on fingernail injuries shows there are successful ways to repair them, but studies contradict each other. There are good outcomes with both conservative and invasive approaches. However, researchers have not conducted studies with control groups to compare them. The situation is also clouded by the complexity of the anatomy which leads to a wide variety of injuries possible for the distal finger. In the face of uncertainty, how do emergency pediatric physicians in Canada commonly repair fingernail injures in children? No previous studies have attempted to evaluate this question. Our hypothesis is that there will not be consistency in how doctors repair them.

Methods

The study is a descriptive, cross-sectional, national survey. All individuals listed on the Pediatric Emergency Research Canada database of physicians who practice pediatric emergency medicine will be surveyed. Our sample size is limited to the finite number of individuals meeting the eligibility criteria. The estimated sample size is 200. This is a census, and no sampling will be applied. Participants will complete a demographics section and a self administered survey online with scenarios of common injuries and will answer what they would do to correct them.

Results

Descriptive statistics will be used to analyze response rates by age, sex, site, workload, speciality, and graduation year. The observed differences will be evaluated using Kendall's tau test, Chi-squared test or Fisher's exact test where appropriate. Alpha will be at 0.05 for all significance tests.

Conclusions

This study is a first step to assess the current treatment of fingernail injuries. The results will guide future research that may include an observation study of different management techniques, a case control study, or a randomized controlled trial of different interventions. Further work may have the possibility of improving the outcomes of fingernail injuries.

Funded By: Resident/Clinical Fellow Trainee Research Grant

Abstract #:	57
Presenter:	Mohamed El-Kalla
Supervisor:	Hien Huynh
Title:	Retrospective analysis of pharmacokinetic infliximab data in pediatric IBD patients
Authors:	Mohamed El-Kalla, Cheryl Kluthe, Matthew Carroll, Eytan Wine, Connie Prosser , Hien Huynh
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology

Introduction:

Infliximab (IFX) is a murine chimeric IgG1 anti-TNFα monoclonal antibody shown in landmark clinical trials to be well-tolerated and effective for induction and maintenance of remission in pediatric and adult Crohn's disease (CD) and ulcerative colitis. A third to half of children with CD in Canada are treated with an anti-TNFα such as IFX. A low IFX trough level (< 2.2 µg/ml) at week 14, i.e. before the 4th infusion predicts IFX discontinuation in adults. It is unclear if targeting a desired trough level after the 3rd dose will result in a better long term remission rate. Currently, there is no clear guideline on how to achieve the desired trough level after the 3rd dose; mainly because the pharmacokinetics of IFX in children is not well studied.

Aim: The aim of this pilot study is to assess the pharmacokinetics of IFX in children after the first three loading infusions in order to guide the interval and dose.

Method: Children with CD deemed to require IFX by the treating physicians were prospectively recruited. Dose of IFX was 5mg/kg given at week 0, 2, 6 and 14 weeks. IFX levels were measured at peak, after the third loading dose, and week 14, just before the 4th infusion.

Result: Fifteen children were recruited so far. Mean PCDAI score was 31.7. Mean dose of IFX at first infusion was 6 mg/kg (5 to 6.9). All received their first three infusions as per protocol. At week 14, seven patients had trough level ≤ 2.2 ug/ml and eight patients had trough level ≥ 2.2ug/ml. 100% of patients who had low IFX trough level less than 2.2 needed adjustment of their IFX infusion to be given every 6 weeks instead of 8 weeks to maintain remission state. Patients with low trough level ≤ 2.2 ug/ml had higher mean PCDI scoring at diagnosis 38.6 while patients who had IFX trough level ≥ 2.2ug/ml had lower mean PCDAI scoring 25.6. All fifteen patients went into remission.

Conclusion: Infusion frequency of IFX seems to be variable among physicians treating patients with Crohn's disease. Additionally, trough levels are not consistently checked. 47% of patients have low trough level that was not detectable at week 14. Higher PCDAI score at diagnosis as well as low albumin levels seem to have a strong correlation with low trough levels suggesting that these factors may play a role in predicting the needed IFX treatment adjustment. This suggests that trough level before the 4th dose is needed to guide maintenance treatment.

Funded By: Trainee Travel Grant

Abstract #:	58
Presenter:	Emma Heydari
Supervisor:	Todd Alexander
Title:	Screening candidate genes for a cause of pediatric idiopathic hypercalciuria
Authors:	Emma Heydari
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Nephrology

Hypercalciuria affects up to 6% of Canadian children causing significant morbidity; “idiopathic hypercalciuria” (IH) is the most common diagnosis. Most filtered calcium is reabsorbed via passive transport from the proximal tubule, the defective segment implicated in the pathogenesis of IH. The objective of our study is to generate a cohort of children with idiopathic hypercalciuria and sequence genes implicated in paracellular calcium reabsorption from the proximal tubule, specifically claudin-2, -12 and -14. Children with IH were recruited. IH was defined as repeated elevated calcium:creatinine (Ca:Cr) ratio with normal serum calcium and parathyroid hormone (PTH) levels. Data collected included demographics, presenting symptoms, family history, initiation of high fluid intake, hydrochlorothiazide therapy, and vitamin D supplementation. DNA from a proportion of patients was collected and claudin-2, -12 and -14 were sequenced to identify polymorphisms.

Funded By: Resident/Clinical Fellow Trainee Research Grant

Abstract #:	59
Presenter:	Waleed G. Masoud
Supervisor:	Elizabeth T. Rosolowsky
Title:	Effectiveness of the Alberta newborn metabolic screening program for congenital adrenal hyperplasia
Authors:	Waleed G. Masoud, Iveta Sosova, Rose Girgis, Fiona Bamforth, Elizabeth T. Rosolowsky
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities

Introduction: Babies born in Alberta are screened for 17 treatable disorders, including congenital adrenal hyperplasia (CAH), which is caused in most cases by 21-hydroxylase deficiency. If undetected, CAH can lead to adrenal crisis and death. Therefore, early detection and treatment are life-saving. The Alberta Newborn Metabolic Screening (NMS) Program began screening for CAH in 2007. In this work, we evaluated the effectiveness of the Alberta NMS Program for detecting CAH from 2008 to 2015.

Methods: Screening for CAH was performed by measuring 17 α-hydroxyprogesterone (17-OHP) levels in 3.2 mm dried blood spots with an immunofluorometric assay (AutoDELFIA Neonatal 17OHP kit, PerkinElmer). The Alberta NMS Program has established borderline and critical 17-OHP cutoff values stratified by birth weight and gestational age. For all borderline results, a repeat specimen was requested, whereas infants with critical results were immediately followed up by a pediatric endocrinologist. Repeat borderline (double borderline) results were treated as critical. Case ascertainment has been achieved through supporting laboratory and clinical data. Data are stored electronically in the provincial NMS Laboratory with the Alberta Health Services.

Results: Between 2008-2015, 419,424 newborns were screened for CAH. A total of 99 infants were deemed to have a positive screen. Of this number, 23 were true positive cases, yielding an incidence of 1:18,236. The positive predictive value (PPV) of our screening was 23.2%. The negative predictive value was 100% as there were no false negative screens. The average birth weight of newborns with critical results was 2596 ± 85 grams, and the average age at the first sample collection was 4.4 ± 0.6 days. Results were available after an average of 5 ± 0.3 days. Our screening method sensitivity was 100% and specificity 99.9%. Predictors of false positive results were prematurity, low birth weight and severe sickness.

Conclusions: These data demonstrate that the Alberta NMS Program is effective in detecting CAH. Our incidence, test characteristics, PPV, and age at the first sample collection match other locally and internationally reported values. The use of different cut-off values for gestational age and newborn weight helped to increase the PPV of our current screening system. Further studies are required to study the correlation between the positive screening results and the electrolyte abnormalities at time of diagnosis.

This study was funded through a Women & Children's Health Research Institute Resident Research Grant.

Abstract #:	60
Presenter:	Marian Thorpe
Supervisor:	Lindsay Ryerson
Title:	Smaller pulmonary artery size is associated with acute post-operative complications in systemic to pulmonary artery shunts
Authors:	Marian Thorpe, Paula Holinski, Mohammed Al Aklabi, Mary Bauman, Lindsay Ryerson
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction: Systemic to pulmonary artery shunts are necessary in the palliation of infants with congenital heart disease and ductal dependent pulmonary blood flow. Acute shunt complications, typically acute thrombosis, increase the mortality in this fragile patient population.

Methods: Retrospective case-control series of all infants who had a systemic-to-pulmonary artery shunt complication at our institution between 2009 and 2015. Infants who had an acute shunt complication, presumed thrombosis, within the first 48 hours post-operatively, were identified prospectively and matched with infants without acute shunt complication. Cohorts were matched according to weight (within 10%), shunt type and size, and use of cardiopulmonary bypass. Nine variables, prospectively identified, including PDA ligation at the time of shunt, source of competitive blood flow post-operatively, proximal pulmonary artery size and time to therapeutic anticoagulation were compared using Chi-square, Fisher's exact, and Mann-Whitney-U tests to determine factors associated with shunt complication.

Results: Seventeen infants with shunt complication were identified in the study period. Two infants were excluded because their shunts clotted in the operating room and were revised; both remained patent post-operatively. Of the cohort with acute shunt complication, 15 had single ventricle physiology and 2 had complex Tetralogy of Fallot; median (IQR) age at time of surgery was 15 days (10-45). There were 10 right modified Blalock-Taussig shunts and five central shunts in each cohort. Shunt size was either 3.5 or 4.0 mm. Shunt thrombosis was confirmed by echocardiography in 11 patients; the remaining 4 patients were treated based on clinical evidence of thrombosis prior to imaging. There was one cardiac arrest secondary to acute shunt complication; the patient died two weeks later. Of the variables examined, pulmonary artery size was the only factor which was statistically significant between the cohort with the acute shunt complication and the cohort without [median (IQR) 3.70 mm (3.25-4.4) vs. 4.50 mm (4.00-5.10); p=0.014].

Conclusions: Systemic to pulmonary artery shunts are a vital procedure in the palliation of infants with ductal dependent pulmonary blood flow. The impact of acute shunt complication on morbidity and mortality remains substantial. Smaller pulmonary artery size, a non-modifiable risk factor, was associated with increased risk of acute shunt complication. Further studies with sufficient power are required to determine additional modifiable risk factors. Although there is great variability in management of these patients, and limited evidence on ways to mitigate the risks, our study contributes new prognostic information which may be considered when placing systemic to pulmonary artery shunts.

Funded By: Resident/Clinical Fellow Trainee Research Grant and Support services

Abstract #: 61
Presenter: Wallace Wee
Supervisor: Carina Majaesic
Title: Dry powder inhaler delivery of tobramycin in in vitro models of tracheostomized children
Authors: Wallace Wee, Scott Tavernini, Andrew Martin, Israel Amirav, Carina Majaesic, Warren Finlay
Affiliations: University of Alberta

Introduction: Pediatric tracheostomies are not uncommon and aerosols allow for targeted lung therapy. However, there is little literature that quantifies aerosol delivery through tracheostomies. Nebulizers, like the PARI LC Plus® (LC Plus), are commonly used in delivering tobramycin but there are drawbacks e.g. time burden. Dry powder inhalers (DPI), such as the TOBI® Podhaler™ (Podhaler), can deliver higher payloads in less time. However, no data exists that assesses DPIs with tracheostomies. Therefore the study's aim was to quantify the amount of aerosolized tobramycin delivered to the lungs of *in vitro* tracheostomized spontaneously breathing pediatric models with the Podhaler and the LC Plus.

Methods: *In vitro* tracheostomized models of a 6- and 12-year old trachea were created. Tobramycin aerosol was delivered to the models using either the LC Plus or Podhaler, and captured on a filter at the trachea's distal end. A colorimetric tobramycin assay was used to quantify the amount of aerosol delivered. Three devices of each type were tested in triplicate to ensure repeatability. Data collected was analyzed using unpaired t-tests to determine statistical significance.

Results: A total of 36 runs were completed and showed that the Podhaler was more efficient compared to the LC Plus. Mass and percentage of nominal dose, mean ± standard-deviation (LC Plus vs. Podhaler with single capsule), was 72.4±11.1mg (24.1±3.7%) vs. 24.2±2.4mg (86.6±8.7%); P-value<0.001.

Conclusions: The study's results show that the Podhaler was significantly more efficient compared to the LC Plus, and three Podhaler capsules delivered approximately the same amount of drug as the Tobramycin inhalation solution. These results suggest that Podhaler's tobramycin delivery is a feasible option in tracheostomized pediatric patients and a clinical study is warranted.

Funded By: Resident/Clinical Fellow Trainee Research Grant and Trainee Travel Grant

Abstract #:	62
Presenter:	Iram Usman
Supervisor:	Dr. Rhonda Rosychuk
Title:	Geographic ariation in time to specialist visit following an emergency department presentation for atrial fibrillation and flutter in Alberta, Canada
Authors:	Iram Usman, Dr. Rhonda Rosychuk
Affiliations:	University of Alberta
Research Activity:	Emergency Department Visits for Attrial Fibrillation and Flutter

Introduction

Atrial fibrillation and flutter (AFF) are the most common arrhythmias in the outpatient setting. For Alberta patients presenting to emergency departments (EDs) for AFF and subsequently discharged, this study aims to identify geographic areas that had longer than expected times to a specialist visit (cardiology or internal medicine) and examines variables associated with longer times.

Methods

All ED presentations during 2010-2011 for AFF that ended in discharge and were made by patients aged ≥ 35 years were extracted from Alberta's Ambulatory Care Classification System. The Alberta Health Care Insurance Plan provided population counts and demographics for the patients presenting (age, sex, year, and geographic unit). The Physician Claims File provided non-ED physician claims data for up to 365 days after a patient's last ED presentation. Statistical analyses include numerical and graphical summaries, the Weibull spatial scan statistic, and multivariable logistic regression.

Results

During 2010-2011, the total number of discharged cases presenting to the ED for AFF are 3,309 (53.6% male) with an average age of 68.04 years. The median time to event for the whole dataset is 280 days and the corresponding 95% confidence interval is 255 to 304 days. The capital health region is detected as a primary cluster of longer than expected time to events, where time to event is defined as 1st contact with the specialist after 365 days of ED presentation for AFF.

Conclusions

This population-based study spans one fiscal year and shows variations in the discharged ED presentation for AFF. The potential cluster identified may represent geographic areas with longer than expected time to specialist after ED presentation for AFF. The cluster is not likely to occur by chance and further investigation and intervention could help reduce the time to see a specialist after ED discharge for AFF.

Funded By: NSERC

Abstract #:	63
Presenter:	Morgan Sosniuk
Supervisor:	Lori West
Title:	Old dogs with new tricks: Optimizing mixed lymphocyte reaction with duraclone flow cytometry phenotyping
Authors:	Morgan Sosniuk, Anne Halpin, Simon Urschel, Patricia Campbell, Lori West
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant

INTRODUCTION: Cardiac transplantation is a lifesaving intervention but despite immunosuppression, the immune system may damage the transplanted organ via responses such as antibody-mediated rejection. In pediatric cardiac surgeries thymectomy is routinely performed. Our overarching goal is to study the impact of thymectomy and its role in the development of *de novo* donor-specific antibody in this population. The Beckman Coulter Duraclone IM flow cytometry phenotyping reagents are widely used within the Canadian National Transplant Research Program (CNTRP) and provide standardized data from centre to centre. Here, we investigate this method incorporated with mixed lymphocyte reaction (MLR) analysis of pediatric post-transplant peripheral blood mononuclear cells (PBMCs).

METHODS: Pre- and post-transplant HLA antibody data were collected from the clinical Histocompatibility laboratory database and analysed. MLR and flow phenotyping were optimized using healthy control adult and pediatric PBMCs and irradiated pooled third-party donor splenocytes. Cell proliferation was quantified using either CellTrace Violet proliferation dye combined with Duraclone IM phenotyping or BrdU incorporation ELISA (n=12). More details on this standardized flow cytometry staining and acquisition system can be found in the October, 2015 WCHRI newsletter.

RESULTS: There were 151 patients, 118 of whom had pre- and post-transplant HLA antibody testing (data not shown) .The BrdU assay demonstrated proliferation but lacks detail regarding individual cell population responses. The proliferation dye was readily detected within the Duraclone IM flow cytometry panel. Unstimulated cells did not proliferate whereas PHA stimulated cells showed abundant proliferation. There were clear phenotypic changes from pre- to post-MLR including the disappearance of monocytes and decreased NK populations. T and B cell populations were clearly labelled and well-defined in the flow analysis. Comparable percentages of cell populations were detected in Duraclone IM tubes using 0.2×10^6 cells or 1.0×10^6 cells thus facilitating the use of small pediatric sample volumes.

CONCLUSIONS: Our preliminary results show that Duraclone IM is a useful system for detecting proliferation responses in MLR in combination with flow phenotyping analysis of cultured cells. These results suggest that Duraclone IM can be used not only as a standardised flow phenotyping method but as a useful tool in the setting of MLR. This assay provides a unique opportunity to exploit the Duraclone IM reagents in the investigation of immune responses. The methods used here to explore HLA alloimmunization are also readily applicable to the study of immune responses in other transplant patient populations.

Funded By: Motyl Endowment for Cardiac Sciences

Abstract #:	64
Presenter:	Kim Ho
Supervisor:	Gary Lopaschuk
Title:	Adaptive or maladaptive? Increased ketone body oxidation in the failing heart is assessed for cardiac efficiency
Authors:	Kim Ho, Liyan Zhang, Cory Wagg, John Ussher, Gary D. Lopaschuk
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction

The failing heart is an energy-starved omnivore that has increased fatty acid oxidation and increased glycolysis uncoupled from glucose oxidation. Amidst these metabolic impairments, alterations in ketone body oxidation during heart failure are still unclear. Two recently published studies performing proteomic and metabolomics analysis have demonstrated increased ketone body oxidation in the failing heart. Whether or not this metabolic alteration is adaptive or maladaptive for cardiac efficiency and function is still unclear. Therefore, we decided to assess ketone body metabolism in a model of heart failure to determine whether these metabolic alterations affect cardiac efficiency. We hypothesize that if ketone body oxidation is elevated in the failing heart, a decrease in cardiac efficiency would be observed and thus, this metabolic alteration is maladaptive.

Methods

C57BL/6J male mice were divided and used in two groups: heart failure and control group. The heart failure group underwent a transverse aortic constriction (TAC) to induce pressure overload hypertrophy over a 4 wk period, while controls underwent a sham surgery (Sham). Oxidative rates of fatty acids, glucose and ketones, as well as glycolysis, were measured in isolated working hearts, at two concentrations of β-hydroxybutyrate.

Results

We observed a decrease in cardiac work in the TAC group compared to the Sham group. Glucose oxidation rates did not change between the TAC and Sham groups. However, glycolysis and palmitate oxidation were both significantly upregulated in TAC alongside a statistically significant increase in β-hydroxybutyrate oxidation. When measuring hydrogen ion production, there were no statistically significant differences between TAC or Sham. Acetyl CoA production from glucose oxidation decreased in TAC and a corresponding decrease in ATP production from glucose oxidation was also observed in the TAC group compared to the Sham group. In contrast, we observed fatty acid oxidation yielding more acetyl CoA and ATP in TAC than Sham. Similarly, ketone body oxidation also showed increased Acetyl-CoA and ATP production in the TAC group compared to Sham. Lastly, when cardiac work was normalized to Acetyl CoA, we observed a decrease in cardiac work per acetyl CoA in the TAC group compared to Sham, indicating a decrease in cardiac efficiency in the TAC group.

Conclusion

These findings directly indicate a dysregulation in metabolism in the failing heart with increased reliance on ketone body oxidation. Our data also suggests that ketones decrease cardiac efficiency in the failing heart.

Funded By: Heart & Stroke

Abstract #: 65
Presenter: Laura Reyes
Supervisor: Sandra Davidge
Title: Effects of prenatal hypoxia on fetal cardiomyocyte proliferation
Authors: Laura Reyes, Amin Shah , Anita Quon, Sandra Davidge
Affiliations: University of Alberta
Research Activity: Maternal Research : Fetal Origins of Adult Disease

Introduction

Many pregnancy complications lead to prenatal hypoxia resulting in intrauterine growth restriction (IUGR); which is known to decrease fetal cardiomyocyte proliferation. TNF-related weak inducer of apoptosis (TWEAK) induces cardiomyocyte proliferation through activation of the fibroblast growth factor-inducible molecule 14 (Fn-14) receptor. The TWEAK/Fn-14 pathway has not being studied in offspring born growth restricted after a hypoxic insult, thus, we hypothesized that IUGR offspring will exhibit reduced cardiomyocyte proliferation due to reduced Fn-14 expression. Moreover, compared to controls, cardiomyocytes from IUGR offspring exposed to recombinant TWEAK (r-TWEAK) will proliferate less.

Methods

Pregnant Sprague Dawley rats were exposed to control (21% oxygen) or hypoxic (11% oxygen, IUGR) conditions from gestational day 15 to 21. Ventricular cardiomyocytes were isolated from female and male, control and IUGR offspring at postnatal day 1 (PND 1). Proliferation was assessed by immunofluorescence and protein expression of Fn-14 was determined by Western blot. Cardiomyocyte proliferation was also assessed in the presence or absence of r-TWEAK (72-hours, 100 ng/mL) and the Fn-14 receptor antibody (72-hours, 100µg/mL).

Results

Being born growth restricted was not associated with differences in the Fn-14 protein expression, or cardiomyocyte proliferation at PND 1 in both male and female offspring. After being in culture for 72-hours, cardiomyocytes from IUGR male offspring had a decreased proliferation compared to controls. The addition of r-TWEAK increased proliferation in both groups. Moreover, Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (164.4% vs. 47.1%; p=0.04), and IUGR (208.5% vs. 70.03%; p=0.02) male offspring. Interestingly, in female offspring, being born growth restricted was not associated with a decreased proliferation. The addition of r-TWEAK increased proliferation in both control and IUGR offspring. Fn-14 receptor antibody decreased cardiomyocyte proliferation in control (175.9% vs. 76.8%; p=0.007), and IUGR (224.4 % vs. 39.9%; p=0.02) female offspring.

Conclusions

IUGR was not associated with a decreased in the cardiac protein expression of Fn-14, or a decrease in cardiomyocyte proliferation in response to TWEAK. We found, however, that male IUGR offspring had a decreased cardiomyocyte proliferation compared to controls, which was absent in the female offspring. Thus, the consideration of sexual dimorphism is essential.

Funded By: Start-up or Retention Funding

Abstract #:	66
Presenter:	Basma Aljabri
Supervisor:	Helly Goez
Title:	Expanding the Phenotypic spectrum of disorders related to ATP1A3 mutations
Authors:	Basma Aljabri, Allison Mathews, John Andersen, Alicia Chan, Oksana Suchowersky, Maja Tarailo-Graovac, Colin Ross, Wyeth Wasserman, Clara Karnebeek, Helly Goez
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development

ATP1A3 (MIM#182350) encodes the alpha 3 subunit of Na+/K+ transporting ATPase, imperative for maintaining the electrochemical gradients of these ions across the plasma membrane. Mutations in ATP1A3 cause neurological disorders including: Rapid-onset Dystonia-Parkinsonism (RDP) also known as (DYT12), Alternating Hemiplegia of Childhood (AHC), and Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy and Sensorineural hearing loss (CAPOS) syndrome. Reports have emphasized distinctions between RDP and AHC, and more recent evidence suggests these conditions may represent a clinical spectrum related to mutation in ATP1A3 gene. This case report adds to the spectrum of clinical presentation attributed to the mutation in the ATP1A3 gene

Case Details:

A four-year old girl presented in our clinic with a history of early onset global developmental delay. At the age of 2 years she developed chorea and limb dystonia post viral infection. In addition, she had axial and appendicular hypotonia and absent deep tendon reflexes (DTR).

Methodology:

Metabolic and genetic work-up, skin biopsy and muscle biopsies, Nerve Conduction Velocity (NCV), MRI brain imaging, were performed and the patient was enrolled with informed consent into the TIDEX discovery study for trio whole Exome sequencing with analysis via a customized bio-informatics pipeline, followed by targeted Sanger sequencing of the variant of interest.

Results:

Blood tests and brain MRI were normal. The NCV was compatible with absent DTR. Her skin and muscle biopsies were normal. Mitochondrial DNA sequencing did not yield compelling variants.

Trio WES analysis identified a rare, pathogenic missense variant in ATP1A3 (c.2267G>A, NM_152296.4; p.Arg756His, NP_689509.1). Sanger analysis confirmed de novo nature of the variant (absent in parents and unaffected sister). This mutation was previously reported as causal of RDP in unrelated patients. This rare movement disorder characterized by abrupt onset of parkinsonism and dystonia usually triggered by physical and psychological triggers with an autosomal dominant mode of inheritance and age of onset ranges from 8-55 years. The clinical presentation of this proband was atypical for RDP, with an earlier age of onset at 4 years as well as additional features of hypotonia, areflexia, limb dystonia, choreoathetosis, motor and speech delay

Conclusion:

This case expands the current available knowledge on the phenotypic spectrum of de novo ATP1A3 mutations.

Funded By: BC Children's Hospital Foundation, NeuroDevNet, CIHR

Abstract #: 67
Presenter: Stephen Hunter
Supervisor: Valerie Carson
Title: A quasi-experimental examination of how school-based physical activity changes impact youth moderate-to vigorous-intensity physical activity
Authors: Stephen Hunter, Scott Leatherdale, Kate Storey, Valerie Carson
Affiliations: University of Alberta
Research Activity: Youth physical activity

Background

The Canadian Physical Activity Guidelines recommend 60 minutes of moderate- to vigorous- intensity physical activity (MVPA) per day for optimal health benefits. However, it was recently reported that only 5% of Canadian children (aged 12 to 17) are meeting these guidelines and are therefore at an increased risk for chronic disease and premature death. While school settings present a unique opportunity to increase MVPA among a large proportion of children, school-based physical activity interventions for high school students remain largely ineffective. Therefore, the purpose of this study was to examine how naturally-occurring changes to school physical activity policy, recreational programming, public health resources, and the physical environment, impact high school students' MVPA over a 1-year period.

Methods

Quasi-experimental longitudinal data from 18,777 grade 9–12 students (mean age = 15.1 ± 0.02 years), and 86 principals from 86 schools, participating in year 2 (2013–2014) and year 3 (2014–2015) of the COMPASS study (Ontario and Alberta, Canada) were used. Total MVPA over the previous week was self-reported at both time points using the COMPASS Student Questionnaire and average daily MVPA was calculated. Changes to physical activity policies, recreational programming, public health resources, and the physical environment were self-reported by school principals. Changes to the number and condition of physical activity facilities were objectively measured during school audits using the COMPASS School Environment Application. Multilevel modeling was used to examine change in student MVPA between schools that made changes and schools that did not. Models were adjusted for several student- and school- level confounders.

Results

Over the 1-year period, 61 of 86 schools made physical activity related changes. Of these, 9 significantly changed student MVPA. However, only 4 of 9 schools' changes increased student MVPA, including opening the fitness centre at lunch (β = 17.2, 95 % CI: 2.6–31.7), starting an outdoor club (β = 17.8, 95 % CI:7.4–28.1), adding a bike rack (β–14.9, 95 % CI:0.7–29.1), and adding weightlifting and run/walk clubs, archery, figure skating, increased access to the sports field, and improved condition of the outdoor basketball court (β = 15.5, 95 % CI: 5.2–25.7).

Conclusions

Changes such as adding or increasing access to facilities and adding multiple recreational programs seemed to be effective for increasing student MVPA over the 1-year period. However, given the specificity of results, a one-size fits all approach may not be effective for increasing MVPA. Instead, school principals may need to consider the resources within and surrounding their school when developing programs to increase student MVPA.

Funded By: Graduate Studentship

Abstract #: 68
Presenter: Steffen Adria
Supervisor: Edmond Lou
Title: Predicting bending flexibility for female brace patients with adolescent idiopathic scoliosis
Authors: Steffen Adria, Edmond Lou
Affiliations: University of Alberta
Research Activity: Adolescent idiopathic scoliosis

Introduction: Adolescent idiopathic scoliosis (AIS) is a 3D spinal deformity which occurs most in adolescent females. Prediction of spinal flexibility can help clinicians optimize the treatment plan, which often incorporates bracing. This study investigates if spinal flexibility of brace candidates can be predicted from patients' demographics and radiographic data.

Methods: Eleven female brace candidates (age: 13.6 ± 1.7 years old) diagnosed with AIS (major curve Cobb angle: 36.6 ± 8.5°) were recruited. There were eight thoracic, nine thoracolumbar and two lumbar curves identified from the 11 subjects. Five factors were investigated to correlate their association with curve flexibility: Cobb angle, Risser sign, apical axial vertebral rotation (AVR) (measured on posteroanterior radiograph using Stokes' method), categorized body mass index (CBMI) and the number of vertebrae of a curve (length), all measured or recorded at the brace prescription clinic.

The flexibility was defined as: Flexibility = ((Cobb Angle at Time of Brace Prescription - Side Bending Angle) / (Cobb Angle at Time of Brace Prescription) x100%

A value of 0% indicates a rigid spine with no correction while bending and a value of >=100% indicates a highly flexible spine. Maximum side bending curvature angle was measured on ultrasound image at the brace casting clinic while the patient maintains the maximal prone side bending position. Analysis was performed on four subgroups: thoracic, thoracolumbar, thoracolumbar-lumbar and aggregate curves. A linear regression method was used to determine the correlation of the flexibilities and the five factors. Maximum residuals (D_{max}) between the predicted line and the data points were also recorded.

Results: Two out of four groups showed statistically significant correlation with Cobb as the selected factor. Thoracic flexibility had strong association with the length value ($p = 0.004$, $D_{max} = 16\%$, Flexibility = 17.74 * Length – 18.44). Thoracolumbar had no statistically significant correlations. The thoracolumbar-lumbar group associated with either Cobb angle ($p = 0.011$, $D_{max} = 18\%$, Flexibility = 1.36 * Cobb + 32.44) or AVR ($p = 0.04$, $D_{max} = 12\%$, Flexibility = -10.80 * AVR + 63.54) and the aggregate curves group were associated with Cobb angle ($p = 0.002$, $D_{max} = 26\%$, Flexibility = 1.13 * Cobb – 32.44).

Conclusion: This pilot study reported that the most common factor for predicting curve flexibility was the Cobb angle. Demographic information did not have any statistically significant forecasting effect.

Funded By: NSERC, Edmonton Orthopaedic Research Society

Abstract #: 69
Presenter: Maliheh Ghaneei
Supervisor: Samer Adeeb
Title: Effects of Schroth exercises added to standard care in adolescents with idiopathic scoliosis on marker-less surface topography asymmetry measurements
Authors: Maliheh Ghaneei, Eric Parent , Samer Adeeb, Sanja Schreiber, Marc Moreau, Douglas Hedden, Douglas Hill, Sarah Southon
Affiliations: University of Alberta
Research Activity: Assessment and monitoring of the condition of scoliosis using surface topography

Introduction
Schroth exercises have shown promise for slowing curve progression and improving posture in AIS. However, few studies have reported quantitative measurements of the effect of scoliosis-specific exercises on the external deformity. Reviews call for randomized and prospective controlled studies on exercises for scoliosis. This study aimed to determine the effect of Schroth exercises added to standard of care (EXP group) to standard of care alone (CTRL group) on asymmetry measurements from marker-less surface topography (ST) analysis.

Methods
Fifty participants with AIS, aged 10-18 years, with curves of 10°-45°, were recruited from a scoliosis clinic and randomized to the EXP or CTRL group. A 6-month long Schroth program was offered for each curve type with weekly supervised visits and daily home program. The compliance with the program and the exercise performance quality were assessed weekly. Full-torso ST scans, acquired at baseline, 3 and 6 months, were analyzed blind to group allocation to calculate the best plane of symmetry by minimizing the distances between the torso and its reflection about the plane of symmetry, which were displayed as deviation color maps. Maximum deviation (MaxDev) and root mean square (RMS) of the deviations corresponding to the largest curve were extracted from the asymmetry patch. Linear mixed models were used to test differences between groups over time while adjusting for self-efficacy and curve type covariates.

Results
At baseline, groups were similar for age, gender, height, use of a brace, curve type (≤1 subject difference per type) and Cobb angle [EXP: 29^{O} (95%CI 25-32) CTRL 27.9^{o} (24-32)]. Six patients dropped out (EXP=4, CTRL =2). For compliance, 76% of visits and 73% of the home exercises were completed. Schroth exercises improved maxDev for the asymmetry patch compared to the deterioration in CTRL significant only at 3 months (p=0.038). Maxdev worsened @3m in the CTRL group (adjmean±SE: 15.1 ±1.4mm, to 16.6 ±1.4@3m, to 13.7±1.4@6m), but improved with exercises (19.1± 1.4mm, 17.7±1.4@3m, 18.2±1.4@6m). Schroth exercises also improved the RMS over the asymmetry patch compared to the deterioration in CTRL significant only at 3 months (p=0.031). RMS asymmetry worsened @3m during follow-up in the CTRL (AdjMean±SE: 7.5 ±0.6 mm, to 8.3 ±0.6@3m, to 7.5±0.6@6m), but was improved with exercises (9.8±0.6mm, 9.1±0.6@3m, 9.5±0.6@6m).

Conclusions
Six months of Schroth exercises added to standard care produced significant short-term improvements in objective 3D marker-less postural measurements.

Funded By: Trainee Travel Grant

Abstract #:	70
Presenter:	Noureen Ali
Supervisor:	Sujata Persad
Title:	Role of β-catenin/Active β-catenin in Osteosarcoma progression
Authors:	Noureen Ali, Geetha Venkateswaran, Elizabeth Garcia
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Oncology

Introduction: Osteosarcoma (OS) is the most common primary bone malignancy with high incidence in children and adolescents, with an overall low survival rate. Wnt signaling pathway is one of the pathways that is deregulated in most cancers. Although a number of studies have shown deregulation of this pathway to be implicated in OS, role of β-catenin (key regulatory component of Wnt signaling) in this cancer is not clear. While some studies support the involvement of β-catenin in OS, others show the contrary. All these studies investigate the role of β-catenin rather than Active Beta Catenin (ABC) which is a fraction of β-catenin that is transcriptionally active. ABC transcribes genes involved in cell proliferation, invasiveness and hence promotes cancer. Therefore in our study we are interested in investigating the role of β-cat/ABC in OS progression.

Methods: We used two pairs of cell lines that represent OS progression: Saos2, Saos2-LM7 (metastatic cell line derived from SaOS2), HOS and HOS-143B (metastatic cell line derived from HOS). OS specific markers like MMP2 and MMP9 were used as a measure of aggressiveness in cell lines. Western blotting, Immuno-fluorescence and high content analysis were carried out for determining the cellular localization of β-catenin and ABC. qRT-PCR was also carried out to measure gene expression levels of downstream targets of β-cat/ABC including MMP2, MMP9, Cyclin D1 and VEGFA.

Results: A significant increase in the cellular level of ABC was observed in metastatic cell lines compared to the respective parent cell lines. In addition to the increased cellular levels of ABC, an increased nuclear localization of ABC was observed in metastatic cell lines. However, no significant changes were observed in the cellular localization of β-catenin with OS progression. With the exception of MMP9 for HOS and HOS-143B, a significantly high expression of all genes was measured in metastatic cell lines compared to parent cell lines.

Conclusion: Our results show a correlation between ABC levels and OS progression, demonstrating its potential to serve as a prognostic marker for OS.

Funded By: Graduate Studentship

Abstract #:	71
Presenter:	Larissa Brosinsky
Supervisor:	Holly Stack-Cutler
Title:	Underserved students engaged in intensive afterschool music instruction: Examining skill development and opportunities for growth
Authors:	Larissa Brosinsky, Holly Stack-Cutler, Alyssa Paterson, Laurie Schnirer
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health

Introduction: The Youth Orchestra of Northern Alberta Sistema (YONA) program offers free, intensive afterschool music instruction to 53 students (2015–2016) in grades 2–5 from two schools. Operating in a low socioeconomic, high-crime Edmonton neighbourhood, YONA encompasses four main values: inclusivity, community, peer support, and intensive instruction. As YONA continues to grow, it is important to examine its student, family, and community outcomes to ensure it is having desired effects similar to those of the original Venezuelan El Sistema program. The Community-University Partnership for the Study of Children, Youth, and Families partnered with the Edmonton Symphony Orchestra, the Edmonton Community Foundation, and University of Alberta researchers to pilot tools and processes to inform the long-term monitoring of YONA student, family, and community outcomes.

Method: We conducted focus groups and semi-structured interviews with YONA stakeholders (*n*=36), including focus groups with parents (*n*=10), classroom teachers, and YONA volunteers (*n*=8), and interviews with YONA staff members (*n*=6). In addition to questions asked as part of a larger community-based study, we asked participants about skills that students developed in the program and opportunities YONA provided to students: *What skills are the students learning in YONA?* and *What opportunities does involvement in YONA give the students?* All qualitative data was categorized into themes using thematic analysis.

Results: Participants reported that participating YONA students developed social skills (reported 47 times), cognitive and academic skills (25 times), self-development skills (24 times), emotional awareness (17 times), and music and motor skills (16 times). Participants stated that YONA offers students the opportunity to be in a positive environment with a supportive program and exposure to healthy role models (reported 28 times), to receive musical and cultural exposure (15 times), and to grow in terms of their skills, sense of personal pride, and future aspirations (12 times).

Conclusions: The present community-based evaluation found that YONA has been successful in developing diverse skills in its students and providing students with opportunities that encourage their development as members of society. Future research could include quantitatively examining YONA's impact on students' academic skills to further explore the benefits of involving underserved children in an intensive afterschool music program. This collaboration has led to new partnerships, increased community-based training for students, and informed methods for community partners and researchers to use when tracking YONA student, family, and community outcomes long-term.

Funded By: Alberta Centre for Child, Family, and Community Research

Abstract #: 72
Presenter: Stephanie Penner
Supervisor: Debra Andrews
Title: Developing skills for developmental disabilities: Teaching module improves medical students' confidence
Authors: Andy Le, Lexa Peters, Stephanie Penner
Affiliations: University of Alberta
Research Activity: Childhood Development: Developmental Disabilities

Introduction:

Medical students feel they have inadequate training on caring for patients with developmental disabilities (PWDD) and behavioural co-morbidities. There is a lack of literature about effective teaching methods on this topic (Troller et al. 2016; Salvador-Carulla et al., 2015). Inadequate education regarding care of PWDD can lead to frustration and negative attitudes toward this complex patient population. Consequently, PWDD may not receive timely and empathetic care (Sahin & Akyol, 2010). To address this educational gap we evaluated a pre-clinical 12-hour elective called "Developing Skills with Developmental Disabilities" (DSDD). Its primary learning objective was to improve student's knowledge and attitudes toward PWDD, with the goal of improving future interactions with this complex pediatric patient population.

Methods:

The DSDD module was an optional elective offered to preclinical medical students for school credit. Students were given 6 hours of didactic teachings from developmental pediatricians and pediatric physiatrists on normal and abnormal childhood development, assessing developmental ages, assistive technologies and devices, and breaking bad news. Students also participated in 6 hours of clinical time at the Glenrose Rehabilitation Hospital, where they interacted with preschool-aged PWDD and their families. An interdisciplinary team (including occupational therapists, psychologists, speech pathologists, and physical therapists) guided students during clinical hours.

Participating students were given pre- and post-module surveys administered on a 5-point Likert scale. Survey questions pertained to students' self-perceived comfort and knowledge regarding PWDD. Scores pre- and post-elective were compared using t-test analysis.

Results:

From 2014-2016 (over 2 academic years), 44 students signed up for the module and 41 completed it (93%). Of the participating students, 19 (46%) had previous work experience and 26 (63%) had personal experience with PWDD. Statistically significant ($p<0.05$) increases were present across all 10 self-reported scores.

Conclusions:

The DSDD module may be a useful tool for medical schools to adopt and adapt into curricula. The module showed significant ($p<0.05$) increases in students' self-reported confidence and knowledge in working with patients with developmental disabilities. Ultimately, if interventions such as DSDD help increase future healthcare practitioners' confidence in working with PWDD, then these patients will hopefully receive better care.

Funded By: MSA-Faculty Joint Fund

Abstract #: 73
Presenter: Jenna Crawford
Supervisor: Sujata Persad
Title: Optimization of the growth period of in vitro neuron isolation
Authors: Jenna Crawford, Christine Dunlop
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Perinatel Stroke

Introduction

Perinatal ischemia can affect motor as well as cognitive development, and plays a role in disorders such as cerebral palsy. Ischemia affects the developing brain by blocking delivery of oxygen and glucose. Oxygen-glucose deprivation (OGD) can be lethal for brain cells, and the post-ischemic reperfusion of oxygen and glucose back into the environment can have lethal effects of its own, increasing the presence of reactive oxygen species (ROS) and potentially increases regulated cell death by apoptosis. Current research indicates that neutraceuticals may provide some protection against the damage of OGD, however it is imperative to understand how brain cells are impacted individually. To do this, neurons were isolated and grown in culture prior to undergoing OGD and survival rates were evaluated.

By convention, related studies grow neurons for seven days in culture prior to OGD treatment. There are no studies indicating a clear reasoning for this, and it was hypothesized that a shorter growth period may be equally suitable and increase the efficiency of these experimental studies.

Methods

Neuronal tissue is isolated and cultured from two-day old Long Evans rat pups, and grown in vitro at 37C and 5% CO2 for either 4 or 7 days. Cells are deprived of glucose and exposed to hypoxia (<1.0% oxygen) for 1, 2, or 4 hours, and then either counted and collected immediately, or reoxygenated and a glucose rich media reintroduced for 24 hours.

Trypan Blue cell death assay was used to determine survival rates, and Western Blot analysis conducted to assess neuronal purity of the samples.

Results

Trypan Blue counts indicated that Day 4 had lower natural death rates compared to Day 7, and the cellular response was comparable for exposure to OGD between the two time points. Western Blot analysis of Day 4 cultures showed astrocyte contamination, whereas no astrocytes were found in the analysis of Day 7 cultures.

Conclusion

Despite the superior survival rate of the neurons on Day 4, this time point is inappropriate for neuron-only experiments due to astrocyte contamination. This does not support our hypothesis but it does provide insight into astrocyte survival under non-ideal conditions, and has implications for experiments that do not require cell-specific isolated cultures. Our results support and provide an explanation for the conventional use of Day 7 as the time point for experimentation on neuronal cultures.

Funded By: Graduate Studentship

Abstract #: 74
Presenter: Rhianna Charchuk
Supervisor: Michael Hawkes
Title: The experience of privately sponsored Syrian refugee families in Edmonton
Authors: Rhianna Charchuk, Stan Houston, Suzanne Gross, Michael Hawkes
Affiliations: University of Alberta
Research Activity: Refugee health

Introduction: In 2016, the Canadian government successfully welcomed 25 000 Syrian refugees, mainly women, children and families. In Canada, refugees are supported either through the Government Assisted Refugee (GAR) or private sponsorship (PSR) programs. When refugees arrive, settlement agencies provide essential services, such as assisting in access to healthcare. Many Syrian refugees have lived in refugee camps for several years where they faced poor sanitation, poor nutrition, and limited access to healthcare. Women and children, in particular, are at risk of health disparities; such as poor dental health, malnutrition and exposure to trauma and violence. Additionally, there are differences in the operation of the private versus government programs which may create disparities in how refugees settle and access healthcare services. With the influx of numerous Syrian refugees in Edmonton, settlement agencies and healthcare services are overwhelmed and it is essential that vulnerable women and children are receiving necessary care. This research aims to explore the experience of newly arrived, privately sponsored Syrian refugee families in accessing healthcare in Edmonton.

Method: I will use a qualitative description method with a community-based research (CBR) framework, to explore the access to healthcare services during the initial settlement of Syrian refugee families. The research question and protocol has been developed with the Edmonton Mennonite Centre for Newcomers (EMCN), which is my primary research partner. Two EMCN staff perform home visits with privately sponsored Syrian refugee families eleven months after their arrival in Canada. During these visits EMCN assesses their needs and allows me the opportunity to join and ask questions specifically about their experience accessing the Canadian healthcare system.

Results: Interviews are currently ongoing. Preliminary findings indicate there are specific barriers that Syrian refugees are facing in accessing healthcare, such as long wait times and limited access to services to treat specific dental health concerns.

Conclusions: My research project will allow researchers, clinicians and service providers to understand the experience of privately sponsored, Syrian refugee women and children in accessing healthcare services. Through my research, I will 1) identify programs, services or support which refugee families have found most useful for accessing healthcare services and understanding the Canadian healthcare system; and 2) identify specific barriers and challenges in accessing healthcare during the initial settlement of refugees. This research will inform settlement agencies and policy makers in order to improve access to healthcare for women and children refugees in Edmonton.

Funded By: Graduate Studentship

Abstract #:	75
Presenter:	Nooshin Jafari
Supervisor:	Kim Adams
Title:	An assistive robotic system to enhance play activities for children with disabilities - preliminary study
Authors:	Nooshin Jafari, Dr. Kim Adams, Dr. Mahdi Tavakoli, Dr. Sandra Wiebe
Affiliations:	University of Alberta
Research Activity:	Assistive technologies for children with disabilities

Title: An assistive robotic system to enhance play activities for children with disabilities- Preliminary study

Introduction: Children with disabilities have fewer opportunities for play, due to their physical and cognitive impairments, compared to their typically developing peers. Limited opportunities for play can, in turn, delay their perceptual, social, cognitive and physical development. Switch-controlled assistive robots (e.g. Lego robots) have been used for remotely manipulating objects, controlled by head or hand switches, to facilitate play performance in children with disabilities, mostly in the area of education and play. However, one limitation of these robots is that the robot usually does the task remotely and oftentimes, a human helper is needed to mediate the interaction of the child with the robot or the environment. In either case, the child may miss the opportunity to directly interact with the environment and also may feel less control over the play activity. Provision of *virtual assistance* (i.e. assistance that is invisible) can give children the sense of control over the play activity while providing them assistance that helps them to be more successful in the task.

Method: This paper presents a novel application of an assistive robotic system with virtual assistance to facilitate play for children in a set of coloring tasks. The system was initially tested with fifteen able-bodied adults to validate the effectiveness of virtual assistance as well as the safety and stability of the robotic system. Participants were given a set of template drawings to color using the robotic system and were asked to use their non-dominant hands in order to increase the challenge and sensitivity to determine the effectiveness of the virtual assistance. One-way ANOVA measure was performed to determine the significance of the assistance condition compared to No-assistance condition.

Result: The assistance condition significantly outperformed the No-assistance condition in terms of: (a) a statistically significant reduction in the ratio of the colored area outside to the colored area inside the template drawings (with large effect sizes, Cohen's d>.8), (b) and a substantial reduction in the travelled distance outside the borders (with large effect sizes).

Conclusion: Theresults validated the effectiveness of the system in improving the user's performance. The system will next be tested with children with disabilities. Future development will include adding artificial intelligence to adaptively tune the level of assistance according to the user's level of performance (i.e. providing more assistance if the user is committing more errors).

Funded By: CIHR, and NSERC

Abstract #:	76
Presenter:	Aleksander Touznik
Supervisor:	Toshifumi Yokota
Title:	In vitro efficacy of locked nucleic acid/DNA mixmer antisense oligonucleotides for treating spinal muscular atrophy
Authors:	Aleksander Touznik, Yusuke Echigoya, Rika Maruyama, Toshifumi Yokota
Affiliations:	University of Alberta

Introduction - Spinal muscular atrophy (SMA) is a recessive autosomal neuromuscular disorder characterized by degradation of motor neurons within the anterior horn of the spinal cord and brain stem, resulting in progressive trunk and limb muscle paralysis. SMA is currently the most common cause of infant mortality, estimated to affect between 1 in 6000 - 11000 live births. SMA is caused by a deficiency in survival of motor neuron (SMN) protein due to a homozygous mutation in the S*MN1* gene. A duplicate gene known as *SMN2* is able to produce approximately 10% of the functional SMN protein. This deficiency is caused by a silencer site on exon 7, which promotes its exclusion in the post-transcriptional mRNA. This project aims to utilize the high-affinity property of the Locked nucleic acid (LNA) base chemistry mixed with DNA bases to inactivate a silencer site to upregulate SMN production.

Methods – Current literature indicates that the ISS-N1 silencer site on intron 7 is the most promising site to target with ASOs. The use of antisense oligonucleotides (ASOs) to knock-up production of functional full-length protein made from the *SMN2* gene is a leading therapeutic approach to treat SMA. Current clinical trials are, however, facing challenges such as delivery and toxicity. We designed several LNA/DNA mixmers varying in length and LNA position. This strategy is promising, as the high affinity of LNA to complementary RNA allows it to work at extremely low concentrations. RT-PCR and Western blotting were used to examine exon 7 inclusion efficiency in mature mRNA and SMN protein production *in vitro*.

Results – RT-PCR results revealed that several LNA/DNA mixmers we designed induced efficient exon 7 inclusion at 5 nM concentration in severe SMA patient fibroblasts. Western blot analysis supported these results, as treatments resulting in the greatest inclusion of exon 7 also showed the highest increase in proper SMN protein production.

Conclusion - Our newly designed LNA/DNA mixmers were demonstrated to have more efficient enhancement of exon 7 inclusion than the ASO currently used in clinical trials in fibroblasts obtained from SMA patients. Cells treated with one of our LNA/DNA mixmers showed high levels of rescued SMN protein *in vitro*. Our new antisense LNA/DNA mixmers identified in this study will potentially offer improvement for the treatment of SMA in the near future.

Funded By: Graduate Studentship

Abstract #: 77
Presenter: Hunter McColl
Supervisor: David Eisenstat
Title: Regulation of the BMI1 and RET proto-oncogenes by the DLX2 transcription factor in the developing gastro-intestinal tract
Authors: Hunter McColl, Marino Novel, Ryan Fung, David Eisenstat
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Congenital Abnormalities

Introduction:

Within the intestinal crypts of Leiberkuhn a stable, non-dividing stem cell group is marked by the oncogene *BMI1*. Unpublished data from the Eisenstat lab demonstrates co-expression of *BMI1* and homeobox transcription factor *DLX2* in intestinal crypts and a regulatory role of DLX2 in the expression of the *Ret proto-onco* gene. *Ret* is responsible for ENS development. Over-expression of Ret induces Multiple Endocrine Neoplasia cancers. Loss-of-function causes Hirschsprung's Disease; partial or complete loss of intestinal innervation. We investigate the regulatory effect of DLX2 on *Bmi1* and *Ret*, with the hypothesis that DLX2 suppresses *Bmi1* while promoting *Ret* expression and is directly binding the targets' promoters during intestinal and ENS development.

Methods:

Chromatin Immunoprecipitation (ChIP) assays determine *in vivo* interactions between DLX2 and targetpromoter regions. Electrophoretic mobility shift assays (EMSAs) and Site Directed Mutagenesis of DLX2 binding sites determine the direct binding of the *Bmi1*/ *Ret* promoters by DLX2 *in vitro*. Reporter gene assays demonstrate the effect DLX2 has on *Bmi1/ Ret* expression *in vitro*. Quantitative PCR is used to determine the effect of knocking out DLX1/2 has on the *in vivo* expression

Results:

ChIP demonstrates DLX2 interaction with *Bmi1* and *Ret's* promoters *in vivo*. EMSA results demonstrate specific binding of DLX2 to the promoters *in vitro*. Luciferase assays demonstrate the *in vitro* regulatory effects of DLX2 on these genes and are supported by the *in vivo* qPCR assays.

Conclusion:

ChIP results confirm occupancy of the *Bmi1* and *Ret* promoters by DLX2 while EMSAs demonstrate direct binding of DLX2 to the promoters *in vitro*. Ongoing immunohistochemistry and qRT-PCR using Dlx1/Dlx2 double knockout (DKO) mouse tissues will determine the *in vivo* biological relevance of DLX2 on expression

Funded By: Graduate Studentship

Abstract #: 78
Presenter: SaiKrishna Annamraju
Supervisor: Ordan Lehmann
Title: FoxF1 influences hedgehog signaling by regulating the primary cilia length
Authors: SaiKrishna Annamraju, Serhiy Havrylov, Ordan Lehmann
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Lung Development

Purpose

Alveolar Capillary Dysplasia [ACD] is a fatal pediatric disorder, characterized by defective vasculature and abnormal lung morphogenesis. It is caused by haploinsufficiency of a Forkhead transcription factor called *FOXF1*, which is known to be regulated via endodermal Sonic Hedgehog [Shh] a critical crosstalk during the lung development. Moreover, vertebrate Hedgehog [Hh] and several other signaling pathways are coordinated by primary cilium. Interestingly, our lab identified that multiple members of the Forkhead family influence cilia structure, and so we hypothesized that mutations in FoxF1 perturb structure of the primary cilia and impair multiple essential ciliary-mediated signaling pathways implied in the etiology of ACD. In this context, we have been examining the role of *FoxF1* in regulating the structure and function of the primary cilia.

Methods

Stable shRNA based FoxF1 knock-down [Kd] NIH3T3 cell lines [murine fibroblast cell lines] were generated using a lentiviral delivery system and the efficiency was confirmed by western blotting. Primary cilia were immunofluorescently stained and visualized using confocal microscopy, to quantify cilial length. To determine the impact of altered *FOXF1* expression on function of the primary cilia, cells were stimulated with Smoothened agonist [SAG] and assayed by measuring Gli1 expression levels.

Results

NIH3T3 cells expressing shRNAs targeting *FoxF1* showed reduced levels of FoxF1 protein [70% Kd] in comparison to control cells and showed significantly stunted primary cilia. In addition, cells with decreased expression of FoxF1 also exhibited attenuation of Hh signaling by 2- fold.

Conclusion

Our results suggest that *FoxF1* may function as a regulator of cilia biogenesis and impact Hh signaling pathway regulated through primary cilia. Our future research will involve investigating alterations in other signaling pathways associated with cilia to gain insights into the mechanistic basis of ACD.

Funded By: Innovation Grant

Abstract #: 79
Presenter: Kelly Fagan
Supervisor: Rachel Wevrick
Title: MAGEL2, a protein implicated in Prader Willi Syndrome, modifies the activity of the RNF41-USP8 complex in leptin sensing neurons
Authors: Kelly Fagan, T. Methsala Wijesuriya, Rachel Wevrick
Affiliations: University of Alberta

Introduction

Prader Willi Syndrome (PWS) is a neurodevelopmental genetic disorder that results in developmental delay and excessive appetite. PWS is caused by the inactivation of several genes including the functionally related Necdin and MAGEL2 genes, on chromosome 15q11-q13. MAGEL2 and Necdin are important in central neurons that detect leptin, a hormone derived from adipose tissue. These neurons regulate energy balance through circuits that modulate appetite and energy expenditure. Individuals with PWS have increased fat mass suggesting they are insensitive to central regulation by leptin. We propose that this leptin insensitivity is due to either reduced availability of cell surface leptin receptors or impaired leptin receptor signalling in central neurons. Specifically, MAGEL2 and Necdin could interact with and control the activity of specific proteins in leptin response pathways. Two such proteins, RNF41 (an ubiquitin ligase) and USP8 (a deubiquitinase), act in concert to target leptin receptors to the cell surface for reuse or to lysosomes for degradation. My project aimed to further elucidate the relationships among MAGEL2, Necdin, RNF41 and USP8.

Methods

Mice with a gene-targeted deletion of Magel2 were used to examine the effects of the loss of Magel2 on levels of RNF41 and USP8. Tissue samples from both the cortex and hypothalamus were collected and the levels of RNF41 and USP8 were analyzed. To measure direct interactions among Necdin, MAGEL2, RNF41 and USP8 with the leptin receptor, we used a proximity biotinylation assay.

Results

We found decreased levels of RNF41 and increased levels of USP8 in brain tissues from mice lacking Magel2. The biotinylation assay showed that MAGEL2 is directly interacting with USP8 and with Necdin. Further interactions are currently being analyzed.

Conclusion

Our result suggests that MAGEL2 could modify the activity of the ubiquitin-regulating enzymes RNF41 and USP8 in leptin sensing neurons in children with PWS and could potentially affect the intracellular sorting of the leptin receptor.

Funded By: Summer Studentship

Abstract #:	80
Presenter:	T.Methsala Wijesuriya
Supervisor:	Rachel Wevrick
Title:	MAGEL2 associates with USP8 and RNF41 to regulate ubiquitination pathways involving the leptin receptor
Authors:	T.Methsala Wijesuriya, K.Vanessa Carias, Kelly Fagan, Leentje De Ceuninck, Jan Tavernier, Rachel Wevrick
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Mental Health

Introduction: Children with Prader-Willi syndrome have neonatal feeding difficulties, developmental delay and excessive appetite. Loss of MAGEL2 causes a neurodevelopmental disorder (Schaaf-Yang syndrome) and may contribute to obesity in children with Prader-Willi Syndrome who lack MAGEL2 and other genes. MAGEL2 is essential in neurons that sense levels of the adipose tissue-derived hormone leptin. The MAGEL2 protein is important for recycling or degradation of proteins in the brain and interacts with and modifies the activity of E3 ubiquitin ligases. RNF41 is a E3 ubiquitin ligase that associates with a ubiquitin-specific protease (USP8). Together with USP8, RNF41 regulates the recycling of the leptin receptor by targeting it either for degradation or for recycling to the cell membrane. We hypothesized that MAGEL2 normally regulates the interaction between RNF41 and USP8, and that loss of this regulation could impair leptin response pathways in the brain in children with PWS.

Methods: Human U2OS cells were transfected with recombinant constructs encoding epitope tagged versions of MAGEL2 and wild type and mutant forms of RNF41. Immunofluorescence was used to visualize the co-localization of different forms of RNF41 with MAGEL2 in intracellular compartments. We expressed recombinant MAGEL2, RNF41 and USP8 in combinations in human U2OS cells and examined the relative abundance of each protein in the presence or absence of the other components of the complex. The interactions between MAGEL2 and other proteins were examined by the Bio ID system.

Results: We identified interactions among components of the RNF41-USP8 complex that depended either on the activity of the RING domain of RNF41 (RNF-SQ mutant form) or the binding domain of RNF41 (RNF-AE mutant form). Co-expression of MAGEL2 with components of the RNF41-USP8 complex modified the abundance of proteins in the complex. Preliminary results suggest that RNF41 enhances USP8 ubiquitylation, and we found that MAGEL2 diminishes the ability of RNF41 to auto-ubiquitinate or to ubiquitinate. Co-expression of MAGEL2 also modified the intracellular localization of components of the RNF41-USP8 complex. We also measured levels of endogenous RNF41 and USP8 level in brain tissues from Magel2 knockout mice and compared these levels to those found in tissues from wild type littermates.

Conclusion: Our results suggest that MAGEL2 could modify the activity of the RNF41-USP8 ubiquitination complex in leptin sensing neurons, providing a possible mechanism for dysregulation of leptin sensing in neurons in children with Prader-Willi syndrome.

Funded By: Trainee Travel Grant

Abstract #: 81
Presenter: Andrew Waskiewicz
Supervisor:
Title: Superior coloboma: A novel disease that reflects a newly discovered feature of ocular development
Authors: Andrew Waskiewicz, Kevin Yoon, Maria Choi, Sophie Koch, Sonya Widen, Ordan Lehmann, Jennifer Hocking
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Congenital Abnormalities

Introduction: The eye primordium arises as a lateral outgrowth of the forebrain, with a transient fissure on the inferior side of the optic cup providing an entry point for developing blood vessels. Incomplete closure of the inferior ocular fissure results in coloboma, a disease characterized by gaps in the inferior eye, and recognized as a significant cause of pediatric blindness.

Results: Here, we identify eight patients with defects in tissues of the superior eye, a congenital disorder that we term *superior coloboma.* The embryonic origin of superior coloboma could not be explained by conventional models of eye development, leading us to reanalyze morphogenesis of the dorsal zebrafish eye. Our studies revealed the presence of a second ocular fissure, the *superior fissure*, located at the 12 o'clock position. Exome sequencing of superior coloboma patients identified a rare and detrimental variant in a Bone morphogenetic protein (Bmp) receptor. Consistent with this result, we find that superior fissure closure defects in a zebrafish Bmp mutant cause phenotypes resembling superior coloboma. Loss of dorsal ocular Bmp is rescued by concomitant suppression of the ventral-specific Hedgehog pathway, arguing that superior fissure closure is dependent on dorsal-ventral eye patterning cues. The superior fissure acts as a conduit for blood vessels, with altered fissure closure resulting in inappropriate connections between the hyaloid and superficial vascular systems.

Conclusions: Together, our findings explain the existence of superior coloboma, a congenital ocular anomaly resulting from aberrant morphogenesis of a novel anatomical structure.

Funded By: Innovation and Summer Studentship

Abstract #: 82
Presenter: Jerry Chen
Supervisor: Oana Caluseriu
Title: Treating Fibrodysplasia Ossificans Progressiva (FOP) with Antisense Phosphorodiamidate Morpholino Oligomers (PMOs) via Exon skipping
Authors: Jerry Chen, Rika Maruyama, Toshifumi Yokota, Oana Caluseriu
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Congenital Abnormalities

Introduction
Fibrodysplasia Ossificans Progressiva (FOP) is an autosomal dominant and highly debilitating genetic disease characterized by progressive bone formation in soft tissues (termed heterotopic ossification). With no effective treatment available, FOP patients gradually lose the mobility needed for essential body functions, leading to an average lifespan of 40 years. In 98% of all cases, FOP is caused by a G>A point mutation in the ACVR1 gene, and subsequently a R206H missense mutation in the resulting protein. The ACVR1 gene codes for the ACVR1 receptor, a type I bone morphogenetic protein (BMP) receptor responsible for normal bone development and repair. In FOP, the mutation causes ACVR1 to be abnormally stimulated by Activin A and becomes hyperactive, resulting in aberrant bone formation. In the hope that reducing ACVR1 expression could provide therapeutic potential, Shi et al. in 2013 were able to knockdown ACVR1 expression in mouse cells using phosphorodiamidate morpholino oligomers (PMOs). PMOs are synthetic DNA/RNA-like oligonucleotides that can downregulate gene expression by being able to induce exon skipping of target exons, which can lead to nonsense-mediated decay of target mRNA. This project seeks to use PMOs to knockdown ACVR1 expression in human FOP fibroblast cells via exon skipping.

Methods
Two human FOP fibroblast cell lines confirmed with the G>A mutation were transfected with PMOs targeting either ACVR1 exon 3 translational start site (for indiscriminate ACVR1 knockdown) or ACVR1 exon 6 mutation-specific site (for mutation only allele knockdown). Semi-quantitative reverse transcription PCR (RT-PCR) was done with primers flanking either exon 3 or exon 6 to measure exon skipping. Subsequent Sanger sequencing of purified RT-PCR bands was done to confirm exon skipping.

Results
RT-PCR of PMO transfected fibroblast cells showed exon skipping in all PMO treatment groups, with four PMOs showing statistically significant exon-skipping efficiency against control PMO treatment. Subsequent Sanger sequencing confirmed PMO induced exon skipping in all PMO treatments.

Conclusions
These results suggest that PMOs are able to induce significant exon skipping of target ACVR1 exons and reduce ACVR1 gene expression. Coupled with the fact that there were no signs of cell toxicity, successful ACVR1 knockdown with PMOs would pave the way for future in vivo trials and hopefully a treatment for FOP.

Funded By: University of Alberta Faculty of Medicine and Dentistry

Abstract #: 83
Presenter: Kana Hosoki
Supervisor: Toshifumi Yokota
Title: Development of phosphorodiamidate morpholino-based antisense therapy for spinal muscular atrophy
Authors: Kana Hosoki, Aleksander Touznik, Yusuke Echigoya, Rika Maruyama, Toshifumi Yokota
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Neuro-cognitive Development

Introduction

Spinal muscular atrophy (SMA) is one of the most common autosomal recessive neuromuscular disorders affecting the motor neurons, usually resulting in rapid progression of muscle weakness and leading to death at a young age. SMA is caused by a deficiency in survival of motor neuron (SMN) protein due to a homozygous mutation in the S*MN1* gene. Humans contain a unique inverted duplication of the *SMN1* gene known as *SMN2*, but it cannot compensate the loss of *SMN1* since the exon 7 of *SMN2* mRNA is excluded (spliced out) due to a single C-to-T nucleotide transition in the exon 7. Our goal is to identify and develop novel antisense oligonucleotides (ASOs) that target splice silencers to enhance the inclusion of exon 7 in the *SMN2* gene using the neutrally charged and less toxic phosphorodiamidate morpholino oligomer (PMO) chemistry.

Methods

Using ASOs to “knock-up” the production of full-length protein made by the *SMN2* gene is a promising therapeutic approach to treat SMA. We designed several PMOs targeting intronic splicing silencer site on intron 7 of *SMN2*, which promotes exon 7 inclusion of the mRNA. Each PMO was transfected into SMA patient fibroblasts. Exon 7 inclusion of post-transcriptional mRNA and SMN protein production were examined by RT-PCR and Western blotting, respectively. To evaluate the *in vivo* efficacy, the PMOs were injected subcutaneously into newborn SMA model mice.

Results

RT-PCR analysis revealed that several PMOs we designed lead to complete exon 7 inclusion in severe SMA patient fibroblasts. The Western blotting showed that the amount of SMN protein was significantly increased in the cells by transfection of the PMOs. Furthermore, a single subcutaneous administration of the PMO improved the motor function and extended the lifespan of SMA model mice dramatically, from approximately two weeks to more than four months. The treated mice showed no symptoms except for the smaller body size and short tails.

Conclusion

We demonstrated that newly designed PMOs induced exon 7 inclusion of *SMN2* and SMN protein production efficiently *in vitro*. In addition, these PMOs rescued SMA phenotypes in vivo. The novel antisense oligonucleotides identified in this study can potentially offer improvement for the treatment of SMA in the future.

Funded By: CIHR

Abstract #: 84
Presenter: Peter Sabiri
Supervisor: Daniel Graf
Title: A role for Bmp7 in sensory nerve development
Authors: Peter Sabiri, Daniel Graf
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Neuro-cognitive Development

Introduction: The anterior aspect of the human head, including most of the tissues of the orofacial region are neural crest cell (NCC) derived. NCCs are multipotent stem cells that play a fundamental role in craniofacial patterning and development. Among the many signaling networks involved in NCC development are Bone morphogenetic proteins (Bmps). Bmps participate in various tissue processes including cell differentiation and homeostasis. Mutations in Bmp7 are exceedingly rare, but when they occur in children, they manifest as ocular, cerebral, otic, palatal, and skeletal anomalies. Currently, it is not known whether individuals carrying a Bmp7 mutation have sensory deficits besides those of the eye and ear. Here we demonstrate an altered sensory phenotype in mice carrying a complete deletion of Bmp7.

Methods: E14.5 Embryos from mice carrying a complete deletion of Bmp7 ($Bmp7^{\Delta/\Delta}$) were harvested and characterized using histological, immunohistochemical and gene expression analysis (qPCR) of various sensory neuronal markers. Air puffs were also directed towards the whiskers of mice carrying a neural crest specific deletion (Wnt1-cre) of Bmp7 to measure nerve responses and characterize sensory differences.

Results: The trigeminal ganglion in embryos carrying a full deletion of Bmp7 is morphologically altered, appearing to be smaller and slightly misplaced in its relation to other craniofacial structures. Immunohistochemical analysis of the trigeminal ganglion proved to be inconclusive due to neuronal variability, however qPCR analysis shows mRNA differences in some receptors (TrkA, Trpv1, Ret, TrkB). To determine whether these molecular differences result in some physiological changes, air puff assays were performed. At low air pressures, mutant mice were less responsive than control mice.

Conclusion: Bmp7 is important for peripheral nerve development. qPCR analysis reveals mRNA differences in neuron receptor expression and air puff assays indicate that mutants have a hypoallodynic response. Future experiments will be aimed at understanding the mechanism by which these changes occur.

Funded By: NSERC

Abstract #: 85
Presenter: Justin Lee
Supervisor: R. Todd Alexander
Title: Identification of novel calcium transport pathway in Jejunum of suckling mice
Authors: Justin Lee, Megan Beggs, Todd Alexander
Affiliations: University of Alberta

Introduction

A positive calcium balance throughout development is crucial for optimal bone mineralization, where this balance is mediated by the interactions between the intestine, kidneys, and bone. Intestinal calcium absorption occurs through the transcellular and paracellular pathways. The current model of calcium absorption in the small intestine includes transcellular transport in the duodenum but not the jejunum or ileum. With limited supporting evidence, young mammals are hypothesized to absorb calcium via the paracellular pathway. Recent unpublished work in the Alexander lab suggests a novel transcellular absorption pathway in the ileum of pre-weaned mice. Thus, we set out to examine the expression of calcium absorption mediators in the jejunum of pre and post weaning mice. We hypothesized that jejunum could also be involved in transcellular calcium absorption prior to weaning.

Methods

Wild-type FVB/N mice at 7 different age groups were examined, N.B. weaning occurred at 3 weeks of age. Jejunal RNA was extracted then reverse transcribed to cDNA. Gene expression of calcium transport mediators (transcellular mediators: *Trpv6*, *Cav1.3*, *CalbD9k*, *Pmca1b*, and *Ncx*; paracellular mediators: *Cldn-2*, *-12*, and *-15*) was quantified using quantitative polymerase chain reaction (qPCR) with specific primers and probes. Protein abundance of Calbindin-D_{9k} and Claudin-2 were examined via immunoblot analysis.

Results

There were significant changes in the expression of calcium absorption mediators at the time of weaning. The transcellular transport mediators, *Trpv6*, *Cav1.3*, *CalbD9k*, *Pmca1b*, and *NCX* were highly expressed prior to weaning with significant decreases (2.5-fold to 12-fold), between 2 weeks and 1 month of age. The paracellular transport mediators showed varying trends of mRNA abundance. *Cldn-2* and *-12* displayed higher expression prior to weaning with significant decreases post-weaning, while *Cldn-15* increased throughout development. Immunoblot analysis of Calbindin-D_{9k} showed highest protein abundance pre-weaning with minimal expression from 2 to 6 months, whereas protein abundance of Claudin-2 did not change throughout development.

Conclusions

These observations suggest a novel transcellular calcium absorption pathway in pre-weaning mice, which disappears after weaning. Future functional studies using Ussing chambers are required to confirm these expression results.

Funded By: Graduate Studentship

Abstract #: 86
Presenter: Robin Featherstone
Supervisor:
Title: Social media to promote evidence in pediatric emergency medicine: Assessment of a knowledge dissemination strategy
Authors: Robin Featherstone, Kassi Shave, Lisa Hartling
Affiliations: University of Alberta
Research Activity: Pediatric Emergency Medicine

Introduction: Translating Emergency Knowledge for Kids (TREKK) is a National Centre of Excellence that was established to address a knowledge-to-practice gap in the emergency department (ED) care of children. A national needs assessment of healthcare providers in general EDs identified clinical topics and informed the selection of guidelines, Cochrane systematic reviews, and other key studies to populate the 'Evidence Repository' on trekk.ca. Stakeholder feedback informed the development of 'Bottom line Recommendations,' summary documents containing diagnosis and treatment guidance on priority topics. Between October 5th and December 27th 2015, the TREKK Social Media Team at the Alberta Research Center for Health Evidence (ARCHE) used blogs and Twitter to promote selected Cochrane Summaries, TREKK's Evidence Repository and Bottom line Recommendations.

Methods: The Social Media Team selected and reproduced 12 Cochrane summaries using a blogging module on trekk.ca. Key points from the Cochrane summaries were shared via 252 Twitter messages that contained 199 hyperlinks to the blog posts on trekk.ca, 34 links to topic areas in the Evidence Repository, 15 links to Bottom line Recommendations, and 4 links to Cochrane Summaries or systematic reviews. We published at a rate of one blog post and 21 Twitter messages per week for 12 weeks; and collected Twitter, web page and link analytics for blogs posts on the trekk.ca website and messages shared by the @TREKKca Twitter account. We also tracked alternative social media metrics (altmetrics) for Cochrane systematic reviews promoted during this period.

Results: During the campaign, TREKK's Twitter account gained 69 new followers (15.3% increase), and its messages were re-tweeted (shared by other accounts) 125 times. Fifty-eight traceable URLs in the Twitter messages were clicked 600 times. The 12 blog posts on trekk.ca received 6,428 page visits during the promotion, 8 Bottom line Recommendations were accessed 566 times, and 8 topic areas in the Evidence Repository were visited 2,299 times. Fourteen Cochrane systematic reviews promoted during the period increased their altmetrics' scores by an average of 10 points (46.2% increase).

Conclusions: Twitter analytics and URL tracking indicate that the social media campaign grew TREKK's online followers and directed web traffic to trekk.ca. Web reports show increased site visits to the promoted Bottom line Recommendations and topics in the Evidence Repository. Altmetrics, page views and URL tracking data suggest increased accessed to Cochrane summaries and systematic reviews. Quantitative evidence collected from a variety of web analytics support blogging and tweeting as effective knowledge dissemination strategies.

Funded By: Partnership resources

Abstract #:	87
Presenter:	Reed Sutton
Supervisor:	Vivian Huang
Title:	An online educational portal improves concerns of inflammatory bowel disease patients regarding pregnancy and medication
Authors:	Reed Sutton, Kelsey Weirstra, Kayla-Marie Smith, Morgan Shipka, Jasmin Bal, Brendan Halloran, Karen Kroeker, Keri-Ann Berga, Richard Fedorak, Vivian Huang
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology

INTRODUCTION:

The impact of a mother's chronic disease on fetal development makes dealing with inflammatory bowel disease (IBD) during pregnancy complicated. Almost 50% of women with IBD have poor reproductive knowledge; this has been associated with unsubstantiated concerns toward pregnancy, and towards IBD medications. To lessen these concerns, we developed an educational web portal.

METHODS:

IBD patients aged 18-45 years were invited to participate in a study to evaluate the effectiveness of an educational web portal covering the topics of heritability, fertility, surgery, pregnancy outcomes, delivery, postpartum, and breastfeeding in the context of IBD and IBD medications. Patients completed pre- and post-study questionnaires about seven IBD-specific pregnancy concerns, and identified Likert scores for nine medication concerns from the Beliefs About Medicines Questionnaire (BMQ).The non-parametric McNemar's test was used to determine if the proportion of patients who had each pregnancy concern decreased post-intervention, . For medication concerns, the Wilcoxon signed-rank test was used to compare median differences between Likert scores. 95% confidence intervals and SPSS Version 23 were used for all analysis.

RESULTS:

Seventy-eight of 111 patients (70.3%) completed pre and post-study questionnaires. Demographics for the 78 are as follows: median age 29.3 (IQR 25.6 - 32.9) years; 54 (69.2%) Crohn's disease; 21 (26.9%) ulcerative colitis; 63 (80.3%) females, 5 (7.9%) currently pregnant and 19 (30.2%) previously pregnant. Medication history: 10 (12.8%) sulfasalazine, 67 (85.9%) mesalamine/5-ASAs, 17 (21.8%) budesonide, 63 (80.8%) steroids, 12 (15.4%) methotrexate, 55 (70.5%) azathioprine/mercaptopurine, 42 (53.8%) biologics, and 38 (48.7%) antibiotics. The intervention significantly decreased the proportion of patients who reported reproductive concerns regarding: fertility, added stress of raising a child affecting IBD, birth defects from IBD, pregnancy causing a flare-up, and inability to breastfeed due to IBD or medications. Concern regarding body image restricting sexual activity and difficulty caring for a child did not change significantly, but neither was directly addressed by topics covered in the portal. The BMQ Likert scores significantly decreased post intervention for concerns about having to take IBD medication, becoming too dependent on IBD medication, and the long-term effects of IBD medication.

CONCLUSIONS:

The educational web portal effectively reduced the proportion of patients who reported certain concerns about pregnancy in IBD, in addition to concerns regarding their IBD medications.

Funded By: CEGIIR

Abstract #: 88
Presenter: Salima Meherali
Supervisor: Shannon Scott
Title: Digital knowledge translation tools on Otitis media for Canadian and Pakistani parents
Authors: Lisa Hartling, Kelli Buckreus
Affiliations: University of Alberta
Research Activity: Knowledge translation tool on common pediatric conditions

Introduction

Knowledge translation (KT) seeks to mobilize research evidence to guide practice decisions in healthcare and aims to reduce the 'evidence-practice' gap by developing, implementing, and evaluating strategies designed to promote behaviour change. Healthcare is moving toward an integrative, collaborative, and patient-centred model; patient/family-centered care is an innovative approach to planning, delivery, and evaluation of care. To ensure appropriate and effective family involvement in their child's care, families must have access to essential and often complex health information. Traditional ways (e.g., standard health information sheets) of sharing health information with healthcare consumers and other audiences often do not facilitate parents'/families' participation in their child's healthcare decisions. Effective healthcare delivery and consumer satisfaction are dependent on approaches to effectively communicate and transfer information and research among diverse audiences. Recently, novel approaches have been explored to engage parents in translating complex health information, including the use of stories or narrative, arts and digital media. The purpose of this research is to build upon the active engagement of healthcare consumers to develop, implement and evaluate innovative KT tools for a common pediatric condition, acute otitis media.

Methods

A multi-methods design will be used to develop, refine and evaluate the usability of arts-based digital tools for pediatric AOM management. First, a knowledge synthesis study on research-based AOM treatment will be conducted. Second, we will interview parents to understand their experience in caring for a child with otitis media. Third, based on the results of the knowledge synthesis and parent interviews, we will develop KT tools for parents. Fourth, before the wide dissemination of this tool, we will conduct a mixed-methods study (qualitative and quantitative; surveys and interviews) to determine the usability and usefulness of these KT tools. Lastly, we will augment these tools in the Pakistani context to evaluate the cultural adaptation of KT tools developed for a Canadian context. Cultural adaptation as a KT strategy in general, and of KT tools in particular, is critically important given Canada's diverse multicultural population.

Significance

This research seeks to empower parents with the required knowledge to be meaningful partners in health decision-making and has great potential to improve health outcomes and healthcare utilization. This research will contribute to knowledge on tailoring KT tools for different cultural contexts. The process of cultural adaptation of the tool will generate important new knowledge that will contribute to the science of KT.

*Acknowledgement: WCHRI awarded Innovation grant for this project.

Abstract #:	89
Presenter:	Allison Gates
Supervisor:	Lisa Hartling
Title:	Informing innovative knowledge translation tools to help parents manage their child's procedural pain in the emergency department: A systematic review
Authors:	Allison Gates, Kassi Shave, Robin Featherstone, Kelli Buckreus, Samina Ali, Shannon Scott, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Pain Management

Introduction. Parents play a critical role in the management of their child's pain and distress during painful procedures, however many lack adequate knowledge of how to effectively do so. The aim of our study is to systematically review the findings of research examining the experiences and information needs of parents with regard to the management of their child's pain and distress during painful procedures in the emergency department.

Methods. We comprehensively searched literature published between 2000 and 2016 reporting on parents' experiences and information needs with regard to helping their child manage procedural pain. We included all study designs, with the exception of reviews, overviews and opinion pieces. Ovid Medline, Ovid PsycINFO, CINAHL, PubMed, abstracts from selected conference proceedings, ProQuest Dissertations and Theses, and reference lists of key studies were searched. Two reviewers screened the articles following inclusion criteria decided *a priori*. Data from each article (including author, year of publication, population, sample size, study design, procedure type, clinical setting and main findings) will be extracted in duplicate utilizing a study-specific data extraction form developed by our team. Any disagreements with regard to study inclusion or data extraction will be resolved by reaching consensus. Data from qualitative studies will be summarized thematically, while those from quantitative studies will be summarized descriptively. The second reviewer will confirm the overarching themes resulting from the qualitative and quantitative data syntheses. The Critical Appraisal Skills Programme Qualitative Research Checklist (CASP UK, 2013) and the Quality Assessment Tool for Quantitative Studies (Thomas, 2003) will be used to appraise the evidence from each included study.

Results. Our online search revealed 2,678 unique records, of which 41 were accepted, following title and abstract screening. After screening by full text, we selected five records for inclusion in the review. We expect to complete the data extraction and quality assessments by December 2016. Based on our preliminary findings, it appears that few studies on the topic currently exist in the literature.

Conclusions. Visiting the emergency department can be anxiety-provoking and overwhelming for children and their parents alike. Parents need to be informed of effective strategies to reduce their child's pain and distress during a painful procedure, and supported in doing so. We will apply the findings of this study to the development and evaluation of tailored, innovative knowledge translation tools to empower parents in taking an engaged role in managing their child's pain and distress during necessary emergency procedures.

Funded By: Partnership resources

Abstract #:	90
Presenter:	Lauren Albrecht
Supervisor:	Shannon Scott
Title:	The development of knowledge translation tools for parents in pediatric acute care
Authors:	Lauren Albrecht, Lisa Hartling, Mandy Archibald, Michele Dyson, Lisa Knisley, Terry Klassen, Shannon Scott
Affiliations:	University of Alberta
Research Activity:	Health services research

Introduction: With increasing demands for family-centered care and patient-oriented health research, strategies are needed for meaningful engagement among researchers, practitioners and health consumers (i.e., patients, caregivers) to effectively bridge the research-practice gap in pediatric acute care. Developing knowledge translation (KT) tools for parents has been proposed as an effective and engaging method of providing complex, evidence-based child health information to support health decision making. The purpose of this study was to develop and pilot test three KT tools, two videos and one eBook, for parents about pediatric croup and acute gastroenteritis (AGE).

Methods: Relevant systematic reviews were identified and literature searches conducted at 3-month intervals from September 2014 - March 2016 to update the evidence underpinning the KT tool content. Qualitative interviews were conducted with parents in the emergency department to understand their experiences and information needs of these conditions. Thematic analysis was conducted to inform the KT tool storyline. Feedback surveys on tool prototypes were conducted with clinicians and parents. Quantitative and qualitative survey data was analysed and incorporated into KT tool revisions. Pilot testing of the final products is currently underway in urban, rural and remote regions.

Results: One new study per condition was incorporated into previously published meta-analyses with no significant changes to intervention efficacy. Composite narratives were constructed from thematic analysis to highlight decision making complexities and emotional aspects of caring for an ill child. Prototype feedback refined tool length, aesthetics, character representation, and additional clinical information. Pilot testing results will be available for presentation in Fall 2016.

Conclusions: By merging rigorous science with parental narratives, these KT tools provide an engaging approach to share systematic review results with the lay public. There is great potential to use this method to develop a number of KT products focused on different conditions and/or interactions between patients/families and the healthcare system.

Funded By: Graduate Studentship

Abstract #: 91
Presenter: Jill Morris
Supervisor: Rhonda Bell
Title: Gestational weight gain, nutrition, and physical activity counselling practices of prenatal health care providers: What influences practice?
Authors: Jill Morris, Hara Nikolopoulos, Tanya Berry, Rhonda Bell
Affiliations: University of Alberta

Introduction

Appropriate gestational weight gain (GWG) is important for maternal and child health. Data from a recent Alberta cohort showed 49% of pregnant women gained weight in excess of Health Canada guidelines. Regional studies have shown low rates of GWG counselling by health care providers (HCPs), including general practitioners, obstetricians, and midwives. Research is needed to determine how to support HCPs to enhance GWG counselling practices. The purpose of this study was to understand current GWG counselling practices, and the influences on practices.

Methods

This mixed method study included semi-structured interviews and an online survey. Interviews were conducted by telephone with prenatal HCPs from Alberta and British Columbia, transcribed verbatim and analyzed using qualitative content analysis. The survey questionnaire was distributed nationally to prenatal HCPs. Responses were compared by HCP discipline using ANOVA, and multiple linear regression examined influences on practices. Data were collected concurrently, analyzed separately, and integrated.

Results

Interview participants (n=23) had a range of practices for GWG counselling. Typically, weight gain information was provided early in pregnancy, but not discussed again unless there was a concern. Among survey respondents (n=508) few routinely provided women with individualized weight gain advice (21%), rate of weight gain (16%), or discussed the risks of inappropriate weight gain to mother and baby (20% and 19%). More routinely discussed physical activity (46%) and food requirements (28%); midwives did these two activities more frequently than all other disciplines ($p<0.001$). Midwives interviewed noted a focus on overall wellness instead of weight, and had longer appointments for in-depth counselling. Regression results found that the priority level that HCPs place on gestational weight gain had the largest influence on providing weight gain advice and discussing the risks ($B=0.71$, $p<0.001$) and discussing physical activity and food requirements ($B=0.341$, $p<0.001$). Interview data linked the priority level of GWG to length of appointments, compensation methods for HCPs, attitudes of HCPs, and the midwifery versus medical model of care.

Conclusions

Interventions for HCPs to enhance GWG counselling practices should consider the range of factors that influence the priority level HCPs place on GWG counselling.

Funded By: Trainee Travel Grant

Abstract #: 92
Presenter: Fabiana Mamede
Supervisor:
Title: Evaluation of expectation and satisfaction of pregnant women in Sao Paulo - Brazil
Authors: Fabiana Mamede, Patricia Prudencio, Kathrein Sena
Affiliations: University of Sao Paulo Brazil
Research Activity: Maternal health prenatal care

Introduction: Satisfaction of women with prenatal care appears to be a factor that encourages pregnant women to seek and to continue prenatal care. Satisfied pregnant with prenatal care tend to recommend the service to other women, again seek the service in a future pregnancy, and present pregnancies with positive results. Meet the expectations of pregnant women regarding prenatal services, influence the satisfaction of the same. This study aims to identify the degree of expectation and satisfaction of pregnant women with prenatal care.

Methods: it is an exploratory, descriptive and cross-sectional study. The sample consisted of 377 pregnant women randomly selected in eight utility prenatal health in a city of São Paulo, Brazil. Of the eight pre-natal services, six in basic health units and two family health units. It was applied to Brazilian Instrument Version Patient Expectations and Satisfaction with Prenatal Care through individual interviews conducted by the researcher in the period from January 2015 to april 2016. The interviews lasted about 20 minutes. Statistical analysis was performed using the statistical software programa R.

Results: It was found that the average age of patients was 27.69 years old (SD=5.6), ranging from 20-43 years old; 196 (52.0%) identified themselves as white, 237 (62.9%) work a home, 322 (85.4%) lived with a partner, 224 (59.4%) reported having completed high school and only 12 (3.2) had higher education, 169 (44.8%) were catholic and 375 (99.5%) did not have a health plan. As for obstetrical data, 288 (76.4%) were multigestas, 264 (70%) initiated prenatal care in the first trimester of pregnancy and 334 (88.6%) had no complications during prenatal care. Gestational age ranged from 27 to 42 weeks, with an average of 32.33 weeks and standard deviation of 3.831. The average number of prenatal visits was 6.23 with a standard deviation of 2.54. It identified low level of expectation 279 (74%) and high satisfaction 220 (58.4%).

Conclusions: Low expectations regarding prenatal shows a negative perception of pregnant women about the service. This may compromise the satisfaction with care, since pregnant women respond to offers of attention according to what they think about their health needs. Therefore, to identify and meet the expectations of pregnant women with prenatal care contributes to increased satisfaction and consequently to improve prenatal care quality in Brazil.

Funded By: CAPES Brazil

Abstract #: 93
Presenter: Juliana Monteiro
Supervisor:
Title: Breastfeeding self-efficacy and duration of exclusive breastfeeding among adolescent mothers
Authors: Raquel Germano Conde, Carolina Guimarães, Mônica Oriá, Juliana Monteiro
Affiliations: University of Sao Paulo Brazil
Research Activity: Child and Youth Development : Nutrition

Introduction: Breastfeeding and its benefits for maternal and child health have been the subject of many scientific studies. Despite the evidence of benefits, it is necessary to understand breastfeeding as a multifactorial process. Maternal age is one of the factors that influence breastfeeding, as adolescent mothers may have greater difficulty in initiate and maintain this practice. In addition, maternal confidence to breastfeed, also known as breastfeeding self-efficacy, has been identified as a modifiable and protective variable to breastfeeding, as it influences the beginning and maintenance of it. The objectives of this study were: to identify the breastfeeding self-efficacy in adolescent mothers; to identify the prevalence of exclusive breastfeeding at 30, 60 and 180 days postpartum; and verify the association between breastfeeding self-efficacy and the duration of exclusive breastfeeding at 30, 60 and 180 days postpartum.

Methods: A prospective longitudinal study was undertaken with a sample of 160 adolescent mothers admitted to a rooming at a public maternity hospital in Ribeirão Preto, Brazil. Data were collected at the maternity hospital using a questionnaire about demographic and obstetrical information and the Breastfeeding Self-Efficacy Scale (BSES). Subsequently, data were collected at 30, 60 and 180 days postpartum using a questionnaire about the children's feeding and the problems during the breastfeeding period. Data were analyzed using the statistical software SAS® 9.0. Fisher's Exact Test was used to evaluate the association between variables.

Results: Most participants (56.90%) demonstrated a high level of breastfeeding self-efficacy. The prevalence of exclusive breastfeeding was 62.00% at 30 days, 52.59% at 60 days and 16.00% at 180 days postpartum. There was no statistically significant association between adolescent's breastfeeding self-efficacy and the duration of exclusive breastfeeding at 30, 60 and 180 days postpartum (p=0.1519, p=0.2570 e p=1.0000 respectively). There was a statistically significant association between adolescent's breastfeeding self-efficacy and the variables "complications during pregnancy" (p = 0.0069) and "complications during labor and/or delivery" (p=0.0316); in other words, participants who did not have these complications demonstrated greater breastfeeding self-efficacy.

Conclusions: The high level of self-efficacy did not influence the duration of exclusive breastfeeding among adolescent mothers. However, we identified that complications influenced the breastfeeding self-efficacy. We emphasize that health professionals should reinforce the exclusive breastfeeding promotion between adolescent mothers in order to improve the breastfeeding rates.

Funded By: Coordination for the Improvement of Higher Education Personnel (CAPES), Brazil

Abstract #: 94
Presenter: Richard Mah
Supervisor: Andrew Woodman
Title: Effect of maternal iron deficiency on fetal glomerular size and density in the prenatal rat
Authors: Richard Mah, Andrew Woodman, Stephane Bourque
Affiliations: University of Alberta
Research Activity: Maternal Research : Fetal Origins of Adult Disease

Introduction

Iron deficiency (ID) is the most common nutritional deficiency worldwide; 2 billion people – over 30% of the world's population – are anaemic, many due to iron deficiency. Pregnant women are most at risk of ID anemia due to blood volume expansion and the demands of the fetal-placental unit. The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that environmental conditions during fetal and early post-natal development influence lifelong health, and can influence susceptibility to chronic diseases in adulthood. Studies have shown that prenatal ID causes fetal anemia, intrauterine growth restriction, and abnormal renal development which may be related to chronic hypertension. However, it is not clear at what stage of development ID causes abnormal renal development and function. Here, we tested the hypothesis that maternal ID causes a reduction in glomerular density and size in fetal kidneys during gestation, which is expected to be more pronounced in males.

Methods

Six week old female Sprague Dawley rats were fed either a low iron (3 mg/kg) diet or iron-replete (35 mg/kg) diet throughout pregnancy. Pregnant dams and pups were euthanized on gestational day (GD) 21, and physical parameters (i.e. body weight, hemoglobin levels) were assessed. Following euthanasia, fetal tissues were fixed in 4% formaldehyde and paraffin embedded for Mayer's' Hematoxylin and Eosin staining. Statistical analyses for maternal hemoglobin levels and bodyweight were conducted using two-way ANOVA with Bonferroni *post hoc* tests. All other data sets were analyzed with two-tailed *t*-tests.

Results

Maternal iron restriction resulted in a 48% reduction in maternal Hb compared to controls by GD21 ($P<0.01$). Accordingly, ID resulted in a 65% decrease in fetal Hb ($P<0.001$). Fetal bodyweight was decreased by 26% in the ID group compared to controls ($P<0.001$), concomitant with an 18% decrease in relative kidney weight ($P<0.05$). In both male and female fetuses, no differences were observed in either glomerular size or number.

Conclusions

These results suggest that reduction in nephron number may occur after birth in perinatal iron deficient offspring, which may lead to the long-term cardiovascular complications observed in these offspring.

Funded By: Innovation Grant

Abstract #: 95
Presenter: Barbara Verstraeten
Supervisor: David Olson
Title: Potential role for pro- and anti-inflammatory cytokines in adverse pregnancy outcomes in a rat two-hit stress model
Authors: Barbara S.E. Verstraeten, J. Keiko McCreary, Ashlee Matkin, Hans Verstraelen, Gerlinde A.S. Metz, David M. Olson
Affiliations: University of Alberta

Introduction: It is widely accepted that maternal stress can have major effects on pregnancy outcomes and that delivery is an inflammatory process mediated in part by Interleukin (IL)-1β and IL-6. IL-1β effects are highly regulated by a complex system of receptors and co-receptors, ligands (IL-1α, IL-1β) and the endogenous receptor antagonist IL-1RA. To further our understanding of the role of stress and IL-1β in parturition, we developed a two-hit stress model in which animals receive psychological and immune stress in late gestation. We showed that combination of both stressors increases adverse pregnancy outcomes, primarily preterm delivery, while neither stressor alone does. These findings resemble those observed in our trans- and multigenerational stress models using only one stressor. In the latter, we also found differences between the ancestral generation and their offspring in circulating IL-10 levels. Here, we hypothesise that two distinct stressors differentially regulate mRNA expression of the aforementioned cytokines and Il-1ra in uteri of F0 and F1 rats when combined, compared to either hit alone.

Methods: F0 dams were exposed to psychological (swimming/restraint on gestational days (GD) 12-18) and immune stress (IL-1β, 5µg/kg/day i.p. from GD17-delivery), resulting in four groups of F0/F1 animals: no stress/saline (NS/S), stress/saline (S/S), no stress/IL-1β (NS/IL-1β) and stress/IL-1β (S/IL-1β), n=3-7/group. mRNA abundance in F0 (weaning) and F1 (adult virgin) uteri was evaluated by qRT-PCR for genes of interest and normalised to Cyclophilin. One-way ANOVA or equivalent with post-hoc testing, $p \leq 0.05$.

Results: In F0 animals, S/IL-1β exposure increased the mRNA abundance of Il-1ra and Il-6 compared to NS/S and S/S offspring ($p < 0.01$/$p < 0.05$ and both $p < 0.05$ respectively), and the Il-1β expression versus NS/S and NS/IL-1β (both $p < 0.05$). The F0 Il-10 abundance was significantly different overall ($p < 0.05$) with a trend towards upregulation after S/IL-1b treatment. In F1 offspring, Il-1α downregulation was observed in the S/IL-1β group compared to S/S and NS/IL-1β animals ($p < 0.05$). F1 IL-1ra abundance was lowest in the double hit group ($p < 0.05$/$p < 0.01$), while Il-1β expression was downregulated most in NS/Il-1β animals ($p < 0.01$/$p < 0.05$).

Conclusions: Cytokine mRNA expression patterns appear opposite in F0 and F1 uteri, suggesting that two-hit ancestral stress not only influences pregnancy and offspring outcomes but also differentially affects the expression of pro- and anti-inflammatory cytokines in uterus of F0 and F1 animals. These findings suggest that the effects of ancestral stress can be transferred, possibly through epigenetic mechanisms, to offspring, thereby alternately programming physiological responses which may lead to adverse (pregnancy) outcomes.

Funded By: PhD fellowship Research Fund Flanders, CIHR, March of Dimes

Abstract #:	96
Presenter:	Brittany Matenchuk
Supervisor:	Margie Davenport
Title:	Prenatal bed rest in developed and undeveloped countries: A meta-analysis
Authors:	Brittany Matenchuk, Rshmi Khurana, Normand Boulé, Linda Slater, Margie Davenport
Affiliations:	University of Alberta
Research Activity:	Exercise, Pregnancy, and Postpartum Health

Introduction: Currently there is no consensus regarding the effects of bed rest on fetal outcomes.

Methods: We performed a meta-analysis of 14 randomized controlled trials comparing standard care to standard care with bed rest after 20 weeks of gestation (2,608 women, 3,328 fetuses). Birth weight was examined according to three endpoints (<2,500g, <1,500g, and small for gestational age [SGA]). Gestational age, admission to the neonatal intensive care unit and perinatal death were also examined. Subgroup analysis compared outcomes from developed and undeveloped countries.

Results: Overall, newborn outcomes were similar between groups; however, there was a 50g greater birth weight with bed rest (Weighted Mean Difference [WMD]: 50g, 95% confidence interval [CI]:0g, 100g, I^2=31%). Divergent effects were observed where bed rest increased birth weight in undeveloped (WMD: 100g, 95% CI: 40g, 170g, I^2=0%) but not developed countries (WMD: -70g, 95% CI: -160g, 30g, I^2=14%, subgroup difference P=0.003). Gestational length was shorter with bedrest in developed (WMD: -0.77 weeks, 95% CI: -1.26, -0.27, I^2 = 0%) but not undeveloped countries (WMD: -0.04 weeks, 95% CI: -0.35, 0.26, I^2=6%, subgroup differences P=0.01). The odds of a very premature birth were also increased in developed (Odds Ratio [OR]: 2.72, 95% CI: 1.22, 6.07, I^2=0%) but not undeveloped countries (OR: 0.88, 95% CI: 0.51, 1.53, I^2=0%; subgroup differences P=0.02).

Conclusions: Women on bed rest in developed countries have worse newborn outcomes while women in undeveloped countries have improved newborn birth outcomes. Improvements in undeveloped countries may be influenced by the confounding effect of hospitalization.

Funded By: Summer Studentship

Abstract #:	97
Presenter:	Laura Adam
Supervisor:	Rhonda Bell
Title:	What is the current knowledge and eating behaviours of low-risk pregnant women in Edmonton?
Authors:	Laura M Adam, Donna P Manca, Rhonda C Bell
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Nutrition

Introduction: Pregnancy can be a complicated time to understand and implement diet and exercise recommendations while juggling food aversions, cravings and morning sickness. The Be Healthy in Pregnancy (BeHIP) study is a pilot randomized-control trial of low-risk pregnant women in Edmonton, Alberta aimed at understanding how support from a Registered Dietitian (RD) in pregnancy can help women meet nutrition and gestational weight gain guidelines. The objective of these analyses is to describe knowledge of nutrition and gestational weight gain guidelines and eating behaviours of healthy, pregnant women in the first half of their pregnancy.

Methods: Sixty-three low-risk pregnant women, <24 weeks gestation, were recruited using mass media and social media. Women completed questionnaires designed to assess knowledge of guidelines, dietary intake, and overall health with a RD.

Results: Although 76% of women reported that they have Above Average knowledge of healthy eating, only 45% of them had Above Average knowledge of healthy eating specific to pregnancy. Seventy percent of women felt clear about how much weight to gain in pregnancy and 65% of women knew how much extra food to eat. Since becoming pregnant, 49% increased juice intake and 46% increased milk intake. Fifty-two percent of the women had increased intake of foods in the grain category, primarily in response to physical symptoms such as aversions or cravings.Increased intake of sweet foods varied between pre- pregnancy BMI groups. 63% of women in the Overweight pre-pregnancy BMI category increased their sweet intake, while 33% and 15% of women in the Underweight/Normal and Obese pre-pregnancy categories increased their intake, respectively (p=0.02). The proportion of women who reported their health as Very Good or Excellent went from 60% in pre-pregnancy to 29% in early pregnancy.

Conclusions: When a woman becomes pregnant, the first half of pregnancy brings many changes. Dietary intake often changes due to cravings and sensory aversions to foods. At the same time, self-reported knowledge of healthy eating in pregnancy decreases. This could reflect increased food safety concerns and changes in nutrition recommendations for pregnancy that women may be less familiar with. Support through these changes and reassurance from healthcare providers is vital.

Funded By: Trainee Travel Grant

Abstract #:	98
Presenter:	Alison Care
Supervisor:	Sandra Davidge
Title:	Regulatory T cell-depletion during pregnancy causes fetal growth restriction and uterine artery dysfunction
Authors:	Alison Care, Stephane Bourque, Emma Hjartarson, Sarah Robertson, Sandra Davidge
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology

Introduction

Regulatory T (Treg) cells are essential for maternal immune tolerance in early pregnancy. Women with pregnancy complications such as preeclampsia, have reduced Treg cells in the circulation and gestational tissues. However, whether this reduced Treg number is causally related to preeclampsia is unknown. We hypothesize that a reduced Treg cell population would cause dysregulation of the immune cell environment, causing uterine artery dysfunction via increased matrix metalloproteinase (MMP)-2-induced cleavage of the inactive precursor bigET-1 to the active vasoconstrictor, ET-1.

Methods

Pregnant mice with FOXP3 promoter-driven expression of the human diphtheria toxin (DT) receptor (*Foxp3-DTR* mice) were injected with DT (37.5ng/g) on gestational day (GD)3.5 and GD5.5 to selectively deplete FOXP3+ cells; DT-treated C57BL/6J mice served as controls. FOXP3+ cell depletion was measured using flow cytometry on GD6.5. Uterine artery blood flow velocity was measured on GD9.5. We assessed uterine artery function ex-vivo on GD10.5 using wire myography. A separate group of mice carried their pregnancies until GD17.5 to assess fetal biometrics.

Results

Regulatory T cell-depletion causes fetal growth restriction (Wild-type+DT: 980.9±16.4mg, *Foxp3-DTR*: 854.4±48.1mg; P=0.01) After DT treatment, FOXP3 expression in uterine draining lymph nodes was reduced in *Foxp3-DTR* mice compared to wild-type mice (-89±5; P<0.001). Preliminary data indicate blood flow velocity in the uterine artery was unchanged by Treg depletion. On GD10.5, *Foxp3-DTR* mice had evidence of fetal resorption (Wild-type+DT: 0.1±0.1 resorptions, *Foxp3-DTR*+DT: 2.3±0.6; P<0.001). Uterine artery conversion of bigET-1 to active ET-1 was enhanced following Treg-cell depletion (P<0.001). In the presence of the MMP-inhibitor GM6001, constriction was reduced by 36% in uterine arteries from wild-type mice, but was unaffected by Treg depletion. Maximal ET-1-induced constriction in the uterine artery was similar for control and Treg-depleted mice (% of phenylephrine maximal constriction, wild-type+DT: 111.2±4.4, *Foxp3-DTR*+DT: 119.6±8.4; P=0.42).

Conclusions

Treg cell-depletion caused fetal growth restriction and increased fetal resorption but did not affect uterine artery blood flow velocity. Contrary to our hypothesis, MMP-induced conversion of bigET-1 to active ET-1 was reduced only in wild-type mice, suggesting dysregulation of the bigET-mediated conversion pathways following Treg depletion.

Funded By: Start-up or Retention Funding

Abstract #:	99
Presenter:	Peter Anto Johnson
Supervisor:	Stephane Bourque
Title:	The effect of prenatal iron deficiency and chronic cold exposure on brown adipose tissue morphology
Authors:	Peter Anto Johnson, Stephana Cherak, Stephane Bourque
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Fetal Origins of Adult Disease

Introduction:

The developmental fetus is highly plastic and therefore vulnerable to early environmental insults. Iron deficiency (ID) is the most common nutritional disorder worldwide, with pregnant women as the most susceptible group. Lack of iron *in utero* has shown to reprogram offspring adipose tissue, altering the developmental trajectory of the fetus and predisposing offspring to fat accumulation, and increasing risk of obesity and linked diseases. However, the exact mechanism is still unknown. Brown adipose tissue (BAT) is a metabolically active fat containing UCP-1, a tissue-specific protein, which works by uncoupling oxidative phosphorylation to generate heat and maintain core body temperature when exposed to cold. Here, we sought to determine whether prenatal iron deficiency (PID) precipitates obesity in the adult offspring by altering normal BAT morphology and thus total metabolism.

Method:

Female Sprague Dawley rats were either fed a control or iron-restricted diet prior to and throughout gestation. At birth, all dams were fed a control diet. At postnatal days (PD) 1, 14, and 28, offspring were euthanized and BAT and white adipose tissue (WAT) were collected. Starting at 4 wk of age, surviving male offspring were subject to the chronic cold exposure (CCE) protocol (4C, 12h/day, 5 wk) or kept at room temperature (RT) (23C). BAT and WAT were then collected from these offspring at PD63 (immediately after CCE) or PD91. Tissues were analyzed by microscopy; multilocular lipid droplets, mitochondria, and immunolabeled UCP-1 were used as markers for BAT, whereas unilocular lipid droplets, lack of mitochondria, and absence of UCP-1 fluorescence distinguished WAT.

Results:

In offspring undergoing CCE, controls had reduced adipocyte area ($P<0.0001$ for PD63 and PD91) and an increase in cell numbers compared to litter-matched offspring ($P<0.01$ for PD63 and PD91) compared to RT, whereas these effects were not seen in PID.

Conclusion:

These results support the hypothesis that PID causes reprogramming of BAT morphology and function, thereby predisposing offspring to obesity. In addition, it suggests that these changes in BAT are irreversible and persist throughout the later stages of life.

Funded By: NACTRC

Abstract #:	100
Presenter:	Mohammad Mehdi Houshmandi
Supervisor:	Lisa K Hornberger
Title:	Improving rate of fetal diagnosis of Coarctation of the aorta in Alberta
Authors:	Mohammad Mehdi Houshmandi, Luck Eckersley, Deborah Fruitman, Lindsay Mills, lisa K Hornberger
Affiliations:	University of Alberta
Research Activity:	Fetal and Neonatal Congenital Heart Disease

INTRODUCTION:

Coarctation of the aorta is one of the most difficult congenital cardiac lesions to detect in the fetus, and despite postnatal oximetry screening programs, remains the one critical heart defect most likely to be undetected prior to neonatal discharge from hospital after birth. Since 2009 new formal Canadian obstetric ultrasound guidelines have been implemented that mandate evaluation of the ventricular outflow tracts, great arteries and arches. In 2013, European and US obstetrical ultrasound guidelines changed similarly. The rate of fetal detection of coarctation of the aorta in Alberta has not been audited following change in guidelines.

METHODS:

We conducted a retrospective analysis of cases of simple coarctation of the aorta diagnosed at the Stollery Children's Hospital, or possible coarctation of the aorta diagnosed in the University of Alberta or Alberta Children's Hospital Fetal Cardiology programs with births between 2004 and 2015. Using medical record and echocardiographic review we established fetal diagnosis, requirement for and timing of operation, and location of residence at birth (2008 onwards). Cases with an operation at greater than one year of age or incomplete data were excluded.

RESULTS:

There were 214 cases of possible coarctation of the aorta detected with complete data. Fetal diagnosis occurred in 59 of 167 cases requiring coarctation repair at less than 12 months of age (35%). The rate of fetal diagnosis of coarctation of the aorta remained stable immediately following the 2009 Canadian guidelines: fetal diagnosis occurred in 31% of cases from 2004 - 2009 and 29% from 2010 - 2012. However from 2013 - 2015 51% of cases were diagnosed during fetal life. Of critical cases (requiring intervention in the first month), 36% were diagnosed prenatally from 2004 - 2009, 37% from 2010 - 2012 and 55% from 2013 to 2015. There were 45 cases of possible fetal coarctation where no infant operation was required (43% false positive rate), 2 false negative fetal echocardiograms and 2 cases with unknown timing of diagnosis. Rate of fetal diagnosis increased from 15% in 2008 – 2011 to 63% in 2012 – 2015 in regional areas outside of Edmonton and Calgary, vs. 32% in 2008 – 2011 to 48% in 2012 – 2015 in Edmonton/Calgary areas

CONCLUSIONS:

Fetal diagnosis of coarctation of the aorta has increased significantly, particularly in regional areas, and now occurs in over half of infantile cases. Further improvement in prenatal diagnosis will likely require mandated imaging of the three-vessel view and aortic isthmus.

Abstract #: 101
Presenter: Esha Ganguly
Supervisor: Sandra Davidge
Title: Effect of maternal antioxidant MitoQ treatment in a rat model of Intrauterine Growth Restriction (IUGR)
Authors: Esha Ganguly, Jude Morton, Christy-Lynn Cooke, Sandra Davidge
Affiliations: University of Alberta
Research Activity: Maternal Research : Fetal Origins of Adult Disease

INTRODUCTION

Chronic hypoxia during pregnancy, associated with intrauterine growth restriction (IUGR), has been linked to fetal programming of cardiovascular disease. A prenatal hypoxic insult reduces placental perfusion, increases placental oxidative stress, and alters gene expression in growth restricted fetuses. Placental factors released due to a stressed placenta have been known to affect fetal development of key organ systems. MitoQ is an antioxidant which, when attached to nanoparticles (nMitoQ), can be used to target maternal and placental oxidative stress without crossing the placenta. We *hypothesized* that treatment with nMitoQ will reduce hypoxia associated placental oxidative stress thus programming the placenta and fetal heart by altering DNA methylation patterns in a sexually dimorphic manner and leading to better pregnancy outcomes.

METHODS

Pregnant rats were exposed to either hypoxia (11% oxygen) or normoxia (21% oxygen) from gestational day (GD) 15-21. On GD15, the rats were intravenously injected with saline or nMitoQ. Placentae and fetal tissues were collected from male and female on GD21. Reactive oxygen species (ROS) in placenta and fetal cardiac tissues were assessed by dihydrorhodamine (DHR) staining. Whole tissue DNA methylation was determined by ELISA assay kit.

RESULTS

Prenatal hypoxia significantly increased ROS levels in placentae of female (normoxia: 0.02±0.001a.u. vs. hypoxia: 0.12±0.03a.u. $p<0.05$) but not male offspring. nMitoQ reduced the generation of ROS in female placentas exposed to hypoxia (hypoxia: 0.12±0.03a.u. vs. hypoxia+nMitoQ: 0.02±0.002a.u. $p<0.05$). Evidence of cardiac oxidative stress was significantly greater in both male (normoxia: 0.02±0.001a.u. vs. hypoxia: 0.13±0.03a.u. $p<0.05$) and female (normoxia: 0.04±0.009a.u. vs. hypoxia: 0.079±0.010a.u. $p<0.05$) hypoxic exposed offspring. nMitoQ treatment reduced cardiac oxidative stress in both male (hypoxia: 0.13±0.036a.u. vs. hypoxia+nMitoQ: 0.02±0.001a.u. $p<0.01$) and female (hypoxia: 0.08±0.01a.u. vs. hypoxia+nMitoQ: 0.04±0.003a.u. $p<0.01$) fetuses. The DNA methylation profile was significantly altered only in hearts of nMitoQ treated prenatally hypoxic male (hypoxia: 0.18±0.06a.u. vs. hypoxia+nMitoQ: 0.58±0.15a.u. $p<0.05$) offspring suggesting differential gene regulation in males and females.

DISCUSSION

Prenatal hypoxia was associated with an increased ROS production in female but not male placentae and fetal hearts of both sexes. Maternal nMitoQ reduced ROS in female placentae. Interestingly, without crossing the placenta nMitoQ was able to reduce ROS in prenatally hypoxic hearts of male and female offspring. In addition, DNA methylation patterns were altered in a sexually dimorphic manner in fetal hearts. Examining the links between physiological and epigenetic alterations may prove important in the search for potential treatments and can provide insights into the development and pathogenesis of disease.

Funded By: CIHR

Abstract #:	102
Presenter:	Dora Gyenes
Supervisor:	Lisa Hornberger
Title:	Exploring Doppler-based predictors of maternal diabetes-induced pathology through first trimester fetal echocardiography
Authors:	Dora Gyenes, Jesus Serrano-Lomelin, Venu Jain, C. Monique Bohun, Winnie Savard, Angela McBrien, Lisa Hornberger
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Cardiology

Introduction: Pregestational diabetes mellitus (DM) is relatively common in pregnancy, affecting 6-7% of women in Canada. It is well established that maternal DM is associated with the development of fetal myocardial hypertrophy in the mid and third trimesters, which is often associated with altered diastolic function. Maternal DM is also associated with fetal structural heart defects, the etiology of which remains incompletely understood. The availability of early fetal echocardiography at <15 weeks of gestation provides an opportunity to examine the influence of maternal DM on the early fetal heart and circulation shortly after the heart is formed. We sought to investigate fetal heart function and the fetal circulation in diabetic pregnancies at 8-15 week by fetal echocardiography with comparison to gestational age-matched healthy controls, and to examine the impact of glycemic control.

Methods: Through prospective recruitment, 45 pregnancies complicated by DM and 90 gestational age-matched healthy controls (2 controls: 1 DM) were identified and studied by fetal echocardiography. Parameters of fetal left (LV) and right (RV) ventricular function and the fetal circulation were measured and compared between DM and control pregnancies. Hemoglobin A1C values were also collected.

Results: Mean gestational age for both groups at fetal echo was 12.4±1.5 weeks. The LV Tei index, an index of global function, was significantly increased in fetuses of DM pregnancies (LV Tei measure: DM 0.52±0.14 vs. control 0.43±0.11, $p<0.001$). Other Doppler-based functional parameters including inflow and outflow velocities, isovolumic relaxation and contraction times, systolic and diastolic time periods, systemic venous Doppler profiles, umbilical arterial flow and heart rate did not differ between diabetic and control fetuses. Maternal HbA1C did not correlate with any functional parameter in our DM cohort.

Conclusion: Our pilot study suggests that maternal DM potentially impacts global LV function of the 8-15 week fetus. Lack of correlation with 1st trimester maternal HbA1C may further suggest altered fetal heart function could be due to additional insults in the DM pregnancy.

Funded By: Summer Studentship

Abstract #:	103
Presenter:	Kate Haynes
Supervisor:	Dr. Vivian Huang
Title:	Maternal-fetal immunotolerance in Inflammatory Bowel Disease
Authors:	Kate Haynes, Garett Dunsmore, Shokrollah Elahi, Vivian Huang
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology

Introduction

Inflammatory Bowel Disease is a group of chronic diseases characterized by inflammation of the digestive tract; it includes Crohn's disease (CD) and ulcerative colitis (UC). IBD affects many women in their reproductive ages. During pregnancy, CD71+ (an immunotolerant cell) levels rise to prevent rejection or harm to the fetus due to inflammation. Women with IBD are at higher risk for poor delivery outcomes due to decreased maternal-fetal immunotolerance. We aim to characterize the percentages of CD71+ cells in the blood samples of CD, UC and healthy patients (H) in the second and third trimester of pregnancy and associated delivery outcomes.

Methods

In this prospective study, blood samples were drawn from pregnant women with IBD and healthy volunteersonce per trimester. Blood was analyzed through flow cytometry for immunoprofiling of CD71+ cells, and compared using non-parametric statistical tests. Delivery outcomes were documented.

Results

There were 43 participants, CD=15, UC=19 and H=9. There were 6 T2 samples (1 CD, 3 UC, 2 H) and 8 T3 samples (0 CD, 3 UC, 5 H). The T2 and T3 CD71+ was much higher in the UC group (T2: UC 12.80%, H 0.34%, CD 2.28% T3: UC: 21.27%, H: 2.61%). No sample was collected for CD during T3. There were 2 preterm, no samples were collected (median GA: 33.715, IQR: 5.43) and 16 full term deliveries (median GA: 39.00, IQR: 2.355). Using the Mann-Whitney U test, the difference in CD71+ cells between CD, UC and H patients was not statistically significant (T2 p= 0.189, T3 p= 0.158) at a significance level of 0.05.

Conclusions

The CD71+ percentages are much higher in UC patients then in CD patients or H volunteers. There is an increase in CD71+ from T2 to T3, and despite the differences in values, there is not enough evidence to associate delivery outcomes with CD71+ at this time. This data is part of an ongoing study; more data is needed to come to a full conclusion.

Funded By: CEGIIR and the Division of Gastroenterology

Abstract #:	105
Presenter:	Kelycia B. Leimert
Supervisor:	David M. Olson
Title:	Optimization of a novel co-culture model to study maternal and fetal components of uterine transformation for labour.
Authors:	Kelycia B. Leimert, Angela Messer, Theora Gray, Megan Malach , Xin Fang, David M. Olson
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Pre-term Birth

Introduction: Parturition requires extensive transformation of the uterus of pregnancy into the active and contractile uterus of delivery. Uterine transformation involves amplificatory up-regulation of a series of uterine activation proteins (UAPs) and inflammatory mediators, resulting in a myometrium sensitized for contraction. This process is not isolated to the myometrium alone, but likely involves interactions with fetal gestational tissue as well. We have designed and optimized a new method to further characterize these interactions. We hypothesize that co-culture communications between maternal and fetal components will advance the transformation process, enhancing IL-6 and COX-2 responses to mediators PGF2a and interleukin (IL)-1b compared to mono-cultures of each tissue.

Methods: Primary human myometrial smooth muscle cells (HMSMC) are plated in 12- well plates with 6mm human fetal membrane explants (FME) situated above in transwell inserts (chorion facing HMSMC), to represent *in vivo* tissue orientation. Via shared culture medium, these tissues can be simultaneously stimulated with IL-1b and/or PGF2a, followed by collection of shared supernatant and extraction of RNA and protein of FME and HMSMC. We can then study IL-6 and COX-2 relative expression levels in each tissue separately in response to both mono-culture and co-culture conditions. Preliminary data n=3, ANOVA with Tukey post-hoc testing.

Results: HMSMC co-cultured with FME for 6h show a 5-fold increase in IL-6 mRNA, and a 3.8-fold increase in COX-2 mRNA, compared to HMSMC mono-cultures. Coculturing for 30h further increases expression, with a 29-fold and 6-fold increase in IL-6 and COX-2, respectively ($p>0.05$). Compared to FME mono-cultures, FME incubated with HMSMC for 6h have 19-fold higher IL-6 mRNA, and 30h co-cultures have 43-fold higher IL-6 expression ($p>0.05$). FME co-cultured with HMSMC for 6h and 30h increase COX-2 mRNA expression 5.5-fold and 6.9-fold. When stimulated with PGF2a or IL-1b, both HMSMC and FME co-cultures increase IL-6 mRNA 6 to 9 times higher than in mono-cultures. COX-2 mRNA levels are amplified in co-incubated FME (13x) and HMSMC (4x) in response to PGF2a, but only have 1.5x higher response to IL-1b.

Conclusions: Indirect contact via shared supernatant results in amplified expression of IL-6 and COX-2 in both HMSMC and FME. In addition, co-culturing increases the responsiveness of the tissues to stimulation by PGF2a or IL-1b. A better understanding of preterm and term labour physiology, especially the role of inflammatory mechanisms, is crucial. Studying *in vitro* communication between gestational layers through this novel method will expand our knowledge of human labour physiology.

Acknowledgements: WCHRI, CIHR, GAPPS.

Funded By: Graduate Studentship

Abstract #: 106
Presenter: Tania Luthra
Supervisor: Sandra Davidge
Title: Effect of STBEVs on the production of reactive oxygen and nitrogen species in endothelial cells
Authors: Tania Luthra, Floortje Spaans, Sandra Davidge
Affiliations: University of Alberta
Research Activity: Maternal Research : Preeclampsia

Preeclampsia (PE) is characterized by *de novo* hypertension with either proteinuria or end-organ dysfunction after 20 weeks of gestation. The only current treatment available involves delivery of the fetus and placenta, which increases the chances of delivering a preterm infant. The exact pathogenesis is unknown, however, failure of spinal artery remodeling is thought to result in a poorly developed and hypoxic placenta, which releases circulating factors responsible for vascular dysfunction. One of these circulating factors is syncytiotrophoblast-derived extracellular vesicles (STBEVs). STBEV levels are increased in plasma of PE women and are suspected to contribute to endothelial dysfunction in these women. We hypothesized that STBEVs induce oxidative stress-mediated damage in endothelial cells.

Human umbilical vein endothelial cells (HUVECs) were isolated and stimulated with increasing concentrations (25 ng – 2.5 µg/ml) of STBEVs (from normal pregnant placentas) for 4, 24 and 48h. Formation of superoxide was assessed with dihydroethidium (DHE), reactive oxygen and nitrogen species (ROS/RNS) via 2',7'-dichlorofluorescein (DCF) and peroxynitrite by nitrotyrosine staining. All cells were analyzed using fluorescent microscopy. STBEVs did not affect superoxide production after 4 or 24h (n=4-8) but appeared to dose-dependently increase superoxide production after 48h of stimulation (n=4). Low concentrations (25-250 ng/ml) of STBEVs appeared to increase ROS/RNS at 24 and 48h (n=1-3). Peroxynitrite production was unchanged after 4 and 24h of STBEV-stimulation (n=4), but appeared higher after 48h (n=2).

Hence, STBEVs may induce low levels of oxidative stress in endothelial cells. Future investigations will increase the n-numbers to verify these results. This investigation will improve our understanding of PE and contribute to potential therapeutic strategies in the future.

Funded By: Support services

Abstract #: 107
Presenter: Jihee Yoo
Supervisor: Stephane Bourque
Title: The effect of prenatal iron deficiency on UCP-1 expression in brown adipose tissue
Authors: Jihee Yoo, Stephana Cherak, Stephane Bourque
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Nutrition

Introduction:

Iron deficiency (ID) is the most common nutritional disorder in the world. Prenatal ID has shown to reprogram offspring adipose tissue, altering the developmental trajectory of the fetus and predisposing offspring to fat accumulation an obesity in later life. Brown adipose tissue (BAT) is a highly metabolically active tissue with a tremendous capacity to expend energy, due to the uncoupling protein-1 (UCP-1) expressed within BAT mitochondria, which acts to uncouple the electron transport chain proton gradient to generate heat. Here, we examined that prenatal ID chronically alters the thermogenic capacity of BAT to precipitate an obese phenotype in the adult offspring.

Methods:

Female Sprague Dawley rats were fed either a control or an iron-restricted diet prior to and throughout gestation. At birth, dams were given normal rat chow, and offspring were weaned onto a high-fat/high-sucrose 'Western diet' at 3 wk of age. At 4 wk of age, offspring were randomized to the chronic cold exposure group (4˚C, 12 h/day, 5 wk) or the room temperature (22˚C) group. Intrascapular BAT was collected directly following cold exposure and analyzed for UCP-1 expression using routine Western Blot analysis.

Results:

Prior to cold exposure, both male and female prenatal ID offspring exhibited lower body weight compared to respective controls. Western diet caused male, but not female, prenatal ID offspring to gain excessive weight. Chronic cold exposure caused increases in BAT mass in all offspring ($P<0.01$ for all groups) with corresponding increases in UCP-1 expression ($P<0.001$ for all parameters), albeit this increase was mitigated in female prenatal ID offspring.

Conclusions:

Taken together, these data show that prenatal ID causes sex-specific programming of BAT quantity and thermogenic capacity. These metabolic changes may underlie the long-term programming of metabolic function by prenatal ID.

Funded By: Start-up or Retention Funding and Innovation Grant

Abstract #:	108
Presenter:	Charlene Nielsen
Supervisor:	Alvaro Osornio Vargas
Title:	Spatial relationships of Alberta's outdoor environment and really small newborns
Authors:	Charlene Nielsen, Alvaro Osornio Vargas, Carl Amrhein
Affiliations:	University of Alberta
Research Activity:	Low birth weight, Small for gestational age, Environmental health

Introduction
The importance of place - where one lives, and even starts out in life during fetal development – contributes to lifelong health. Environmental exposures that mothers experience during pregnancy may contribute to adverse birth outcomes. Newborns that are too small or too early are the second leading cause of infant death in Canada, or may lead to physical/mental disabilities and chronic health problems later in life. The province of Alberta has higher rates than Canadian averages, and has been increasing since 2000. We examined the coincidence of maternal ambient health hazards with births that are small for gestational age (SGA: below tenth percentile weight for pregnancy duration) and low birth weight at term (LBW: less than 2,500 grams at 37 or more weeks gestation).

Methods
A Geographic Information System (GIS) was used to calculate and map outdoor pollutant/hazard estimates – a common source of shared maternal exposures. These were overlaid with double kernel densities (DKD) of SGA and LBW from Alberta registered births for 2006-2012. DKD were calculated as ratios of the spatial distributions of each birth outcome divided by spatial distributions of total births, and are not constrained by geographical or administrative boundaries. Spearman's rank correlations were examined for relationships. Standard deviational ellipses were generated to help understand central tendency, dispersion, and directional trends of SGA, LBW, and the potential pollutant sources having higher correlations.

Results
Positive associations with most built-environmental sources were found. Density of roads, emissions of particulate matter and sulphur dioxide had Spearman correlation coefficients from 0.46 to 0.25. Negative associations with numbers of oil and gas wells and proportion of cropland were between -0.54 to -0.30. Standard deviational ellipses showed that higher correlations closely matched the direction and size of the SGA/LBW ellipses, which were concentrated north-south along Alberta's core of major cities. Negative associations had less overlap, with a slight northwest-southeast trend.

Conclusion
We examined spatial relationships for the entire time period and although weakly associated are consistent with the scientific literature. SGA and LBW is typically an urban issue and coincides with transportation and industrial pollutant sources. Annual variation, additional chemicals, and choice of radii for the densities (what distance some of these other factors may have associations) will need further investigation. Our ongoing research is part of the Data Mining and Neonatal Outcomes (DoMiNO) project, which may provide insight to support preventative or remedial policies where they CIHR, NSERC may be needed.

Abstract #:	109
Presenter:	Hein Min Tun
Supervisor:	Anita Kozyrskyj
Title:	How pets make our babies healthier: Their influence on gut microbiome of infants following caesarean delivery
Authors:	Hein Min Tun, Tedd Konya, David Guttman, Allan Becker, Piush Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, James Scott, Anita Kozyrskyj
Affiliations:	University of Alberta
Research Activity:	Development of infant gut microbiota (SyMBIOTA)

Purpose

Infants born by cesarean section exhibit a dysbiosis in gut microbiota which are important for immune gut maturation and barrier function. We, and others, have found that household pets can alter infant gut microbial diversity and composition. In this study, we examined the impact of prenatal and postnatal pet exposures on fecal gut microbiota of infants born by cesarean versus vaginal delivery.

Methods

The study population comprised 746 infants enrolled at Edmonton, Vancouver and Winnipeg sites of the Canadian Healthy Infant Longitudinal Development (CHILD) population-based birth cohort. Gut microbial diversity and composition at 3 months and 1 year after birth was assessed using high-throughput 16S rRNA sequencing. Delivery method recorded in the birth chart was defined as vaginal (with or without intrapartum antibiotic prophylaxis, IAP), elective cesarean and emergency cesarean. Pet exposure (prenatal and postnatal at 3 months of infant age), ethnicity and other covariates were retrieved from the standardized questionnaires completed by mothers. Statistical analyses were performed in SAS V9.4. Infant gut microbial profiles according to pet exposure and delivery mode, and adjusted for ethnicity, were examined by linear discriminant analysis effect size (LEfSE) with an LDA log score cut-off of 2.

Results

In total, 53.9% of the households reported owning ≥ 1 furry pet while the mother was pregnant and 47% when the infant was 3 months old. Statistically significant differences in prenatal pet ownership were observed by ethnicity, with higher rates reported by Caucasian than Asian women. Regardless of ethnicity, a 7-10% reduction in pet ownership was seen postnatally at 3 months. With prenatal pet exposure alone, a trend of higher microbial species richness was observed in fecal samples of infants regardless to their delivery mode. Pet exposure at both pre- and postnatal increased the relative abundance of genus *Oscillospira* (p=0.04) with 3 folds increased risk (OR 3.13) in infants at 3 months who were born by elective cesarean. Among infants born by emergency cesarean, pet exposure at both pre- and postnatal increased the abundance of two genera including *Ruminococcus* (p=0.01) and *Oscillospira* (p=0.02) with more than 2 folds increased risk (OR 2.53 and 3.54 respectively).

Conclusions

This study provides new evidence that exposure to pets can modify gut microbial composition of infants following cesarean delivery, which may confer future health benefits for infants.

Funded By: Trainee Travel Grant

Abstract #: 110
Presenter: Samaneh Khanpour Ardestani
Supervisor: Sunita Vohra
Title: Parents and clinicians' opinions about probiotic therapy in prevention of pediatric antibiotic-associated diarrhea
Authors: Samaneh Khanpour Ardestani, Joan Robinson, Hien Huynh, Levinus Dieleman, Hsing Jou, Sunita Vohra
Affiliations: University of Alberta

Background: Probiotic therapy may be effective in preventing pediatric antibiotic-associated diarrhea (AAD). Some limitations in previous studies include a lack of patient or formal clinician input in the determination of minimal important difference (MID) and selection of relevant outcomes.

Objectives: a)To establish the MID that would prompt parents and clinicians to use probiotics to prevent AAD and b)To obtain parents and clinicians' opinion about the most important outcomes in clinical trials of AAD.

Methods: In this survey, parents of children presenting to the emergency department of a Canadian tertiary care children's hospital and pediatricians working in that hospital were approached. A range of potential MIDs were presented and participants selected the MID that they would require to use probiotics for AAD prevention. Additionally, participants were asked to rate a list of outcomes they would consider to be important in clinical trials of AAD.

Results: In total, 127 parents and 45 pediatricians were recruited. Sixty four parents (56%) and 21 clinicians (51%) reported they would use probiotics if it would reduce the risk of AAD by 40% (i.e. reduce the risk of AAD from 19% to 12%; yielding a Number Needed to Treat of 13 and a relative risk of 0.61. In comparison to parents, pediatricians more frequently "agreed" or "strongly agreed" that probiotics were "effective" (34 (77%) clinicians vs. 60 (48%) parents, p=0.002) and "safe" (43 (98%) clinicians vs. 76 (62%) parents, p=0.001) for prevention of AAD. Three (2.5%) parents and none of the clinicians "disagreed" or "strongly disagreed" that probiotics were safe for prevention of AAD. Stool consistency and frequency, diarrhea duration, prevention of dehydration, disruption of normal daily activities, need for hospitalization and physician revisit were among the most important outcomes both groups required to be measured in clinical trials of AAD.

Conclusion: There is good agreement between parents and clinicians regarding how effective probiotics would need to be in preventing AAD to warrant use. This information along with outcomes they perceived important will help designing future trials.

Funded By: Graduate Studentship

Abstract #:	111
Presenter:	Jessica Wu
Supervisor:	Justine Turner
Title:	Does registered dietitian counseling improve the knowledge of Celiac Disease in parents of children with Celiac Disease?
Authors:	Jessica Wu, Daniela Migliarese Isaac, Diana Mager, Justine Turner
Affiliations:	Nutrition Services (Child Health), Alberta Health Services
Research Activity:	Child and Youth Development : Nutrition

Introduction: Multidisciplinary care is important in the care of patients with celiac disease (CD), however there is a gap in the literature regarding the specific role of the Registered Dietitian (RD) in education for families with children with CD. We aimed to determine whether dietetic counseling by the RD improved knowledge about CD and the gluten-free diet (GFD) in caregivers (parents or guardians) of children newly diagnosed with CD.

Methods: A 22 item survey was administered to caregivers of children with newly diagnosed CD before and after a 60 to 90 minute counseling session with an RD at the Stollery Children's Hospital in Edmonton, Alberta. Survey questions included demographic questions about the parent's education level, sex, and age; questions about general knowledge of celiac disease and treatment; and questions regarding the gluten content of thirteen common foods that RDs identified as foods most often asked about during teaching sessions. Caregivers were also asked which sources of information about a GFD they utilized prior to dietetic counseling, and were asked to rate the usefulness of those sources of information.

Results: Twenty-six caregivers (80% mothers, aged 30 to 39 years) completed the before and after survey between January and June 2016. The ability of caregivers to correctly identify gluten-free or gluten-containing food was significantly improved (71.7% before versus 88.2% after, p=0.004). At baseline, 80% of the caregivers were aware that the GFD was the treatment for CD, increasing to 100% post dietitian counseling (p=0.03). Prior to RD counseling, only 57% of caregivers recognized the treatment requirement was an absolute gluten-free diet (GFD), and 37% reported not knowing if some gluten intake was acceptable. After counseling, 92% correctly identified that the requirement was for an absolute GFD (p=0.05). The internet was the most utilized resource (86% of caregivers), followed by another person with CD (68%), cookbooks (45%), and newspapers/magazines (45%).

Conclusion: RD counseling improved caregiver knowledge of CD and the GFD. These results highlight the essential contribution of an RD in providing care to CD patients. As the quality of information on the internet and other CD patients can be variable, these sources should not be relied upon for teaching on the GFD. Expert RD counseling can provide accurate, informative, and personalized counseling to families to ultimately encourage better health outcomes for the child with CD.

Abstract #:	112
Presenter:	Ryan Fung
Supervisor:	David Eisenstat
Title:	Tales from the Crypt: Regulation of intestinal stem cell markers Lgr5 and Bmi-1 by DLX2 during intestinal development and regeneration
Authors:	Ryan Fung, Hunter McColl, David Eisenstat
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities

Short bowel syndrome is a condition where patients are unable to properly absorb sufficient nutrients from their diet due to missing sections of their small intestine. This condition is prevalent in premature or sick infants that suffer from neonatal necrotizing enterocolitis (NEC), a condition where the small intestine can become ischemic. Treatment of neonatal NEC may require surgical resection of non-viable small intestine. The purpose of this project is to determine the effect of the homeobox transcription factor, DLX2, on expression of the intestinal stem cell markers Lgr5 and Bmi-1 during intestinal development, with relevance to NEC and other causes of short bowel syndrome. DLX2 is expressed in the embryonic gastrointestinal tract (GIT). Intestinal stem cells are the precursors for many different cell types in the intestine where Lgr5+ stem cells are important for maintaining the intestinal mucosa while Bmi-1+ stem cells are important for epithelial renewal after injury. To date, our lab's preliminary data shows that DLX2 and BMI-1 are co-expressed in the crypts of the small intestine of mice and that DLX2 occupies the Bmi1 gene promoter in vivo. Current assays being conducted include chromatin immunoprecipitation, immunohistochemistry, immunofluorescence, and quantitative real-time polymerase chain reaction towards determining the interaction between DLX2 and the Lgr5 promoter. We predict that if DLX2 represses the expression of Lgr5 and Bmi-1 in embryonic and adult intestinal tissue, then DLX2 expression may prevent differentiation of mature and functional intestinal cells required for nutrient absorption. Regenerative strategies to restore intestinal cell function in children with short bowel syndrome will have to incorporate our understanding of the gene network controlled by DLX transcription factors.

Funded By: AIHS

Abstract #:	113
Presenter:	Maha Alsaif
Supervisor:	Andrea Haqq, Carla Prado
Title:	Fasting and postprandial glucose, insulin and GLP-1 levels in children with Prader-Willi Syndrome
Authors:	Maha Alsaif, Michelle Mackenzie, Carla Prado, Andrea Haqq
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition

Background: Prader-Willi Syndrome (PWS) is a unique clinical model of severe childhood obesity with increased insulin sensitivity. The incretin hormone, glucagon-like peptide 1 (GLP-1), has potent effects to stimulate insulin secretion in response to glucose; however, it is not clear if GLP-1 levels are altered in children with PWS. Therefore, the purpose of our study was to compare fasting and acute postprandial concentrations of glucose, insulin and GLP-1 in children with and without PWS.

Methods: Ten children with PWS and seven controls completed three separate study visits. A fasting blood sample and anthropometric measurements were completed at each study visit. Participants consumed one of the following breakfast meals at each visit: standard (350kcal, 55%CHO, 30%fat, 15%PRO), higher protein/lower carbohydrate (350kcal, 40%CHO, 30%fat, 30%PRO), higher protein/lower fat (350kcal, 55%CHO, 15%fat, 30%PRO). Blood samples were taken at 60-minute intervals for 3 hours after the meal.

Results: PWS and controls were of similar age and BMI-z score. PWS had lower fasting levels of glucose (p=0.033) and showed a trend (although not significant) for lower insulin and HOMA (p=0.055 for both) at baseline. Fasting GLP-1 levels in PWS children were comparable to controls. Fasting and AUC values of GLP-1 were not correlated with glucose and insulin. Glucose concentration increased over time in the PWS group (p=0.031) but not in the controls. However, insulin and GLP-1 concentration increased over time in both PWS (p<0.0005 and p=0.001) and control groups (p=0.003 and p=0.013). Postprandial absolute glucose and insulin levels were higher in the PWS group compared to the control group at three hours (p=0.003 and p=0.005, respectively) following the meal. PWS had higher glucose relative to fasting at 3 hours and higher insulin relative to fasting at 1, 2, and 3 hours compared to controls. Glucose, insulin and GLP-1 AUC were not different between meals in the control group. However, insulin AUC was higher in response to the higher protein/lower fat meal than the higher protein/lower carbohydrate meal in the PWS group only (p=0.048).

Conclusion: This study indicates thatfasting glucose is lower while insulin and HOMA trend to be lower in PWS, suggesting that PWS children are more insulin sensitive than controls. Fasting GLP-1 levels were comparable in PWS and control children, suggesting that it is not the primary driver of insulin sensitivity in PWS. The prolonged insulin and glucose response in PWS are suggestive of insulin resistance, implying potential abnormalities in glucose control.

Funded By: Innovation Grant

Abstract #:	114
Presenter:	Ghazal Danesh
Supervisor:	Eytan Wine
Title:	Bacteria isolated from terminal ileum washings of pediatric Crohn disease patients activate the NLRP3 inflammasome
Authors:	Ghazal Danesh, Michael Bording-Jorgensen, Deenaz Zaidi, Misagh Alipour, Eytan Wine
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Infection, Inflammation, Immunology

INTRODUCTION: The nod-like receptor protein-3 (NLRP3) inflammasome is a multi-protein complex that leads to immune activation and has been linked to Crohn disease. It is responsible for the maturation and secretion of the proinflammatory cytokine, interleukin (IL)-1β. The production of reactive oxygen species (ROS) is increased with inflammasome activity and is thought to activate NLRP3 through an unknown mechanism. We hypothesize that this pathway contributes to Crohn disease through effects on bacterial killing, based on previous work in our lab. In this pilot study, we isolated and characterized bacteria from terminal ileum (TI) washings collected during endoscopy of two patients with Crohn disease and one without. To investigate the effect of bacteria from different sources on inflammasome activation, IL-1β and ROS production were measured in infected THP-1 human monocytes.

METHODS: We devised a new method to co-culture aerobic THP-1 cells and facultative or strict anaerobic bacteria isolated from the TI washings of pediatric patients with and without Crohn disease. To prompt infection, THP-1 cells were grown on coverslips and placed onto a lawn of bacteria grown on agar in the wells of a 24-well plate. Medium was added to these wells and collected after two hours. This medium was used to analyze IL-1β and ROS generation.

RESULTS: Bacteria from Crohn disease patients induced greater overall IL-1β and ROS production. We identified two bacterial species isolated from these patients that increased IL-1β secretion, while some bacteria did not elicit any IL-1β release. There was significant variation in inflammasome responses for different bacteria.

CONCLUSION: Bacteria isolated from pediatric patients with Crohn disease result in increased IL-1β and ROS production, suggesting an increase in inflammasome activation, compared to a non-disease control. However, there was significant variation in inflammasome responses for different bacteria. Further work will focus on defining patient and bacterial factors that contribute to inflammatory bowel diseases to better manage Crohn disease in pediatric patients.

Funded By: Summer Studentship

Abstract #:	115
Presenter:	Krista MacDonald
Supervisor:	Diana Mager
Title:	Body composition, handgrip strength, dietary intake, physical capacity & markers of cardiometabolic & liver dysfunction in children with NAFLD & PWS.
Authors:	Krista MacDonald, Andrea Haqq, Jason Yap, Diana Mager
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition

Introduction: The study purpose was to describe and contrast body composition and markers of muscle strength, dietary intake, physical capacity, cardio-metabolic and liver dysfunction in obese children with nonalcoholic fatty liver disease (NAFLD) and Prader-Willi Syndrome (PWS).

Methods: Children aged 7-18 years with NAFLD (n=7), PWS (n=9) and healthy lean controls (n=14) were recruited from the Stollery Children's Hospital and the community. Anthropometrics (weight, height, circumferences, skinfolds), body composition (Dual X-ray absorptiometry;DXA), handgrip strength (HGS), 6 minute walk test (6MWT), dietary intake (3-day food record, glycemic index; GI, glycemic load; GL and Canadian healthy eating index; HEI-C), cardiometabolic and biochemical (blood pressure, triglyceride (TG), total-cholesterol (TC), HDL-and-LDL-cholesterol, glucose, insulin) measures were assessed. Insulin resistance was assessed using the homeostasis model of insulin resistance (HOMA-IR).

Results: Overall meanage was 12.6 ± 3.4 years, with no differences between groups ($p>0.05$). NAFLD and PWS children had higher weight-z, BMI-z, waist-to-height-z ratio, waist-circumference-z, insulin and HOMA-IR values compared to healthy controls ($p<0.05$). However, NAFLD children had significantly higher WC-z, BMI-z, bicep skinfolds and fasting concentrations of ALT when compared to PWS children ($p<0.05$). PWS children had a trend towards lower serum insulin levels ($p=0.06$) and HOMA-IR values ($p=0.07$) compared to NAFLD children. No other differences in biochemical (TG, HDL, LDL, TC, glucose) measures were observed between NAFLD and PWS, although NAFLD children had significantly higher values for TG, LDL, TC and lower values for HDL than controls ($p<0.05$). Body fat% was 43.3% and 44.9% in NAFLD and PWS children, respectively ($p>0.05$). Children with PWS had significantly lower HGS compared to NAFLD ($p=0.01$) and control children ($p<.001$). There was a positive correlation between fat free mass and HGS ($p<0.01$). NAFLD and PWS children had a significantly lower total distance walked in the 6MWT than controls ($p<0.05$), but no differences between PWS/NAFLD children were observed ($p>0.05$). Children with PWS had higher HEI-C scores (81 ± 5) than NAFLD (67 ± 17) or healthy controls (66 ± 9), but no differences in macro-and micronutrient, GI or GL intake.

Conclusion: Obese children with NAFLD/PWS experienced similar derangements in cardio-metabolic markers, body composition and functional physical scores when compared to lean children. However, PWS children demonstrated significantly reduced muscle strength when compared to NAFLD or lean children. Further investigations elucidating the potential factors influencing these findings are warranted

Funded By: Graduate Studentship

Abstract #:	116
Presenter:	Jordan Rycroft
Supervisor:	Radha Chari
Title:	The impact of premature rupture of membranes and gestational age on infant gut microbiota at three months
Authors:	Jordan Rycroft , Rebecca Entz, Mon Tun , Tedd Konya, David S Guttman, Allan B Becker, Piush J Mandhane, Stuart E Turvey, Padmaja Subbarao, Malcolm R Sears, James A. Scott, CHILD Study Investigators, Radha Chari, Anita L. Kozyrskyj
Affiliations:	University of Alberta

Introduction: Bacterial colonization in early life facilitates establishment of the infant gut microbiome, initiating the development of the human mucosal immune system. Recent studies have demonstrated that mode of delivery, intrapartum antibiotic prophylaxis, and infant breastfeeding can influence the developing microbiome, though additional pre-birth and birth characteristics have yet to be addressed. Our study looks at the impact of the premature rupture of membranes (PROM) and the gestational age (GA) on the developing microbiome of the infant at three months.

Methods: Data from 917 late preterm to full term infants who were enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort, were analyzed to determine if PROM and the GA at delivery altered microbiota profiles of infant fecal samples at three months, sequenced at the V4 region of the 16SrRNA gene. Gut microbial composition was measured by taxon relative abundance and groups differences tested by Mann-Whitney. To adjust for birth and infant diet factors, comparisons were restricted to exclusively breastfed infants who were vaginally delivered and whose mothers received no intrapartum antibiotic prophylaxis (IAP).

Results: In our study population, 27.3% of infants were exposed to PROM and 4.3% were late pre-term (< 37 weeks), 23.6% were early term (37-38 weeks), 56.6% were full term (39-40 weeks), and 15.5% were late term (41 + weeks).We found changes by PROM and GA within exclusively breastfed infants who were vaginally delivered and not exposed to IAP[AK1] [JR2] . Among infants exposed to PROM, we found significant decreases in the relative abundance of species *Eggerthella lenta* (0.02), *Bacteroides fragilis* (0.002), and *Bacteroides uniformis* (0.039), as well as increases to genus Clostridium (0.004) and Peptostreptococcaceae (0.003). In late term infants, there was a significant increase in the levels of both Bifidobacteriaceae (0.053) and Veillonellaceae (0.043) compared with early term infants. In comparison to the full term group, a significant increase in Coricobacteraceae (0.019) and decrease in Enterobacteriaceae (0.032) was found for the late term group.

Conclusions: Both PROM and GA may impact the development of the infant gut microbiome, independent of birth mode and infant nutrition. Therefore, these perinatal factors require further research to expand our understanding of a possible link between pregnancy, obstetrical management, and child health outcomes.

Funded By: Summer Studentship

Abstract #:	117
Presenter:	Justine Klaver-Kibria
Supervisor:	Irena Buka
Title:	Indoor air quality and asthma in children: A review of residential indoor air quality hazards with a special focus on renovations and indoor chemicals
Authors:	Justine Klaver-Kibria, Irena Buka, Lesley Brennan
Affiliations:	Children's Environmental Health Clinic
Research Activity:	Child and Youth Development : Lung Development

Introduction:

Asthma is a disorder in which inflammation of the airways is precipitated by specific or non-specific stimuli in the environment. Over the past several decades, an exponential growth in, and use of, home building materials, furnishings, and personal care products has occurred. The chemical emissions from these common indoor products are becoming a concern for children's environmental health and asthma research.

Methods:

Using PubMed and Embase databases, we reviewed the literature on indoor residential chemical pollutants and childhood asthma (0-18 years) from 2005 to 2015. Only studies published in peer-reviewed journals and in the English language were included. Asthma exacerbation in the home environment (not schools or daycares) was the health outcome. Although, indoor chemical pollutants and renovations are mainly a 'developed world' phenomenon, we did consider studies from anywhere around the world, with the exclusion of research that included biomass burning. We also excluded studies that compared rural (or farm living) to urban populations because of confounding. Keywords include: volatile organic compounds (VOCs), benzene, toluene, phthalates, aromatic hydrocarbons, Halogenated Diphenal Ethers, pesticides, formaldehyde, chlorinated hydrocarbons, xylene, flame retardants, renovation, paint, floor coverings, construction materials, housing, and polyvinyl chloride (PVC).

Results:

In total 22 articles met our inclusion criteria. Literature generally fell into four categories: volatile organic compounds (VOCs) (n=8), phthalates (n=6), renovations (n=6) and multiple pollutants (n=1) (one review study spanned three categories, for a total of 22 articles). In line with previous research, our review supports the association between increased childhood asthma and indoor chemical pollutants such as formaldehyde, recent renovation, PVC building materials and painting. We found weak or inconclusive evidence of an association between phthalates and asthma in children.

Conclusions:

A growing body of epidemiological evidence suggests that chemical pollutants in the home environment are associated with childhood asthma.

Funded By: CHRC Seed Research Grant

Abstract #:	118
Presenter:	Tim Dalmer
Supervisor:	Robin Clugston
Title:	Retinoic acid signalling and congenital diaphragmatic hernia-associated genes: evidence from humans and mice
Authors:	Tim Dalmer, Robin Clugston
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities

Introduction: Congenital diaphragmatic hernia (CDH) is a debilitating diseaseaffecting approximately 1 in 3,000 live births, greatly impacting a newborn's ability to survive. Caused by incomplete development of the diaphragm, CDH results in improper separation of the thoracic and abdominal viscera. This affects lung development, triggering pulmonary hypoplasia and hypertension, which greatly restricts a newborn's ability to breathe. Retinoic acid, the active metabolite of Vitamin A, has been an area of focus in understanding the ambiguous etiology of CDH. The retinoid hypothesis states that abnormal retinoic acid signaling in the developing diaphragm is a key factor in CDH development and in need of further study. Our goal is to compile a database of known CDH-associated genes and assess their expression in the developing murine diaphragm. Methods: Candidate genes are identified from articles reporting genetic anomalies in CDH patients as well as CDH murine model studies. Expression analysis is accomplished by RT-PCR of extracted murine diaphragm mRNA using gene-specific primers. We will measure mRNA levels at differing stages of gestation, creating a timeline of each gene's expression pattern throughout diaphragm development. Results: We have compiled a list of more than 150 CDH-associated genes, and categorized them according to various criteria, including retinoid activation/signalling, phenotype of the diaphragm defect, and CDH occurrence in humans and mice. Conclusion: Understanding the role of retinoic acid in diaphragm development and the ability to identify mutations associated with CDH as early as possible is key towards enabling the best chance of survival for CDH newborns.

TRAD was supported by an Office of the Provost and VP (Academic) Undergraduate Summer Research Award. The Clugston Lab is gratefully supported by a WCHRI Innovation Grant.

Abstract #: 119
Presenter: Giseon Heo
Supervisor:
Title: Contribution of craniofacial form to the pathogenesis of pediatric obstructive sleep apnea
Authors: Giseon Heo, Matthew Pietrosanu, Mathieu Chalifour, Steven Luoma
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Sleep and Breathing Disorders

Introduction

Obstructive sleep apnea (OSA) is a substantial health concern occurring in 1-5% of children. Although the peak period for pediatric OSA development is during adenotonsillar hypertrophy, not all children with large tonsils and adenoids develop the condition, suggesting that airway size is of greater importance in the presentation of OSA. It is well-known that airway size is dictated by craniofacial form, particularly of the cranial base, maxilla, and mandible, and changes most rapidly during childhood. An understanding of the contribution of craniofacial form to the occurrence of pediatric OSA may therefore lead to childhood treatment options that will prevent further progression of OSA into adulthood, substantially decrease health-care utilization, and increase overall quality of life. We hypothesize that craniofacial form is strongly associated with OSA severity and can be used to indirectly and independently of the current polysomnographic gold standard to asses OSA risk in children.

Methods

Children aged 2-17 have been recruited through the Stollery Clinic at the University of Alberta Hospital since October 2015. All participants undertook a polysomnography (PSG) exam, the current gold standard in the diagnosis of pediatric OSA. Furthermore, patients also have 3D photos taken of their faces at the Graduate Orthodontics Clinic at the University of Alberta. These 3D photos are analyzed in two different ways: (i) an orthodontist evaluated the photos and categorized patients into 4 groups in terms of predicted OSA severity (minimal, mild, moderate, or severe), and (ii) the shape of the face was analyzed using a statistical technique inspired by Moire topography that combines methods from geometric and topological data analysis.

Results

We developed a new shape analysis technique, called heatmap pseudo-multifiltration that generalizes existing methods in geometric and topological data analysis. We demonstrated and validated our new technique on pre-segmented maxillary sinus data.

Conclusions

Our method has demonstrated its ability to detect differences in curves or surfaces. We are continuing our analysis of the faces of pediatric OSA patients and plan to present our results at the WCHRI Research Day on November 16.

This research is conducted jointly with Matthew Pietrosanu, Mathieu Chalifour, and Steven Luoma, and is funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute, NSERC, and the McIntyre Memorial Fund in the School of Dentistry.

Funded By: Seed Grant

Abstract #: 120
Presenter: Brianne St. Hilaire
Supervisor: Silvia Pagliardini
Title: A new chemogenetic rodent model of central sleep apnea
Authors: Brianne St. Hilaire, Xiu Ding, Silvia Pagliardini
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Sleep and Breathing Disorders

Introduction

Central sleep apnea (CSA) is a condition marked by a cessation of breathing caused by decreased inspiratory drive from respiratory rhythmogenic neurons within the brainstem, in an area known as the pre-Bötzinger complex (pre-BötC). CSA is implicated in several disorders in children, including sudden infant sleep disorder (SIDS), apnea of prematurity, and cardiovascular disorders. There are currently no effective treatments for CSA, which necessitates the development of an animal model in order to test potential therapies. This project aimed to create a model of CSA in rats using a chemogenetic approach, in which a genetically modified opioid receptor (KORD) is expressed through a viral vector in pre-BötC neurons. The receptors can then be activated by their exogenous ligand, Salvanorin B (SalB), leading to hyperpolarization of inspiratory neurons, and causing apneas.

Methods

In our experiment, two viruses expressing the KORD receptors were injected in the pre-BötC through a stereotactic surgery, and rats were then implanted with EEG and EMG electrodes to identify sleep states and respiratory muscle activity, respectively. After recovery, respiratory disturbances were monitored using plethysmographic studies. Three weeks after viral infection, rat were tested for respiratory and sleep behavior in control conditions and after systemic application of SalB. Immunohistochemistry was performed on rat brainstems after the experiment to confirm virus localization in the pre-BötC.

Results

While rats did not display respiratory disturbance in control conditions, hyperpolarization of pre-BötC neurons with SalB induced frequent apneas during sleep. Respiratory disturbances increased from 6 apneas/hour in control conditions, to 20 apneas/hour with administration of SalB. In addition, apnea length increased during experimental conditions.

Conclusions

We conclude that KORD expression in the pre-BötC can be used as a rodent model for CSA in our laboratory in order to further test mechanisms and therapies related to sleep disordered breathing. We will use this method in order with other chemogenetic models to test the phenomenon of abdominal recruitment during sleep, which has been associated with stabilization of breathing after apneas.

Funded By: AIHS

Abstract #:	121
Presenter:	Alexandra Bain
Supervisor:	Jane Schulz
Title:	Improving access to health information regarding Pelvic Floor Disorders to a urogynecology clinic population
Authors:	Alexandra Bain, Jane Schulz, Momoe Hyakutake
Affiliations:	University of Alberta
Research Activity:	Women's Health : Urology/Gynecology

Introduction

Pelvic floor disorders (PFDs) occur as a result of weakness or injury to the pelvic floor. Common presentations include urinary incontinence, fecal incontinence, and pelvic organ prolapse. Approximately one in four women over age twenty will experience at least one PFD, increasing to one in two women by the age of fifty. Despite this high prevalence, many women do not seek medical help due to embarrassment, myths regarding cause, and uncertainty about treatment options. Our study objective was to determine the preferred medium for providing health information and education regarding PFDs to our patient population.

Methods

We developed and distributed a survey to women attending the tertiary care urogynecology clinic at the Lois Hole Hospital for Women. The survey inquired about their current sources of health information, their comfort level using electronic health information tools, and their preferences for various health information delivery methods, including face-to-face encounters and online tools such as vodcasts.

Results

The survey response rate was 88% (221 surveys were distributed, of which 194 were completed). 40% and 60% survey participants were new patients and returning patients, respectively. Out of the 194 surveys completed, it was determined that 86% of patients own a computer and 76% of patients access the internet daily via their electronic source of choice. 77% of patients access health information online however, only 20% of patients are familiar with My Health Alberta website, which is a website promoted by Alberta Health Services as a reliable electronic resource for health information. 82% of patients said they would find it useful to have online health information provided by their urogynecology clinic. The preferred modes of health information delivery included one on one sessions with a health professional, an online vodcast accessible at any time, and printed handouts.

Conclusion

These results strongly suggest that the patient population accessing the urogynecology clinic for PFDs would benefit from more innovative and accessible health information regarding their gynecological concerns.

Funded By: Summer Studentship

Abstract #: 122
Presenter: Daniel Nisakar Meenakshi Sundaram
Supervisor: Hasan Uludag
Title: Targeting integrin-β1 to reduce attachment and migration of breast cancer cells
Authors: Daniel Nisakar Meenakshi Sundaram, Cezary Kucharski, Manoj Parmar, Remant Bahadur KC, Hasan Uludağ
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology

Purpose: Cell surface integrins, which play important role in the survival, proliferation, migration and invasion of cancer cells, is a viable target for treatment of metastatic breast cancer. This line of therapy still remains challenging due to the lack of proper identification and validation of effective targets as well as the lack of suitable therapeutic agents for treatment. We have focused on one such molecular target for this purpose, namely integrin-β1 and achieved effective lowering of integrin-β1 levels on a breast cancer model (MDA-MB-231 cells) by delivering a dicer substrate siRNA targeting integrin-β1 with lipid-modified low molecular weight polyethylenimine (PEI) polymers anticipating the breast cancer cells to attach less as well as reduce their ability to migrate.

Methods: Integrin β-1 silencing experiments were carried out in MDA-MB-231 breast cancer cells through Immunostaining, qRT-PCR, fibronectin-binding, human Bone Marrow Stromal Cell (hBMSC) adhesion, scratch (migration) assay and Transwell migration assay.

Results: Three specific lipopolymers with different lipid substitutions displayed effective silencing at 40 nM siRNA concentration based on immunostaining of cell-surface integrin β-1, but 1.2PEI-LA (with linoleic acid substitution) exhibited the best silencing among them. The surface level of integrin β-1 was significantly silenced after treating with 1.2PEI-LA/siRNA complexes, and similarly the mRNA levels were also strongly silenced till day 9. The functionality of this effective silencing was assessed by studying its ability to attach to fibronectin and human bone marrow stem cells as integrin β-1 is a primary receptor for fibronectin. In both these assays, significant reduction in the cell attachment was observed in 1.2PEI-LA treated cells. Finally, the well-established scratch assay as well as Transwell migration revealed strong inhibition in the migration of MDA-MB-231 cells.

Conclusions: Silencing integrin β-1 gene in invasive MDA-MB-231 cells was shown to be feasible with a practical dose of specific siRNA, which was effectively delivered by non-viral (polymeric) carriers. Both the fibronectin binding and hBMSC adhesion assay showed that the extent of integrin silencing at cell surface was adequate to reduce its binding and the Transwell as well as scratch assays showed reduction in their migration ability thereby revealing the functional benefit of integrin β-1 silencing. In addition to silencing integrin β-1, identifying other targets could be beneficial to fully reduce the attachment and migration of breast cancer cells. Nevertheless, this study provides a viable method to specifically abolish an important mechanism behind breast cancer metastasis.

Funded By: CBCF, NSERC, Canada-China Initiative Grant provided by the U. of Alberta Office of Research

Abstract #:	123
Presenter:	Beate Sydora
Supervisor:	Sue Ross
Title:	Change over time in patient-reported symptoms and quality of life in Edmonton's interdisciplinary menopause clinics
Authors:	Beate Sydora, Vikas Chadha, Nese Yuksel, Lori Battochio, Lori Reich-Smith, Shelly Hagen, Tami Shandro, Sue Ross
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mature Women's Health

Introduction:

Symptoms experienced by women during menopause transition can be debilitating and impact quality of life (QOL). Edmonton has two specialized, multidisciplinary menopause clinics operating one day per week at Lois Hole Hospital for Women (LHHW) and twice weekly at Grey Nuns Community Hospital (GNCH). Women with severe menopause symptoms are referred by their physician. Both clinics routinely use a generic menopause symptom severity questionnaire (MSSQ) at each clinic visit, but this does not address QOL. The study's objectives were to test the use of a validated QOL tool, the menopause-specific quality of life (MENQOL) questionnaire, and to evaluate patient outcome in these clinics.

Methods:

We conducted a prospective cohort study of consecutive new patients seen at the LLHW and GNCH menopause clinics between May and October 2015. Consenting women completed MSSQ as part of usual care at each clinic visit, supplemented by a baseline MENQOL questionnaire at their first clinic, and again at 3-5 month follow-up visit. Demographics and medical and obstetric histories were extracted from patient clinic charts. Women on the wait list for the menopause clinics were enrolled as controls; they completed demographic and medical history at baseline, and MENQOL and MSSQ at baseline and 3-5 month follow-up in mailed-in surveys. Data were anonymized and entered in a REDCap database. Descriptive statistics were applied to baseline characteristics. Paired statistics compared baseline and follow-up MENQOL and MSSQ scores.

Results:

Baseline and follow-up data were available from 71 clinic patients (52 GNCH and 19 LHHW) and 25 wait list patients. There was no significant difference between clinic and wait list patient demographics (age, BMI) and lifestyle (smoking, alcohol, caffeine consumption). Symptom severity was significantly reduced in clinic but not in wait list patients as assessed by reduction in mean MSSQ scores (-0.34, $p<0.001$ for clinic versus -0.08, $p=0.33$ for wait list patients). Similarly, MENQOL results showed significant reduction in mean "bother" scores ($p<0.01$) for all 4 MENQOL domains for clinic patients. Differences in baseline and follow-up scores were not significant for wait list patient ($p=0.08$, 0.55, 0.95, and 0.31 for vasomotor, psychosocial, physical, and sexual domain).

Conclusion:

Women attending Edmonton's Menopause Clinics experienced significant reduction in symptom severity and improvement in QOL at follow-up compared to initial clinic visit. Women on the clinic wait lists did not demonstrate significant changes over a similar timeframe. MENQOL appears a useful tool to measure the impact of treatments on women's QOL.

This study was approved by the University of Alberta HREB board (Pro00055860) and supported by a seed grant from WCHRI.

Abstract #: 124
Presenter: Xiaoyun Tang
Supervisor: David Brindley
Title: Doxycycline attenuates breast cancer related inflammation by decreasing lysophosphatidate and inhibiting NF-κB activation
Authors: Xiaoyun Tang
Affiliations: University of Alberta

We previously discovered that tetracyclines increase the expression of lipid phosphate phosphatases at the surface of cells, thus increasing the degradation of exogenous lysophosphatidate. Extracellular lysophosphatidate signals through six G protein coupled receptors and is a potent promoter of tumor growth, metastasis and chemo-resistance. These effects depend partly on the stimulation of inflammation by lysophosphatidate. In this work, we used a syngeneic mouse model of breast cancer and showed that treatment with doxycycline decreased circulating lysophosphatidate concentrations and tumor growth.

Doxycycline, also decreased the concentrations of several cyotkines/chemokines (IL-6, IL-9, IL-10,CCL2CCl11, CXCL1, CXCL2, CXCL3, CCl11, G-CSF, LIF, VEGF) in the tumor. These results were compatible with the effects of doxycycline in decreasing the numbers of F4/80+ macrophages and CD31+ blood vessel endothelial cells in the tumor. Doxycycline also decreased the lysophosphatidate-induced growth of breast cancer cells in 3D culture. Treatment of breast cancer cells with doxycycline also decreased the translocation of NF-κB to the nucleus and the mRNA concentrations for IL-6 in the presence or absence of lysophosphatidate. These results contribute a new dimension for understanding the therapeutic effects of tetracyclines. These actions of doxycycline make it a potential candidate for and adjuvant therapy of cancer and other inflammatory diseases.

Funded By: Innovation Grant

Abstract #:	125
Presenter:	Powel Crosley
Supervisor:	Mary Hitt
Title:	PAC-1 combination with TRAIL enhances apoptosis in cell-line and primary cultured adult granulosa cell tumour cells
Authors:	Powel Crosley, Kate Agopsowicz, Marjut Pihlajoki, Markku Heikinheimo, Anniina Farkkila, Mary Hitt
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology

Introduction: Granulosa cell tumour (GCT) constitutes ~5% of ovarian neoplasms and generally responds poorly to chemotherapy.

Procaspase activating compound-1 (PAC1) is a small-molecule drug shown *in vitro* to sequester inhibitory zinc ions from the Caspase-3 (CASP3) zymogen allowing CASP3 to auto-mature and execute apoptosis.

TNF-related apoptosis-inducing ligand (TRAIL) is a pro-apoptosis ligand that can bind membrane-bound death receptors and trigger the extrinsic apoptotic pathway resulting in activation of CASP3 to execute its proteolytic role and programmed cell death.

We hypothesise that combining PAC1 activation of CASP3 with induction of apoptotic signaling by exogenous TRAIL will significantly heighten biologic effect thereby reducing disease, and that these effects will be obtained at doses lower than those required by either agent alone.

Methods: The GCT cell line KGN was treated *in vitro* with a 6-log range of PAC1 concentration for 48 hours to establish a dose-response curve (using a real-time cell analyzer, RTCA). In parallel, KGN cells were treated with a 6-log range of TRAIL concentration to establish its dose-response curve. Calculated EC_{50} values were then used for both PAC1 (20 μM) and TRAIL (10 ng/mL) to evaluate the biologic response of simultaneous treatment with PAC1 and TRAIL, and TRAIL delayed 24 hours after PAC1 treatment (using resazurin viability assay and RTCA). Separately, cells from fresh primary and recurrent tumour samples were cultured *in vitro* for 5 days, then treated with PAC1 (20 μM), TRAIL (10 ng/mL), or the combination, and finally assayed for viability and caspase 3/7 activity 48 and 72 hours later.

Results: Dose-response assays indicate treatment with PAC1 strongly reduces viability of KGN cells compared to untreated control ($p<0.05$). Similar assays with TRAIL only reduced viability of KGN cells at the highest concentration tested (1 μg/mL). The assays also suggest a ~24 hour delay in PAC1 reduction of GCT viability while TRAIL appears to induce a time-limited response. Using calculated EC_{50} concentrations for both PAC1 (20 μM) and TRAIL (10 ng/mL), assays for both KGN and patient-derived primary GCT cells were tested with each drug alone, both drugs applied concurrently or TRAIL applied 24 hours after PAC1. Combination of PAC1 with TRAIL was dramatically more cytotoxic than TRAIL or PAC1 treatment alone ($p<0.05$).

Conclusion: Combining CASP3 activator PAC1 with apoptosis-inducing agents may be an effective strategy for treatment of GCT and warrants preclinical assessment.

Funded By: Innovation Grant

Abstract #:	126
Presenter:	Shehzad Kassam
Supervisor:	Ginetta Salvalaggio
Title:	Managed alcohol programs: Integrating a public health intervention into an acute care setting
Authors:	Shehzad Kassam, Hannah Brooks, Elaine Hyshka, Ginetta Salvalaggio
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mental Health

Introduction: Managed alcohol programs (MAP) provide regular doses of beverage alcohol to patients with severe alcohol use disorders (AUD) to prevent withdrawal. MAP in community settings have shown positive public health outcomes, including uptake into housing and improved healthcare. MAP may also be a promising strategy for short-term stabilization of inpatients with severe AUD in acute care settings, and have the potential to prevent leaving against medical advice, premature discharge, costly readmissions, and poorer health outcomes. However, few studies exist to offer guidance on this practice in inpatient settings. Our objectives were to: 1) describe the academic and grey literature on MAP in either community or inpatient settings; 2) outline gaps in the literature related to these services; and 3) inform implementation of MAP in acute care settings with considerations of gender-specific needs and barriers to accessing services.

Methods: A scoping review was conducted. CINAHL, PsycINFO, MEDLINE, EMBASE and PubMed databases, Google Scholar and ten grey literature databases were searched. Two authors developed inclusion/exclusion criteria and independently reviewed texts for data extraction related to MAP operations. A secondary analysis of the team's recent process evaluation of a local inner city acute care service was also conducted; MAP-relevant content from these qualitative patient interviews was analyzed to complement the scoping review.

Results: A total of 5121 search results yielded 60 relevant peer-reviewed manuscripts and grey literature reports for analysis. Preliminary results indicate that while some literature has documented benefits of community-based MAP, few studies describe standardized protocols or procedures for provision of alcohol in acute care settings. Analysis of gender representation in the literature shows that most studies conducted had ‘all male’ participation as compared to ‘male and female’ or ‘all female’. Community-based MAP also seem to predominantly focus on male clients with programs being either mixed or males only, with little mention of services specific for females. Secondary analysis of interviews showed support for MAP implementation from both male and female participants. While a few participants opposed MAP due to beliefs that it may enable drinking, many felt MAP would alleviate withdrawal symptoms and keep patients in hospital.

Conclusion: This review highlights the potential public health benefits of community-based MAP and the current and historical practices related to alcohol provision in inpatient settings. However, several gaps regarding MAP implementation in acute care settings remain, particularly in the inclusion of female participation in research studies and providing appropriate services for women.

Funded By: Summer Studentship

Abstract #:	127
Presenter:	Mohammed Bahari
Supervisor:	Michael van Manen
Title:	Exploring Canadian neonatologists perceptions of targeted neonatal echocardiography
Authors:	Mohammed Bahari, Kumar Kumaran, Michael van Manen
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction:

Over the past decade, Targeted Neonatal Echocardiography (TnEcho) has become available in Neonatal Intensive Care Units (NICUs). TnEcho helps in understanding the function of the neonatal heart, the hemodynamics of the systemic and pulmonary circulation during transition and in the evaluation of the hemodynamic effects of a patent ductus arteriosus. While evidence would suggest that this is a valuable tool, use of TnEcho in NICUs has faced many obstacles. Inter-specialty conflict, variation in training, and concerns regarding reliability are a few examples. The objective of this study is to explore Canadian neonatologists' attitudes and perceptions regarding the use of TnEcho.

Methods:

We have developed and validated an online survey to elicit and study Canadian neonatologists' attitudes and perceptions regarding the use of TnEcho. All neonatologists working in level III NICUs in Canada will be invited to participate. There will be no exclusion criteria. The survey will be distributed between October and December 2016. Participation will be voluntary. All information collected from the surveys will be anonymous with no efforts made to identify respondents. Descriptive analyses will be completed. Significance tests such as t-test, ANOVA, Chi-square, and Fisher exact test will be used to explore the relation between the different variables. A p-value less than 0.05 will be considered statistically significant. IBM SPSS will be utilized for statistical analysis.

Results

We anticipate this study to help us to better understand Canadian neonatologists' attitudes and perceptions regarding the use of TnEcho. Identifying perceived barriers and facilitators as well as potential benefits and risks for the use of TnEcho is an important step in the development and application of TnEcho in Canadian NICUs.

Conclusions

Although TnEcho allows the understanding of specific clinical problems, the use of TnEcho by neonatologists in NICUs has encountered resistance and challenges. This study will help us to better understand the role of TnEcho in Canadian NICUs to facilitate development of TnEcho programs.

Abstract #: 128
Presenter: Proscovia Mugaba
Supervisor: Lisa Hornberger
Title: Cardiac MRI as an alternative to routine cardiac catheterization in single-ventricle infants undergoing a bidirectional Glenn at the Stollery Hospital
Authors: Proscovia Mugaba, Lindsay Ryerson, Lisa Hornberger
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Cardiology

Introduction: In 2007, a study from Boston's Children's Hospital found Cardiac MRI (CMR) to be a safe and adequate alternative to routine cardiac catheterization in the evaluation of infants with single-ventricle physiology before bidirectional Glenn (BDG). Following this report, the use of routine pre-BDG CMR was adopted at the Stollery Children's Hospital (SCH), for low risk patients. Currently, this approach has not been validated outside the Boston experience. This study aims to evaluate the SCH experience with the use of routine pre-BDG CMR. We shall test the hypothesis that CMR can be safely and accurately used in the pre-BDG evaluation of infants.

Methods: A retrospective cohort study was conducted including infants (1 to 12 months) with single-ventricle physiology who underwent BDG at the SCH from January 1 2007 to December 31 2015. A medical chart review was performed to obtain data on patient demographics, preoperative imaging, BDG surgery and post-operative outcomes. This project was designed using REDCap software. Data collection is nearing completion and complete analysis is expected by end of December 2016.

Results: A total of 231 infants were included. They were referred from Edmonton (80), Calgary (58), Saskatchewan (46), Winnipeg (37) and Vancouver (10). Systemic ventricular morphology included 143 right, 87 left, and 1 indeterminate. All infants underwent echocardiography, 142 underwent cardiac catheterization and 107 underwent CMR; 32 underwent both CMR and catheterization. About 25% of catheterizations involved an intervention, including pulmonary angioplasty (4), aortic angioplasty (21) and coiling of aortopulmonary collaterals (9). One infant had an adverse event during CMR compared to 14 undergoing catheterization. Median bypass time at BDG was 59 minutes (16-268). There were 11 cases (5%) of a preoperatively missed diagnosis. Post-operative complications were reported in 132 infants, the commonest being chylothorax among 38 infants. Twenty two infants underwent an unplanned cardiac reoperation during the same admission; 11 attributed to residual lesions after BDG and none attributed to a preoperatively missed diagnosis. At the end of the hospital admission following BDG, 227 (98.3%) were eventually discharged home, including 23 discharged via another hospital; 4 (1.7%) died prior to discharge.

Conclusion: These preliminary results show that since adopting a policy of routine use of pre-BDG CMR at the SCH, a significant number of infants still underwent cardiac catheterization; the underlying reasons are yet to be fully explored. Reassuringly, preoperatively missed diagnoses were infrequent and overall outcomes following BDG are reassuring.

Funded By: Resident/Clinical Fellow Trainee Research Grant

Abstract #:	129
Presenter:	Sonia Rawat
Supervisor:	Gary Lopaschuk
Title:	Cardiac hypertrophy in congenital neonatal heart disease delays maturational increases in fatty acid oxidation through myocardial acetylation control
Authors:	Sonia Rawat, Arata Fukushima, Liyan Zhang, Alda Huqi, Victoria H. Lam, Cory S. Wagg, Khushmol K. Dhaliwal, Lisa K. Hornberger, Ivan M. Rebeyka, Gary D. Lopaschuk
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction: Congenital heart disease (CHD) affects more than 1% of newborns, causing atypical functioning and blood flow in the heart, and the possible development of hypertrophy. Cardiac hypertrophy delays the normal maturational process by reducing fatty acid oxidation, resulting in a decrease in energetic capacity and an increase in the susceptibility to ischemic injury during corrective surgery for CHDs. Protein lysine acetylation has emerged as a novel post-translational modification that enhances fatty acid oxidation. However, the importance of lysine acetylation in human newborn heart metabolism and hypertrophy has yet to be elucidated. Therefore, we investigated how changes in lysine acetylation contribute to metabolic changes in hypertrophied neonatal hearts following maturation.

Methods: Human myocardial samples were collected during corrective heart surgery from infants at the University of Alberta Hospital (Edmonton, Alberta, Canada), and stratified in three age groups (0-20 days, 21-100 days and 101-200 days) and further stratified based on the presence or absence of hypertrophy assessed by echocardiography. The heart tissues were processed for acetylation status using immunoprecipitation and for enzyme activities.

Results: The overall acetylation of myocardial proteins was significantly increased with age in non-hypertrophied hearts, whereas the age-dependent increase was blunted in hypertrophied hearts. The increase in the acetylation of myocardial proteins was also evident with mitochondrial proteins. In particular, an age dependent hyperacetylation of fatty acid oxidation enzymes long chain acyl CoA dehydrogenase (LCAD) and β-hydroxyacyl CoA dehydrogenase (β-HAD) was positively correlated with their enzymatic activity (β-HAD R^2=0.54; LCAD R^2=0.50) only in non-hypertrophied hearts. In line with this, a reduced acetylation of LCAD and β-HAD was also observed in hypertrophied hearts from 21-day old rabbits subjected to aorto-caval shunt, in which a decrease in fatty acid oxidation rates occurred. In addition, a decrease in the acetylation of mitochondrial acetyltransferase GCN5L1 was observed in the hypertrophied hearts, and silencing GCN5L1 mRNA reduced acetylation of LCAD and β-HAD, as well as fatty acid β-oxidation rates *in vitro*.

Conclusions: Cardiac hypertrophy in CHD patients prevents the normal increase in myocardial acetylation following birth, resulting in a delayed maturation of fatty acid oxidation.

Funded By: Innovation Grant

Abstract #: 130
Presenter: Andrej Roczkowsky
Supervisor: Richard Schulz
Title: Intracellular MMP-2 activation is an early event in doxorubicin-treated cardiomyocytes
Authors: Andrej Roczkowsky , Brandon Chan , Bryan Hughes , Mathieu Poirier, Ramses Ilarraza, Richard Schulz
Affiliations: University of Alberta
Research Activity: Cardio-oncology

Introduction

Doxorubicin is an effective anticancer drug used to treat a variety of cancers in both children and adults. Its therapeutic utility, however, is hindered because its major chronic side effect is dose-dependent myocardial injury, which can lead to heart failure. The mechanism of doxorubicin-induced myocardial injury is unclear. It is associated with increased oxidative stress, impaired calcium handling, and myofibrilysis in the heart. Oxidative stress directly activates matrix metalloproteinase-2 (MMP-2), an intra- and extra-cellular protease implicated in many cardiovascular diseases. Once active, MMP-2 impairs cardiac contractile function by cleaving sarcomeric and other intracellular proteins, including troponin I. We hypothesise that intracellular MMP-2 plays a role in doxorubicin cardiotoxicity by cleaving substrates in the sarcomere and sarcoplasmic reticulum (SERCA2a and phospholamban).

Methods

Neonatal rat ventricular myocytes (NRVM) and human fibrosarcoma (HT1080) cells were treated with doxorubicin (0.5 μM) ± selective MMP-2 inhibitors ARP-100 (1 μM) or ONO-4817 (1 μM) for 2-24 hr. Cell death was measured by lactate dehydrogenase release, MMP-2 activity was measured by gelatin zymography, and MMP-2 protein and its protein target levels were measured by immunoblot. mRNA expression of MMP-2 substrates was measured by RT-qPCR.

Results

Doxorubicin was used at a concentration which caused 15% cell death in neoplastic HT1080 cells but none in NRVM after 24 hr. In NRVM, doxorubicin increased intracellular MMP-2 activity by 311% after 12 hr, which persisted at 24 hr. Increased MMP-2 activity was attenuated 67% with ARP-100 or ONO-4817. MMP-2 protein levels were increased 213% by 24 hr doxorubicin. Doxorubicin reduced protein levels of a confirmed MMP-2 target, troponin I, by 40%, which was not restored by ARP-100 or ONO-4817. Doxorubicin decreased phospholamban and SERCA2a protein levels by 44% and 39%, respectively, via a MMP-2 independent mechanism. Doxorubicin caused a 97% reduction in troponin I mRNA expression, trended to decrease phospholamban mRNA expression, and had no effect on SERCA2a mRNA expression.

Conclusions

Doxorubicin at an antitumor concentration increases MMP-2 activity in cardiac myocytes, in part by an increase in MMP-2 protein levels. Doxorubicin decreases protein levels of troponin I possibly by reducing its mRNA expression. A limitation of this study was the use of neonatal cardiomyocytes which have an immature sarcomere and sarcoplasmic reticulum. Therefore, future studies should measure targets of doxorubicin-activated MMP-2 in adult cardiomyocytes.

Funded By: Summer Studentship

Abstract #:	131
Presenter:	Chantal Allan
Supervisor:	Lori West
Title:	Physical fitness after pediatric solid organ transplantation: A review
Authors:	Chantal Allan, Sunita Mathur, Lori West
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant

Introduction: For the most part, pediatric solid organ transplant recipients are surviving into adult life. However, the quality of their prolonged lives does not meet the same standards as their healthy counterparts. Recently, to address this finding, physical rehabilitation programs have been established in pediatric transplant centers. Several studies have evaluated the fitness of individuals enrolled in these programs, but there is no review of these studies to date.

Methods: Several databases were searched for peer-reviewed publications since 1990. Articles were selected for their relevance to age (0-17 years), condition (solid organ transplant), and fitness assessment (assessed by at least one fitness test). Fitness assessment results were compared among studies and to the normal population. Aerobic capacity was assessed in most studies, so the mean VO2max per type of organ transplant was calculated.

Results: Twenty-seven studies were reviewed. A majority of articles relate to heart and kidney transplant patients, with few studies on other types of transplant. For lung transplantation, the lack of studies may be explained by the small number of procedures. However, liver transplant recipients are proportionately less studied. All assessed fitness parameters were lower in the pediatric transplant population. VO_2max (ml/kg/min) was lower in thoracic organ transplant recipients (heart = 29.0±6.81, lung = 19.6±6.48) than abdominal organ transplant recipients (kidney = 30.8±7.52, liver = 26.8±9.18). Muscle function was assessed in only 9 of 27 studies, and the type of assessment varied. Therefore, limited comparisons of muscle function could be made among types of organ transplant.

Conclusion: This review highlights a lack of studies that address muscle strength and endurance in pediatric transplant recipients. Furthermore, there is a clear need for further research into the fitness assessment of pediatric transplant recipients, especially non-heart transplant or kidney recipients. Though fitness parameters are impaired in the pediatric transplant population, the cause of this impairment is not well understood. Underlying causes should be investigated to identify the aspects of clinical care that could be targeted to improve physical functioning.

Acknowledgements: The Women and Children's Health Research Institute; the University of Alberta Faculty of Medicine and Dentistry, and Faculty of Graduate Studies; the Canadian National Transplant Research Program; and, the American Society of Transplantation – Transplantation and Immunology Network.

Funded By: Support services

Abstract #: 132
Presenter: Devin Chetan
Supervisor: Jennifer Conway
Title: Successful treatment of VAD pump thrombosis in four pediatric patients
Authors: Devin Chetan, Holger Buchholz, Mary Bauman, Vijay Anand, Paula Holinski, Jennifer Conway
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Cardiology

Purpose: Pump thrombosis is the most commonly reported cause of device failure in adults on continuous flow ventricular assist device (CF-VAD). Recent studies have shown the rate of pump thrombosis in adults ranges from be 4-8% depending on device type. The guidelines for management of this complication are largely based on expert opinion with no algorithms reported for the pediatric population. We report our early experience with pediatric patients who developed pump thrombosis on a CF-VAD and suggest treatment strategies adapted from the adult population.
Methods: The charts for all patients who underwent implantation of a CF-VAD (n=7) at the Stollery Children's Hospital from 2005-2014 were retrospectively reviewed. Pump thrombosis was defined as a rise in LDH with associated changes in pump parameters +/- rise of plasma-free hemoglobin. All patients were managed on heparin postoperatively. Patients less than 30kg were transitioned to warfarin (INR 2.5-3.5), ASA, and clopidogrel while two patients were switched to warfarin (INR 2-3) and ASA.
Results: Of the 7 patients reviewed, 4 patients had 6 pump thrombosis events. Please see table 1 below outlining the demographics, time to pump thrombosis, and management strategy. None of the patients had ischemic brain injury secondary to pump thrombosis.
Conclusion: Our limited experience suggests that the treatment of pediatric VAD thrombosis can be approached with similar principles to the adult population. Our current strategy includes:
i) Initiating treatment with bivalirudin with an isolated rise in LDH with no corresponding rapid rise in plasma free hemoglobin which may prevent further progression
ii) Treatment with a low-dose systemic TPA protocol as opposed to targeted therapy via catheter intervention if bivalirudin fails
iii) If there are concerns with respect to impact on kidney function or the patient is close to a previous surgery, device exchange can be considered

Table 1.

Demographics and Device	Episode	Time to Clot	Diagnosis and Pre-Thrombosis Anticoagulation	Treatment and Anticoagulation	Status
Patient 1: 7 yo M Heartware HVAD®	1	3 months	Myocarditis, biventricular dysfunction Heparin infusion	Pump exchange Bivalirudin à ASA, warfarin, clopidogrel	Cardiac transplant after 2nd pump thrombosis
	2	6 months		Bivalirudin	
Patient 2: 5 yo M Heartware HVAD®	1	2 weeks	Congenital heart disease with a mechanical mitral valve and biventricular dysfunction Heparin infusion	Pump exchange Mitral valve replacement (tissue) Bivalirudin à ASA, warfarin, clopidogrel	Cardiac transplant
Patient 3: 9 yo F Heartware HVAD®	1	1 month	Shone's Complex, biventricular dysfunction, and pulmonary hypertension Heparin infusion, ASA, clopidogrel	1. Integrillin therapy (failed) 2. Intracavitary TPA (failed) 3. Systemic TPA Bivalirudin à ASA, warfarin, clopidogrel	Still on device (23 months); several admissions for rising LDH, all treated with bivalirudin with good response
Patient 4: 17 yo F Thoratec HeartMate II ®	1	2.5 months	Dilated Cardiomyopathy secondary to iron overload, biventricular dysfunction ASA, warfarin	Integrillin and TPA	Subarachnoid bleeds following integrillin and TPA requiring left temporal and right posterior fossa craniotomies
	2	5 months		LVAD replacement (Heartware HVAD®) Heparin à ASA, warfarin	No thrombosis issues post-Heartware HVAD® implant (2.5 years since device implant)

Funded By: Trainee Travel Grant

Abstract #:	133
Presenter:	Ali Hajar
Supervisor:	Simon Urschel
Title:	Age-related differences in the regulatory capacity of CD5+CD1d+ B-cells in the context of heart graft acceptance
Authors:	Ali Hajar, Lavinia Ionescu, Ying Ling, Lori West, Simon Urschel
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant

Background:

Infants benefit from improved graft survival and reduced immunosuppression needs following heart transplantation. The CD5+CD1d+ subpopulation of B-cells contains IL10-producing “B10 cells” found to have immune regulatory capacity in animals. We found this subtype to be ten times more prevalent in infants than adults and hypothesized they contribute to the more tolerogenic environment. We aimed to determine if human IL10-producing B-cells are contained only within the CD5+CD1d+ B-cell subset, and if they impact B- and T-cell proliferation. Age-related differences in functionality were explored.

Methods:

Splenocytes were sorted by flow cytometry (FACS) to separate CD5+CD1d+ or CD24+CD38+ (transitional) B-cells from other B-cells and obtain 4 populations, which were cultured with stimuli inducing T-dependent (TD; aIgM+CD40L) or T-independent (TI; CpG) activation. IL10 secretion was measured by ELISA. To assess effects on proliferation, CellTrace-marked splenocytes were stimulated with Staphylococcal enterotoxin B, aIgM+CD40L, CpG, or aCD3+aCD28 in absence of CD5+CD1d+ B-cells as well as 1(natural proportion, CONTROL), 2 and 5 times their natural proportions.

Results:

CD5+CD1d+ B-cells produced IL10 following TD and TI activation. However, TI-activated non-CD5+CD1d+ B-cells produced higher amounts of IL10 than the CD5+CD1d+ subset. In adult samples, IL10 secretion and the variation between subsets were greatly reduced. Compared to the CONTROL, B-cell proliferation after TD activation was higher in CD5+CD1d+ depleted cultures and reduced in samples with 2X the natural proportion ($p = 0.081$). The effects were mainly on memory (CD27+) B-cells. No effects on the proliferation of T-cells or TI-activated B-cells were observed. As with IL10 secretion, CD5+CD1d+ B-cell effects on B-cell proliferation were diminished in adult samples.

Conclusion:

CD5+CD1d+ B-cells encompass many, but not all, regulatory B10 cells. The presence of these regulatory cells in increasing proportions decreases B-cell proliferation following TD activation. Further analysis is required to confirm suspected age-related differences in IL10 secretion and suppression of proliferation.

Funded By: Summer Studentship and Trainee Travel Grant

Abstract #:	134
Presenter:	Abbas Hyderi
Supervisor:	Lisa Hornberger
Title:	Healthy teens with preterm birth have increased LV twist parameters. Is it a mechanism of LV compensation to an impaired diastolic performance?
Authors:	Abbas Hyderi, Prasad Ravi, Michael Stickland, Joanna Maclean, Ian Adatia, Lisa Hornberger
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Cardiology

Introduction:

LV twist and twisting rates increase with increasing age and are postulated to be a compensatory mechanism for progressive diastolic impairment. Our previous study showed that healthy infants with preterm birth have impaired left ventricular (LV) diastolic function and a similar enhancement of LV twisting parameters at 1 month post birth. This study sought to examine LV function (conventional, tissue Doppler's, regional strain and twist mechanics) in healthy teens born at ≤28 weeks of gestation (PT) with comparison to control teens born at term (TT).

Methods:

We prospectively recruited 49 PT (12.8±1.3yrs) and 27 healthy, age and gender matched TT (12.5±1.6 yrs.). LV function 2D, M mode and Doppler based parameters were assessed by Echocardiography. LV twist, peak twist and untwist rate were derived from basal and apical short axis grey scale images using speckle-tracking echocardiography. Torsion was calculated as LV twist divided by LV length. Comparisons were made between PT and TT using an unpaired t-test. Sub-analysis was performed between PT 24-26wks vs. 27-28wks, and birth weight <10th centile vs. >10th centile.

Results:

Age at echo did not differ between PT and TT (12.8 ± 1.3 vs 12.5 ± 1.6 years, respectively).Conventional measures of LV function including ejection and shortening fraction ,ventricular inflow velocities and E/A wave ratio, E/e', isovolumic relaxation time and global longitudinal strain did not differ between PT and TT. PTs, however had higher peak LV twist (11.3± 4.6° vs. 8.9±3.4°, p=0.008), peak twist rate (102 ± 30°/s vs.88 ± 25°/s, p=0.02), peak untwist rate (-112 ± 44°/s vs. -92± 29°/s, p=0.02) and peak torsion (1.68 ± 0.68°/cm vs. 1.36 ± 0.56°/cm, p=0.02) compared to TT. Sub-analysis of PT born at 24-26 wks had higher peak twist (13.11 ± 4.8°vs 10.13 ± 4.25°p=0.008),peak untwist rate(-130.4 ± 53.7°/s vs -100.15 ± 34.6°/s,p =0.01)and torsion(1.89 ± 0.66 °/cm vs 1.52 ± 0.69°/cm, p= 0.03) and a tendency to increased peak twist rate(110.45 °/s vs 96.24°/s,p=0.08).

Conclusions:

Although healthy teens with preterm birth have an increased LV twist, peak twist rate, untwisting rate and torsion similar to findings in older healthy adults. This finding is greater in those with a history of more extreme prematurity that could suggest greater compensation for myocardial pathology. Increased LV twist parameters in this population may reflect LV compensatory mechanism for persistent mild myocardial diastolic impairment. Further, larger prospective studies are required to confirm.

Funded By: Resident/Clinical Fellow Trainee Research Grant

Abstract #:	135
Presenter:	Joren Manz
Supervisor:	Denise Hemmings
Title:	Sphingosine-1-phosphate mediated vascular adaptations and the impact TNF on vascular tone in pregnancy
Authors:	Joren Manz, Denise Hemmings
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Preeclampsia

Many vascular adaptations occur during pregnancy to deal with increased blood volume and to regulate fetal blood supply. Sphingosine 1-phosphate (S1P) is a bioactive lipid that may contribute to the required increased vasodilation in pregnancy, but has not yet been investigated. S1P generates nitric oxide (NO), an important vasodilator, but can also induce constriction and permeability depending on receptors and cell types that bind to it. We hypothesize that S1P contributes to the adaptive vasodilatory response in pregnancy while maintaining the endothelial barrier, whereas in non-pregnant (NP) conditions the same level of S1P will induce permeability leading to constriction. TNFα, a proinflammatory cytokine that doubles in preeclampsia, a hypertensive pregnancy disorder, is reported to induce constriction and increase permeability. TNFα signaling generates S1P, but whether these vascular effects are mediated by SIP is unknown. We therefore further hypothesize that TNFα will abnormally increase S1P levels leading to increased permeability and constriction. Vascular tone, the degree of constriction experience by a blood vessel relative to its maximally dilated state, and permeability were measured after infusion of S1P (1μM) or TNFα (10ng/mL) inside pressurized uterine arteries from pregnant and NP mice using a pressure myograph system. S1P did not alter vascular tone (0.074±1.57%), but did so when the NOS inhibitor LNAME was added (35.0±3.35%). The same S1P concentration induced constriction in arteries from NP mice (16.0%,n=1). Contrary to our hypothesis, TNFα did not induce constriction in pregnant or NP mice (3.48±2.55; -2.95±0.976%). However TNFα+LNAME induced constriction in pregnant mice (29.9%,n=1) indicating that TNFα generates NO. Blocking with LNAME shows that it also induces constriction. We do not yet have definitive evidence that these TNFα responses are mediated by S1P. Further experiments using S1P receptor inhibitors are planned. Our results suggest that S1P is important in the adaptive vasodilatory effects critical for normal pregnancy but that the same conditions in NP cause vascular dysfunction.

Funded By: NACTRC, U of A FoMD

Abstract #:	136
Presenter:	Aamena Kapasi
Supervisor:	Carmen Rasmussen
Title:	Executive functioning and adverse childhood experiences in children with prenatal alcohol exposure
Authors:	Aamena Kapasi, Isabel Light, Jacqueline Pei , Gail Andrew, Carmen Rasmussen
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Fetal Alcohol Syndrome

Prenatal alcohol exposure (PAE) is related to a wide range of physical, emotional, and cognitive disabilities, and may result in Fetal Alcohol Spectrum Disorder (FASD). Individuals with FASD and PAE often face a “double jeopardy” with both organic deficits in neurological functioning and high rates of adversity in their childhood environments compared to typically developing children. Common adversity for children with PAE include abuse, malnutrition, domestic violence, neglect, child welfare involvement, and multiple home placements. Furthermore, executive functioning (EF), often conceptualized as facilitative of goal-directed cognitive process and behavioral planning, is known to be compromised in many individuals with PAE, including problems with cognitive flexibility, set-shifting, inhibition, and delay of gratification. In the general population, adverse childhood experiences (ACEs) are related to many negative health outcomes, including executive functioning deficits. We examined overall rates of ACEs, as well as the association between EF difficulties and ACEs in children with PAE.

Methods: Data on childhood adversity and EF was retrospectively collected from 333 clinical files of patients with confirmed PAE assessed at an Alberta hospital FASD clinic (189 males, $M_{age=}$9.3, 65% diagnosed with FASD). Childhood adversity was measured with the ACE Questionnaire, which measures experience of 10 ACEs, resulting in a score from 0 to 10. Of the total sample, 123 clinical records contained executive functioning data. Measures included the Rey-Osterrieth Complex Figure Test (RCFT) and the Delis-Kaplan Executive Functioning System (DKEFS). All children completed the RCFT (71 males, M_{age}=10.9 years, 61% diagnosed with FASD), and forty-one children completed the DKEFS (18 males, M_{age}=13.2 years, 54% diagnosed with FASD).

Results: Children with PAE experienced high rates of ACEs, with a mean ACE score of 3.4 (SD=1.8; range=0 to 9). The most frequent adverse experiences were not being raise by both biological parents, substance use in the household, parental mental health problems, and neglect. Correlational analysis was conducted between the DKEFS and RCFT scores, and the ACE scores. None of the scores were significantly correlated with ACE scores.

Conclusions: Children with PAE have high rates of ACEs compared to the general population. In this study, a significant relationship between EF and ACE scores was not found. This study provides further evidence of the high level of ACEs among children with PAE, and provides information for those seeking to understand EF in children with PAE. Further research examining other factors related to EF problems in PAE is needed.

Funded By: CanFASD, ACCFCR

Abstract #:	137
Presenter:	Rotem Lavy
Supervisor:	Fred Berry
Title:	foxc1a genetically interacts with ripply1 to regulate mesp-ba expression and somitogenesis
Authors:	Rotem Lavy, W. Ted Allison, Fred Berry
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities

Introduction

Somitogenesis is an important segmentation process laying the foundation for the formation of the vertebrate body. The transcription factor *mesp-ba* has an important role in determining somite boundary formation. Its expression in somitogenesis is regulated by the activator Tbx6 and the repressor Ripply1 via a feedback regulatory network. Loss of *foxc1a* function in zebrafish leads to lack of anterior somite formation and reduced *mesp-ba* expression. We examined how *foxc1a* interacts with the *tbx6-ripply* network to regulate *mesp-ba* expression.

Methods

We used morpholino oligomers to facilitate gene knockdowns in zebrafish embryos. Bright field microscopy was used to visualize somite formation and embryonic development. Whole-mount in-situ hybridizations were used to assess gene expression.

Results

In *foxc1a* morphants, anterior somites did not form at 12.5 hours post fertilization (hpf). At 22 hpf posterior somites were seen, whereas anterior somites remained absent. In *ripply1* morphants, no somites were observed at any time point. *mesp-ba* expression was reduced in the *foxc1a* morphants and expanded anteriorly in *ripply1* morphants. Expression of *tbx6* was unaffected in the *foxc1a* morphants, but expanded anteriorly in the *ripply1* morphants. Double knockdown of *foxc1a* and *ripply1* resulted in lack of anterior somite formation while posterior somites did form, suggesting rescue of the *ripply1* phenotype. Unlike in the single *foxc1a* morphants, *mesp-ba* expression, detected as 1-3 stripes, was restored in the anterior PSM. *E*xpression of *tbx6* was expanded anteriorly in the double morphants.

Conclusions

Both *foxc1a* and *ripply1* morphants displayed defects in somitogenesis, but their individual loss of function had opposing effects on *mesp-ba* expression. Loss of *ripply1* appears to have rescued the *mesp*-ba expression in the *foxc1a* morphant, suggesting that intersection of these parallel regulatory mechanisms is required for *mesp-ba* expression and somite formation.

Funded By: Innovation Grant

Abstract #: 138
Presenter: Dorothea Hui
Supervisor: Sandra Wiebe
Title: Is parenting style related to language development in early childhood?
Authors: Dorothea Hui, Aishah Abdul Rahman, Luciano Hood, Valerie Carson, Sandra Wiebe
Affiliations: University of Alberta
Research Activity: Child and Youth Development: Language

Introduction: Language is key for preschool children's success in regards to both learning and social interactions. Good language is linked with better emotional and psychosocial adjustment. Language delays, on the other hand, have been found to put children at an increased risk for developing behavioural, social, and emotional problems, as they face difficulty learning and getting along with others. Children between 2 and 5 years of age are undergoing rapid development and have high neural plasticity, and during this preschool period, they are particularly dependent on their parents. As a result, preschool language development is largely influenced by parenting. Baumrind's model is arguably the most influential framework used for classifying styles of parenting, and it identifies three distinct styles – authoritative (both demanding and responsive), authoritarian (demanding but unresponsive), and permissive (responsive but not demanding). The authoritative parenting style might support language as frequent parental talk while reasoning and explaining expectations and rules exposes children to a large variety of words and concepts. Additionally, less frequent parental talk may occur when parents are unresponsive and expect rules to be followed without explanations or when parents do not set clear rules for children, hindering language development. Few studies have addressed the possible influences of parenting styles on language development, hence, the current study seeks to examine whether parenting style is related to preschool language development.

Methods: Participants included 69 children between the ages of 2.5-5.01 years and data was obtained through the first wave of the Physical Activity and Cognition in Early Childhood (PACE) study. Parents filled out the Robinson Parenting Questionnaire, and they received a score for each style instead of being categorized into a specific parenting style. Child language was assessed using the Peabody Picture Vocabulary Test (PPVT-IV), a receptive vocabulary and standardized test.

Results: Regression analyses were conducted with language as the dependent measure and parenting styles as the predictors. The preferred model included authoritative parenting style and child age as a covariate. Authoritarian and permissive parenting styles were not significant predictors and therefore did not stay in the model. The strength of association between authoritative parenting and child language (R^2) was 0.094.

Conclusion: This study is observational and does not allow any causal conclusions. However, the results suggest that authoritative parenting styles benefit preschool language development as being responsive, and reasoning and explaining entail abundant parent talk.

Funded By: Innovation Grant

Abstract #:	139
Presenter:	Uyen (Evelyn) Tran
Supervisor:	Samina Ali
Title:	Acute pain management: The medical students' perspective
Authors:	Uyen Tran, Janeva Kircher, Priya Jaggi, Hollis Lai, Tracey Hillier, Samina Ali
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Pain Management

Introduction: Acute pain is a common presenting complaint, which if addressed appropriately, can enhance patient outcomes and satisfaction. Pain management teaching begins in medical school. We aimed to describe medical students' perspective on their curriculum, comfort levels, and preferred pain teaching modality.

Methods: An online survey was distributed to medical students at University of Alberta from May-July 2015. We collected student demographics, curriculum content and duration, knowledge about acute pain medication dosing, and perceived barriers and facilitators to pain management.

Results: 124/670 (19.6%) surveys were returned. Students recalled a median of 2 (IQR=4), 5 (IQR=3.75), 4 (IQR=8) and 3 (IQR=3.75) hours of formal pain education from 1st-4th year of medical school, respectively. Students reported 0-25% of the pain curriculum was dedicated towards pediatric pain. While students rated the importance of pain treatment at a median of 90mm on a 100mm VAS scale (IQR=19.5), they felt its teaching was not prioritized (32mm, IQR=34). Increasing training improved comfort in treating adult pain (52.1% pre-clerks 'uncomfortable' versus 22.9% of clerks). However, managing pediatric pain remained relatively challenging (83.6% pre-clerks 'uncomfortable' versus 52.1% of clerks). 31% (15/46) of clerks felt unable to accurately assess children's pain. Only 60%, 52% and 44% of clerks correctly dosed ibuprofen, acetaminophen and morphine, respectively, for adults. Notably, 46%, 46% and 21% correctly dosed the same medications for pediatric patients. The majority of pre-clerks favour lectures (51.7%), whereas clerks prefer bedside instruction (43.7%) and small group sessions (23.9%). Top identified barriers to adequate pain management were fear of adverse effects and contraindications, patient mindset and potential for addictions. Facilitators were medication compliance, pain scores and education.

Conclusion: Medical students recall minimal training in pain management, and report significant discomfort in treating and assessing both adult and pediatric pain. Overall, additional methods to didactic teach for learning about pain such as small groups and bedside examples were preferred by students. This study looked at the current pain curriculum from the medical students' perspective and identified that protected time for pain education is lacking. Early interventions are needed to ensure that future physicians receive enhanced education in pain management.

Abstract #:	140
Presenter:	Stephanie Powley Unrau
Supervisor:	Valerie Carson
Title:	Update of the Canadian Physical Activity Guidelines for the Early Years (Aged 0-4 Years)
Authors:	Stephanie Powley Unrau, Eun-Young Lee, Lyndel Hewitt, Stephen Hunter , Cally Jennings, Corey Kuzik, Jodie Stearns, Veronica Poitras , Kristi Adamo, Valerie Carson
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development: Physical Activity

Introduction: Physical activity is a behavioural determinant of health in the early years (aged 0-4 years). Knowledge users (e.g., parents, child care providers, health practitioners) of early years children have the opportunity to facilitate children's physical activity, and can be informed on the amount of physical activity that leads to optimal health by up-to-date, evidence-based guidelines. The objective of this study was to update the existing guidelines by conducting a systematic review of all available evidence, published in English or French, on the relationship between physical activity and various health indicators.

Methods: Databases searched were MEDLINE, Embase, PsycINFO, SportDiscus, and the Cochrane Central Database. To be included in the review, studies needed to be peer-reviewed, written in English or French, and meet a priori study criteria. No date or study design limits were imposed. The population of interest was apparently healthy children aged 1 month to 4.99 years. The intervention was physical activity, defined as any bodily movement produced by skeletal muscles resulting in energy expenditure, and included objective and subjective measures. The comparator was various volumes, durations, frequencies, patterns, types and intensities of physical activity. The outcome included health indicators ranked as critical: adiposity, motor development, psychosocial health, cognitive development, and fitness; and health indicators ranked as important: bone and skeletal health, cardiometabolic health, and risks/harm/injury. Article screening by two reviewers was comprised of two levels: titles and abstracts at level one, and full text articles at level two. Data extraction of descriptive, exposure, outcome, and risk of bias information for included articles followed level two. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system will be used to assess the quality of evidence for each health indicator.

Results: Database searches identified 26,293 records; an additional 98 records were identified through review article reference list searches. After de-duplication, 20,678 titles and abstracts were screened at level one and 873 full text articles were screened at level two. A total of 99 articles met the inclusion criteria and had data extracted. In the proceeding stages, this information will be synthesized and analyzed, and the quality of evidence will be assessed.

Conclusions: This systematic review followed a rigorous search, screening, extraction, and quality assessment process. Findings will be used to generate updated evidence-based guidelines that will inform knowledge users about the optimal amount of physical activity needed for healthy growth and development of children in the early years.

Funded By: Summer Studentship

Abstract #:	141
Presenter:	Lesley Brennan
Supervisor:	Irena Buka
Title:	Mold exposure in the home: Insights from the Children's Environmental Health Clinic (ChEHC)
Authors:	Lesley Brennan, Alvaro Osornio-Vargas, Alexander Doroshenko, Anne Hicks, Jamal Tarrabain, Harold Hoffman, Donald Spady, Irena Buka
Affiliations:	University of Alberta
Research Activity:	Children's Environmental Health

Introduction

The Children's Environmental Health Clinic (ChEHC) addresses the effect of environmental factors on children's health. Mold is a common exposure associated with health effects in multiple systems. The purpose of this study was to review all mold cases evaluated at ChEHC over the past 4 years to better understand the impact of mold on our patients.

Methods

All ChEHC cases from 2012-2015 in which mold exposure was identified by the referring physician or by ChEHC assessment were included in analysis. Demographic information and details regarding exposures and symptomatology were reviewed.

Results

Thirty-three cases, representing 26% of ChEHC cases from 2012-2015, were analysed. Approximately half (52%) of referrals were for mold, the remainder were identified by a detailed environmental patient history. The presence of mold was defined by patient report. Common symptoms reported were cough/wheeze/breathlessness (79%), nasal congestion/rhinitis/nasopharyngitis (51%), and fever (27%). In 79% of cases, other residents in the home experienced similar symptoms.

Residences frequently affected were single-family homes (64%) built >30yrs ago (73%); renters were more likely than homeowners to report mold (58% vs. 42%). Common co-exposures included living near heavy traffic (82%), owning pets (52%), using scented products (48%), and environmental tobacco smoke (33%).

In each case, we assessed symptoms in relation to mold exposures and provided a management plan including provision of evidenced-based information, resources, and follow-up care. Most families (82%) responded to mold by cleaning, remediation, or relocating. Of these families, two-thirds reported an improvement in symptoms, 11% noted no improvement, and 22% did not follow-up.

Conclusions

Mold exposure represents a significant concern for ChEHC patients. Symptoms are varied and home environments are complex. Future goals include expanding our patient database and our tools for mold assessment so that we may improve our capacity for evaluating and communicating risk and enhance management strategies.

Funded By: Covenant Health

Abstract #: 142
Presenter: Catherine Stewart
Supervisor: Sarah Curtis
Title: Dog related injury in the Stollery emergency department
Authors: Catherine Stewart, Marcella St. Louis, Sarah Curtis, Melanie Rock, Sylvia Checkley, Manasi Rajagopal
Affiliations: University of Alberta
Research Activity: Pediatric Emergency Medicine

Introduction

Previous research has identified pediatric dog-bites as a significant type of injury seen in emergency departments but a neglected consideration during development of policy and practice of municipal legislation and health services. This chart-review aims to evaluate incidence and management of dog related injuries and dog bites seen in the Stollery Children's Hospital in Edmonton, AB, Canada from the years 2002-2016.

Methods

Charts being reviewed include children aged 1 day to 16 years old who have sustained a dog bite or injury from a dog and require a visit to the Stollery Emergency Department (ED). Following both Ethics HREB and Operational & Administrative approvoal, 732 charts were identified via discharge diagnosis terms including 'Bite', 'Dog Bite', and 'Animal Bite'. Relevant data being extracted includes: (1) Visit details (2) Demographics and medical history of the child (3) Dog characteristics and circumstances of bite/injury (4) Characteristics of bite/injury (5) ED management of bite/injury (6) Consultations within/outside AHS. Data is entered into the Research Electronic Data Capture (REDCap) software. Further analysis will be performed with the assistance of a statistician and descriptive statistics will be used to describe categorical variables as proportions and continuous variables as means or medians.

Results

To date, 697 charts have been reviewed and entered into REDCap. Interim data from these charts will be presented.

Funded By: Summer Studentship

Abstract #:	143
Presenter:	Allison Smith
Supervisor:	Monica Gorassini
Title:	Motor pathways in children with perinatal stroke receiving intensive therapy
Authors:	Allison Smith, Ephrem Zewdie, Donna Livingstone, Kelly Brunton, Michelle Teves, Caitlin Hurd, Elizabeth Condliffe, Adam Kirton, Jaynie Yang, Monica Gorassini
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Perinatel Stroke

Introduction: The sensorimotor regions of the brain are common sites of damage early in development. Individuals with cerebral palsy (CP) experience reorganization of sensorimotor pathways resulting in limited limb activity and motor impairment. Current therapies aimed at improving walking emphasize intensive activity-based therapy applied in infancy. Such interventions have shown promising functional results; however, the degree to which they influence underlying motor systems is unknown. Here we investigated the effects of intensive leg therapy to improve walking function in children with perinatal stroke to mainly one side of the brain.

Methods: Children between 8 months and 3 years received therapy which encouraged stepping and weight bearing in the most affected leg. Therapy was provided for 1 hour/day, 4 days/week, for 3 months. Motor pathway excitability was measured by applying transcranial magnetic stimulation (TMS) over the leg representation of each motor cortex. We examined the onset latency and prevalence of motor-evoked potentials (MEPs) in lower limb muscles (vastus lateralis, tibialis anterior, hamstrings, and gastroc-soleus). Data will be presented from an on-going, randomized, controlled trial with a delayed-treatment group acting as controls.

Results: The onset latency of ipsilateral and contralateral MEPs evoked from the less affected cortex progressively decreased with age across the sample size, typically with latencies of 60ms at 8 months to 20ms at 54 months. Following the delay (control) period, ipsilateral muscles showed the greatest increase in prevalence of MEPs. In 7 children, ipsilateral MEPs increased by 14% while contralateral MEPs increased by 4% after TMS application over the less affected cortex. Similarly, when applying TMS over the most affected cortex in 5 children, ipsilateral MEPs increased by 20% while contralateral increased by 15%. Following the therapy period, ipsilateral muscles continued to show the greatest increase in prevalence of MEPs. 18 children showed a 9% increase in ipsilateral MEPs and a 7% decrease in contralateral MEPs evoked from the less affected cortex. Similarly, 11 children showed a 21% increase in ipsilateral MEPs and no change in contralateral MEPs evoked from the most affected cortex.

Conclusions: Greater prevalence of ipsilateral pathways supplying leg muscles is unexpected given that a greater representation of ipsilateral MEPs in the upper limb is associated with poorer motor outcome in CP. It is possible that such pathways serve different functional purposes to the lower limb. These preliminary results suggest the possibility of reorganization of underlying motor systems in response to early intensive therapy and/or development.

Funded By: CIHR, AIHS

Abstract #: 144
Presenter: Jacqueline Crossman
Supervisor: Tarek El-Bialy
Title: The effect of low intensity pulsed ultrasound on the temporomandibular joint in mice
Authors: Jacqueline Crossman, Nadia Alzaheri, Mohamed-Nur Abdallah, Faleh Tamimi, Patrick Flood, Tarek El-Bialy
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Infection, Inflammation, Immunology

Introduction (Purpose)

Juvenile idiopathic arthritis (JIA) is a type of rheumatoid arthritis, a chronic and inflammatory disease, that affects children and youth. One of the most common joints affected by JIA is the temporomandibular joint (TMJ). JIA in the TMJ can result in TMJ condylar resorption, which leads to disturbances in normal craniofacial development, causing abnormalities like micrognathia. Current treatments of JIA include anti-inflammatory drugs, corticosteroids, antirheumatic drugs, and surgery. These treatments only affect some patients, research evidence is lacking, and surgery is painful, risky, and costly. Low intensity pulsed ultrasound (LIPUS) is a type of mechanical waves that are commonly used in medicine. LIPUS accelerates bone fracture healing, it has an anti-inflammatory effect, and it stimulates mandibular growth in rats, rabbits, baboons, and humans. The aim of this research was to evaluate the effect of LIPUS on the TMJ condyle in MRL-lpr/lpr mice, a mouse model used to study rheumatoid arthritis.

Methods

Sixteen 9-week old MRL-lpr/lpr mice were divided into 4 groups. Four mice received LIPUS treatment (20 minutes/day, 30 mW/cm^2 of the transducer's area, 1.5 MHz frequency pulsing at 1kHz) to the right TMJ for 2 weeks, 4 mice received LIPUS treatment to the right TMJ for 4 weeks, and the remaining 8 mice served as the corresponding control mice to these two treatment groups and did not receive LIPUS treatment. Micro-computed tomography (microCT) scanning (SkyScan model 1172) and analysis were performed in order to measure TMJ condylar length, width, and height. Three-way ANOVA and Student t-tests (SPSS 16.0) were used to statistically analyze this data.

Results

Condylar length was significantly greater in the group that received LIPUS treatment for 4 weeks compared to the group that received treatment for 2 weeks ($p < 0.05$). Also, condylar length was significantly greater in the group that received treatment for 4 weeks compared to its corresponding control group that did not receive treatment ($p < 0.05$). There were no significant differences in condylar width and height.

Conclusions

LIPUS may have an effect at decreasing the destructive effects of JIA in TMJ condyles. The use of adult mice was a limitation of the current study, and it is recommended that future studies analyze the effect of LIPUS on growing condyles in juvenile mice.

Funded By: Innovation Grant

Abstract #:	145
Presenter:	Kim Cuong Nguyen
Supervisor:	Lawrence Le
Title:	In-vitro evaluation of tooth-periodontium using a high resolution phased array ultrasound system
Authors:	Kim Cuong Nguyen, Julyana Gomes de Oliveira Carvalho, Neelambar Kaipatur, Edmond Lou, Paul Major, Lawrence Le
Affiliations:	University of Alberta
Research Activity:	Oral health for children

Background and Objectives

Malocclusion or tooth misalignment is the most common dental anomaly that can affect oral health and function, and if left untreated, will lead to problem in jaw movement, chewing, or speech, and higher susceptibility to periodontal diseases. Correction of malocclusion requires comprehensive orthodontic treatment. Cone-beam computed tomography has immensely helped orthodontic clinicians and researchers further evidence-based orthodontic treatment. However, children are increasingly susceptible to deleterious effects of ionizing radiation due to the fast rate of cellular growth, organ development, and longer life expectancies. Ultrasound imaging, which is a non-invasive and ionizing radiation-free technique, uses echoes of mechanical waves and the acoustic properties of the target to produce an image. The objectives of this study are to investigate the reliability of a medical ultrasound system to image the connective soft and hard tissues surrounding and supporting the tooth, and compare the results with the gold standard micro-CT, a small scale of computed tomography imaging modality with enhanced spatial resolution in the range of one millionth of a meter.

Methods

The samples used were the center incisors of two 6-month-old piglets. The samples were scanned by micro-CT with 18-micrometer resolution prior to ultrasound experiment. The ultrasound scanner used in this study was a high resolution phased array system with a 20 MHz frequency transducer. The experiment was set up so that the long axis of the probe aligned with the longitudinal axis of the incisor. The distance between the gingival margin and cementum-enamel junction, the distance between the gingival margin and alveolar crest, and the distance from cementum-enamel junction to alveolar crest were measured three times using images from both modalities by two raters. The intra and inter-rater reliabilities of ultrasound and its agreement with micro-CT were calculated using ICC and Bland-Altman methods.

Results

The calculated intra and inter-rater reliabilities of measurement reflected a strong agreement and correlation between three occasions of both raters with all ICC values > 0.9. The mean difference between ultrasound and micro-CT of three distances was 0.04 mm with the limits of agreement (95% confidence) between the two methods between -0.44 mm and 0.52 mm.

Conclusions

This preliminary study demonstrated that ultrasound has a promising potential to become a non-invasive diagnostic imaging tool to assess tooth-periodontal structures and to deliver a significant impact in the practice of dentistry with less ionizing radiation and better oral care, especially for pediatric and adolescent patients.

Funded By: Support services

Abstract #:	146
Presenter:	Julyana Gomes de Oliveira Carvalho
Supervisor:	Lawrence Le
Title:	Reliability of cone beam computed tomography for alveolar bone level assessment in the adolescent population: A pilot study
Authors:	Mengxun Li, Julyana Gomes de Oliveira Carvalho, Kim Cuong Nguyen, Neelambar Kaipatur, Paul Major, Lawrence Le
Affiliations:	University of Alberta
Research Activity:	Oral health care for children

Background and Objectives: Morphological condition of alveolar bone is an important indicator for dentists. Patients with malocclusion are easy to suffer from alveolar bone loss. The change of periodontal support may lead to loose teeth or even teeth loss in the long term. Therefore it is of great importance to assess the alveolar bone morphology both before, during, and after orthodontic treatment. Cone-beam computed tomography (CBCT) is superior to intraoral radiography in the context of providing a much better diagnostic image without tissue overlap. In addition, CBCT images render information relevant to alveolar bone level on the buccal or lingual aspects of the teeth, which intraoral radiographs cannot provide. Even though much research effort has been spent to evaluate the reliability of CBCT in the assessment of alveolar bone, the results appear controversial. The aim of this work is to evaluate the potential application of CBCT in alveolar bone level assessment by investigating the repeatability of CBCT image measurements in the adolescent patient population.

Methods: A total of 52 incisor images from the upper jaw (maxilla) and lower jaw (mandible) were acquired from 13 orthodontic adolescent patients using i-CAT 17-19 high resolution dental CBCT system (Imaging Sciences International, Hatfield, PA, USA with a short scan protocol (120KVp, 5mA, 13cm field of view, 4s scanning time, and 0.3mm voxel size). Distance from cemental-enamel junction to alveolar bone edge was measured three times by two independent raters. Intra-class correlation coefficient (ICC) was determined for intra and inter-rater reliability tests.

Results: For the inter-rater reliability, ICC from maxillary measurement was 0.89, indicating good consistency within raters. However, for mandibular measurement, ICC value was significantly lower (0.55). When it came to intra-rater reliability, we found that ICC was higher for rater 1 than rater 2, showing inconsistency between raters. The result of mandibular alveolar bone assessment was far from satisfactory due to inability to detect on the CBCT images thin structures of the alveolar bones especially close to the crest.

Conclusions: CBCT is still an optimal clinical imaging method at present to assess alveolar bone level on the buccal or lingual aspects of the teeth. However, CBCT also has its limitations: high radiation and low resolution. Due to lack of resolution of the CBCT images, the mandibular incisor bone crest in the adolescent patient is hard to be identified in many cases.

Funded By: Seed Grant

Abstract #:	147
Presenter:	Haroon Ahmed
Supervisor:	Mosarrat Qureshi
Title:	Lack of awareness about prevalence of Developmental Coordination Disorder (DCD) in preterm infants in the Northern Alberta Neonatal Program
Authors:	Haroon Ahmed, Patti Sollereder, Amber Reichert, Paulene Kamps, Mosarrat Qureshi
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Neuro-cognitive Development

Introduction:

Developmental Coordination Disorder (DCD) has a prevalence rate of around 5% among school aged children but is more common among Low Birth Weight male infants born preterm ≤32weeks gestational age (GA). Data on DCD in Northern Alberta is lacking. We hoped to elucidate the prevalence of DCD among preterm infants admitted to the RoyalAlexandraHospital (RAH) Neonatal Intensive Care unit (NICU) and identify risk factors associated with DCD to aid in its diagnosis and to provide therapy.

Methods:

Analytics, Data Integration, Measurement & Reporting (DIMR) services of Alberta Health Services provided a list of preterm infants (<37 weeks) who were born in Northern Alberta from 2000-2008, admitted to RAH NICU, and were diagnosed with DCD based on ICD code. Data abstracted from Clinical records and Glenrose Neonatal and Infant Follow up clinic database included Perinatal variables, Neonatal variables, and developmental testing scores. When applicable, schools were approached after parental consent for results of developmental assessments. Infants with cerebral palsy, significant cognitive delay (full-scale IQ<70), and/or legal blindness (VA<20/200) were excluded. Approval was granted by Human Research Ethics Board of University of Alberta.

Results: Out of the total 11,787 infants born <37 weeks during this study period in Northern Alberta, 150 infants were identified by DIMR as having DCD. 2 of the 150 were term, 50 were excluded, and 10 were lost to follow up. Upon review of clinical or school records, 67 patients were miscoded as DCD while they did not have formal developmental testing at ≥5 years of age. Only 15 infants fulfilled the criteria for DCD with GA 33.0±3.6 weeks (mean±SD) & BW 1915±666 g (mean±SD) with 69.2% males. Information is still awaited on 6 patients.

Conclusions: Our research on DCD in Northern Alberta revealed significantly lower number of DCD cases in preterm infants than is reported in the literature. This suggests a serious lack of awareness about DCD in regional, educational and health care systems. Information from Health Information Management (HIM) also seems significantly deficient. Research shows that without proper diagnosis and help, the motor difficulties in children with DCD can impact activities of daily living, academic achievement, emotional, behavioral, and psychological functioning as well as social engagement all of which can be a huge cost to the medical system. A prospective study using the Little DCD questionnaire to screen preterm infants and thereafter diagnosing them at 5 years of age would benefit these children and their parents.

Funded By: Neonatal Education and Research fund

Abstract #:	148
Presenter:	Rika Maruyama
Supervisor:	Toshifumi Yokota
Title:	Development of antisense oligonucleotide therapy for Fibrodysplasia Ossificans Progressiva
Authors:	Rika Maruyama, Justin Elliott, Yusuke Echigoya, Oana Caluseriu, Toshifumi Yokota
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Congenital Abnormalities

Introduction

Fibrodysplasia Ossificans Progressiva (FOP) is a rare autosomal-dominant disorder characterized by progressive heterotopic ossification. The worldwide prevalence is approximately 1 case in 2 million individuals and the age of onset ranges between birth and adulthood. The median lifespan of the patients is approximately 40 years of age. Currently, there is no effective treatment available. More than 95% of cases are caused by a recurrent mutation of (617G>A; R206H) in ACVR1, a bone morphogenetic protein (BMP) type I receptor. The mutation renders ACVR1 responsive to Activin A, by which WT ACVR1 is not activated. The ectopic activation of $ACVR1^{R206H}$ by Activin A induces heterotopic ossification. Because $ACVR1^{R206H}$ is a hyperactive receptor, a promising therapeutic strategy is to decrease the activity of ACVR1 in patients. To accomplish this goal, we aim to develop new therapies utilizing antisense Locked Nucleic Acid Gapmers (LNA Gapmers). LNA Gapmers are DNA oligonucleotides with fully modified phosphorothioated backbones and have locked nucleic acid (LNA) modification at both ends; they hybridize to a target sequence of mRNA, which induces the mRNA degradation by RNase H.

Methods

We designed and screened LNA Gapmers specific to ACVR1. The Gapmers were transfected into FOP patient fibroblasts. ACVR1 expression was measured by semi-quantitative RT-PCR and Western blotting.

Results

Several of our custom-designed LNA Gapmers successfully reduced the expression of ACVR1 both at RNA and protein level in the FOP patient fibroblasts. Furthermore, the Sanger sequence result suggested that one of the FOP allele-specific Gapmers achieved preferential knock-down of the mRNA transcribed from the FOP allele.

Conclusions

We demonstrated that LNA Gapmers efficiently reduced the expression of ACVR1 in vitro. The in vivo efficacies of the Gapmers will be tested by FOP mouse and xenograft models. Our study provides a proof of principle for applying antisense oligonucleotide therapy for FOP, and possibly for the treatment of other autosomal-dominant disorders with toxic gain of function mutations.

Funded By: Gilbert K. Winter Fund

Abstract #: 149
Presenter: Maria Choi
Supervisor: Andrew Waskiewicz
Title: Investigating the genetic and cellular factors underlying superior coloboma, a novel birth defect affecting development of the eye
Authors: Maria Choi, Kevin Yoon, Andrew Waskiewicz
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Congenital Abnormalities

Introduction:

Ocular coloboma is a congenital disorder in which the eye fails to form properly during early development. This disorder represents the second leading cause of pediatric blindness. It is observed in the inferior aspect of the eye upon the failure of the choroid fissure to close during development, resulting in a cleft (coloboma). Recently, patients have been identified with coloboma in the superior aspect of the eye. While investigating this novel disorder, referred to as superior coloboma, our lab discovered a novel optic structure: a transient superior fissure whose location aligns with the position of the patient superior coloboma. Our lab and others have previously shown that bone morphogenetic protein (BMP) signalling is a critical developmental signalling pathway that regulates proper dorsoventral axis patterning of the eye. Exome sequencing of patient DNA uncovered alterations in eye patterning genes, such as T-box 2 (*TBX2*). To expand our understanding of the causality of this novel disorder, we aimed to investigate the role of *TBX2* in the formation of superior coloboma.

Methods:

We performed in situ hybridization to examine how BMP signalling regulates *tbx2a* and *tbx2b* (zebrafish paralogues of human *TBX2*) expression. We used transgenic *fby* zebrafish that had a null allele for *tbx2b*. We analyzed the phenotypes and genotypes of embryos to determine if *tbx2b* mutants had a superior fissure closure defect. We also used immunohistochemistry and confocal laser scanning microscopy to image embryos in agarose whole mount. To evaluate the effects of a total loss of *tbx2*, we used morpholinos to knockdown *tbx2a* in *fby* embryos.

Results:

When BMP signaling was decreased, we observed less *tbx2b* expression, reflecting what has been discussed in the literature. Also, preliminary data suggests that a loss of *tbx2b* may delay superior fissure closure. Moreover, embryos with decreased levels of both *tbx2a* and *tbx2b* appear to have an exacerbated superior fissure closure defect phenotype.

Conclusions:

Our research implicates *TBX2* in the causality of superior coloboma, although further research is required. Preliminary data suggests that *tbx2b* regulates superior fissure closure and that *tbx2* loss may exacerbate superior fissure closure defects. We will be developing a CRISPR-Cas9-mediated knockout of *tbx2a* to further evaluate the effects of a total loss of *tbx2*. To analyze how increased TBX2 levels and how the *TBX2* variant found in patient DNA influence eye development, we will also develop an overexpression construct and a patient variant construct, respectively.

Funded By: Summer Studentship

Abstract #: 150
Presenter: Megan Beggs
Supervisor: Todd Alexander
Title: Novel calcium transport pathways mediate intestinal calcium absorption pre-weaning
Authors: Megan Beggs, R. Todd Alexander
Affiliations: University of Alberta

Introduction: Calcium (Ca^{2+}) is essential to vital physiological functions including bone mineralization where the rate of deposition peaks in infancy and mineral content peaks by early adulthood. Maintenance of a positive Ca^{2+} balance is thus crucial during development. Calcium homeostasis is mediated by interactions between the intestines, kidneys, and bones. Intestinal absorption occurs via an active, transcellular or passive, paracellular pathway. Currently evidence adults indicates the duodenum and large intestine are sites of transcellular absorption whereas the jejunum and ileum are proposed to mediate exclusively paracellular absorption. However, whether this hold true throughout development is not known. We therefore set out to describe intestinal Ca^{2+} absorption pathways pre and post weaning.

Methods: Wildtype FVB/N mice (n=12) pre-weaning at 1 day, 1 and 2 weeks and post weaning at 1, 2, 3 and 6 months of age were examined (weaning occurs at three weeks in mice). Gene expression from intestinal segments was studied using quantitative PCR with specific primers and probes. Protein was semi-quantified using immunoblot analysis. Functional studies were performed using Ussing chambers in the presence and absence of the L-type Ca^{2+} blocker, nifedipine.

Results: *Trpv6* and *Cabp9k,* mediators of transcellular calcium transport, mRNA expression increase six-fold between two weeks and one month of age in the duodenum with a similar increase in $Calbindin_{D9k}$ protein. In the ileum, mediators of transcellular transport – *Trpv6, Cav1.3*, and *Cabp9k* – are highly expressed prior to weaning. Net Ca^{2+} absorption in the ileum was observed only prior to weaning and was completely inhibited by nifedipine, suggesting a novel Ca^{2+} absorption pathway during early in life. Abundance of *Cldn-2* and *-15* mRNA, mediators of paracellular absorption, peak at 7 days in the duodenum. In the ileum, *Cldn*-2 mRNA peaks at 14 days with a 10-fold decrease by 1 month, where abundance of *Cldn-15* increases 3-fold during this time to peak after weaning. Preliminary results from the proximal large bowel also suggest a significant role of transcellular Ca^{2+} absorption prior to weaning that continues throughout life.

Conclusions: These observations suggest that weaning marks a significant shift in mechanisms mediating intestinal calcium transport. Of particular interest is the identification of a novel transcellular Ca^{2+} absorption pathway in the ileum of mice prior to weaning. Future studies to delineate the mechanisms underlying the observed changes are required in order to understand how a positive calcium balance is maintained during development.

Funded By: Graduate Studentship

Abstract #:	151
Presenter:	Kassi Shave
Supervisor:	Lisa Hartling
Title:	Procedural pain in children: utilizing parent expertise in research and knowledge translation
Authors:	Kassi Shave, Samina Ali, Shannon Scott, Lisa Hartling
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Pain Management

Introduction: Procedural pain makes up the majority of the average child's experience with acute pain. Poorly managed procedural pain can have short-term and long-term effects, which can extend and complicate both a procedure and the emergency department (ED) stay. There are many interventions available to manage pain and distress in children undergoing procedures; however, their use varies significantly across Canadian EDs. Knowledge translation (KT) tools are essential to ensure the uptake of evidence in practice. Parents are an underutilized resource in pediatric research, and can bring distinct knowledge, experience, and expertise to KT efforts. Our objective is to describe how parents were engaged in the "Procedural pain in children: A qualitative study of caregiver experiences and information needs" project and the implications it had on the research process.

Methods: The goal of this qualitative research project was to gather information from parents to inform the development of a KT tool on management strategies for procedural pain. Semi-structured interviews were conducted with a purposeful sample (n=12) of caregivers of children who attended the ED at the *Stollery Children's Hospital*, and required an intravenous insertion or venipuncture. The key stakeholder for the research was Translating Emergency Knowledge for Kids (TREKK), a Networks for Centres of Excellence initiative in Knowledge Mobilization. TREKK has a parent advisory group (PAG) that provides input on all TREKK activities. In conducting the study, the TREKK PAG was involved with interview guide development and piloting, and provided ongoing feedback on data collection, analysis, interpretation of the results, and next steps for KT tool development.

Results: TREKK PAG input resulted in changes to (1) data collection; (2) data analysis; and (3) plans for next steps. Ongoing feedback during data collection resulted in changes to the interview guide in terms of both language used and topics addressed. Input received during data analysis affected our interpretation of the results. Finally, feedback received from the PAG directed our focus for KT tool development.

Conclusions: This research generated new knowledge through collaborative researcher-stakeholder partnerships.Parents are a valuable resource, and provide meaningful guidance in conducting patient-relevant research.

Funded By: Graduate Studentship and Trainee Travel Grant

Abstract #: 153
Presenter: Stephanie Kowal
Supervisor: Tania Bubela
Title: Conducting ethically robust pediatric clinical trials of bio-therapeutics for chronic, manageable diseases: Lessons from a scoping review
Authors: Stephanie Kowal, Emma Camicioli, Liz Dennett, Tania Bubela
Affiliations: University of Alberta
Research Activity: Pediatric Research Ethics

Introduction

Novel bio-therapeutic interventions, including gene and stem cell therapies, are currently under investigation globally in adults with various chronic manageable diseases. In some cases, these clinical trials are beginning to recruit pediatric participants and expectations about the benefits of participation are high. While there is a long tradition of conducting pediatric clinical trials of bio-therapeutics (e.g., bone marrow transplantation) for fatal diseases such as cancers, the clinical research community has less experience in running such trials for chronic, manageable, or non-fatal diseases. It is timely, therefore, to consider the specific ethical raised by such trials. Most pediatric trials require parental consent, which is influenced by disease severity, age of the child, trial risks, potential benefits, and logistics. Adding to the complexity, ethics requirements and regulatory standards for design and conduct of pediatric trials are not harmonized, internationally.

Our scoping review explored whether: 1) current laws and regulations around pediatric clinical trials for non-cancer research are sufficient to protect children; and 2) clinical investigators have support for and adequate knowledge of the ethical conduct of pediatric clinical trials that meet regulatory requirements.

Methods

We conducted a scoping review of ethical issues of pediatric trials for chronic, manageable diseases, using 8 peer-reviewed and grey literature databases. Of the 4962 articles returned, 37 empirical articles met our inclusion criteria and gave recommendations about ethical issues in pediatric clinical trials. We qualitatively analysed each article for substantive and practical recommendations for ethical clinical trial conduct.

Results

There is a general paucity of evidence to guide clinical trial conduct for chronic manageable diseases that cause disability (n=4). Furthermore, only 1 article discussed the conduct of trials for novel bio-therapeutics. Regardless, the 37 articles agreed that current regulatory standards adequately balance the safety of pediatric clinical trial participants and the desire of the research community to proceed with clinical translation. Recommendations captured in our scoping review offer insights into supports required and practical techniques investigators can use in adhering to ethical best practices in clinical trial design and conduct.

Conclusions

With proper training, guidance and support from funders, government, and institutions, researchers can meet site-specific standards for pediatric trials with thoughtful design (e.g. appropriate risk analysis, placebo use) and local knowledge of ethical practices for informed consent/assent (substance and form) and recruitment.

Funded By: AIHS, CIHR, Choroideremia Research Foundation, Foundation Fighting Blindness

Abstract #: 154
Presenter: Rhonda Rosychuk
Supervisor:
Title: Stratified regression analysis of recurrent events with coarsened censoring times
Authors: Rhonda J Rosychuk, X. Joan Hu
Affiliations: University of Alberta
Research Activity: Research Methodology

Introduction

A typical administrative database collects information over time from a target population starting on a calendar date. Scientifically meaningful analyses, however, often use an individual time of the study subjects, the elapsed time since an individual-specific event such as age. Moreover, many situations demand inference on a population larger than the one from which the data are collected. These, together with other practical constraints, result in various types of incomplete data. On the other hand, researchers are often interested in understanding temporal patterns of factor/exposure effects based on the longitudinal data.

Methods

We present weakly structured methods for analysing doubly censored recurrent event data where only coarsened information on censoring is available. Administrative records of emergency department (ED) visits from a provincial health administrative database were extracted and the available information of each individual subject is limited to a subject-specific time window determined up to concealed data (e.g. missing birthdates as start times). To evaluate time-dependent effect of exposures, we adapt the local linear estimation with right censored survival times under a stratified Cox regression model with time-varying coefficients.

Results

Using generated birthdate procedures based on a uniform distribution of intervals informed by ages (in years) at the ED visits, we approximate the likelihood estimating function to estimate age-dependent covariate effects. We established the pointwise consistency and asymptotic normality of the regression parameter estimator. When applied to ED data on patients presenting to the ED for asthma, we quantified important exposure differences that vary over age.

Conclusions

We address missing start times of the underlying counting processes, which results in missing censoring times and coarsening information of the recurrent events. With the evaluation of covariate effects over time, effects can be quantified and adjusted by other variables to provide new insights on the general understanding of ED presentations.

Funded By: CIHR

Abstract #:	155
Presenter:	Shelly Jun
Supervisor:	Amanda S Newton
Title:	Point-of-care cognitive support technology in emergency departments: A scoping review of technology acceptance by clinicians
Authors:	Shelly Jun, Sarah Curtis, Amy C Plint, Sandy M Campbell, Kyrellos Sabir, Amanda S Newton
Affiliations:	University of Alberta

Introduction: Point-of-care (POC) cognitive support technologies in the emergency department (ED) have been shown to enhance clinician adherence to guidelines, improve timeliness of diagnosis and treatment decisions, and reduce medical errors. These tools guide clinician practice and have the potential to optimize emergency care; however, limited adoption by clinicians can prevent successful implementation in the ED. To address this predicament, a better understanding of technology uptake is needed. This scoping review aims to synthesize emerging evidence on clinicians' acceptance of POC cognitive support systems in the ED.

Methods: This review is guided by the Arksey and O'Malley framework, with enhancements as recommended by Levac. We conducted a systematic search of 12 electronic databases (MEDLINE, EMBASE, PubMed, PsychInfo, CINAHL, CBCA Complete, Inspec, SCOPUS, Proquest Dissertation and Theses Global, PROSPERO, EBM Reviews, and Health Technology Assessments) and two online archives of conference proceedings (Society for Academic Emergency Medicine and American College of Emergency Physicians). Primary studies published between January 2006 and July 2016, describing ED-based POC cognitive support systems and user acceptance were included. Additional articles are being identified from reference lists of selected studies. Two reviewers have independently screened studies for eligibility. Disagreements were resolved through third party consultation. Methodological quality of included studies is being assessed by two independent reviewers using the Mixed Methods Appraisal Tool. Outcomes of interest are clinician, patient, organizational, and technical factors related to technology acceptance. A descriptive analysis will identify patterns in study characteristics, and a thematic analysis guided by domains of the Adapted Technology Acceptance Model 2 will determine consistency in findings for acceptance variables.

Results: To date, we have screened 1,459 unique articles identified by the electronic database search strategy for potential eligibility. Twenty-two studies have been included from this strategy. Initial reviewer agreement, prior to 100% consensus for study inclusion, was excellent (kappa=0.901). Additional articles are still being identified through study reference lists. Data extraction and quality assessment of included studies are currently underway; results will be reported at the presentation.

Discussion: This scoping review may identify key barriers and facilitators to POC cognitive support technology acceptance by ED clinicians. Results from this review will be used to develop technology implementation strategies that encourage high uptake in clinical practice within the ED. The results of this review will be relevant to clinical and system administrators who seek to deploy technology-based health care solutions, yet, may be unaware of clinician concerns.

Funded By: University of Alberta

Abstract #: 156
Presenter: Maryam Nesari
Supervisor: Shannon Scott
Title: Study design for developing evidence-based digital knowledge translation tools on fever for Canadian and Iranian parents
Authors: Maryam Nesari, Lisa Hartling , Kelli Buckreus, Shannon Scott
Affiliations: University of Alberta

Introduction

Parental/caregiver management of fever, one of the most prevalent pediatrics' health conditions, depends on variables such as parents'/caregivers' health literacy, knowledge, perceptions, attitudes and experiences. Misconceptions regarding the pathophysiology of fever, its associated risks, and the need for antipyretic medications, for instance, influence how the condition is managed at home, as well as decisions are made by parents/caregivers to seek medical care for their chid. Within a broader framework of patient-centred care, wherein parents/families actively engage in health-care decision-making for their children, it is fundamental to empower parents to make appropriate health decisions. Essential to this mission is enabling them to have access to reliable and easy-to-understand healthcare information. This is especially challenging within Canada's multicultural context. The variable qualities of health information on the Internet, overlaid by the fact that 55% of Canadians have limited health literacy, create an urgent need for trusted sources to support healthcare consumer knowledge. Therefore, the purpose of this study is to develop, implement and evaluate innovative knowledge translation (KT) tools to connect parents with the best available evidence-based information on pediatric fever, and to evaluate these tools for cross-cultural relevance.

Methods

Arts-based digital tools for parents/caregivers on pediatric fever management will be developed and evaluated through a multi-modal study design carried out in five phases: Phase 1) A knowledge synthesis project on parents' information needs regarding pediatric fever will be conducted. Phase 2) 12-15 parents will be interviewed to learn about their experiences of caring for a child with fever and seeking medical care. Phase 3) The development of KT tools for parents will be informed by phase 1 and will include a narrative synthesizing the parental experiences shared through the interviews. Phase 4) A mixed-methods study (qualitative and quantitative) will then determine the usability and usefulness of these KT tools for parents, prior to wider public dissemination. Phase 5) Finally, the KT tools will be adapted for an Iranian context to evaluate their cross-cultural appropriateness.

Results &Conclusion

By creating KT tools which offer the best available evidence on children's fever management, this project will make a significant contribution towards empowering parents to make evidence-informed healthcare decisions for their children. This has great potential to improve pediatrics' health outcomes, healthcare utilization, and consumer satisfaction. Further, this research is unique in terms of the cultural adaptation of KT tools, an initiative that is crucial for responding to the needs of Canada's diverse multicultural populations.

Funded By: Innovation Grant

Abstract #: 157
Presenter: Osnat Wine
Supervisor: Alvaro Osornio Vargas
Title: The barriers and facilitators of integrated knowledge translation in environmental health context: Preliminary deliberations of the DoMiNO project
Authors: Osnat Wine, Osmar Zaine, Alvaro Osornio Vargas, Katharina Kovacs Burns
Affiliations: University of Alberta
Research Activity: Maternal Research : Pre-term Birth

Introduction:

The DoMiNO research project team (DoMiNO: Data Mining & Neonatal Outcomes, NSERC/CIHR 2013-2017), investigates the relationship between early births and small babies with industrial emissions, and socioeconomic variables, by using new data mining computing systems to analyze large sets of existing data. The complexity and sensitivity of environmental health research requires collaboration between researchers and knowledge users. Therefore, DoMiNO has established a partnership between interdisciplinary researchers, practitioners and decision-makers representing academia, governmental agencies and the public using an integrated knowledge translation approach(iKT). In this presentation we present the facilitators and barriers of the on-going collaborative research.

Methods:

This is part of a case study exploring DoMiNO's iKT approach. Participants include all 24 DoMiNO team members. The team have been working together since April 2013 and have recently gathered for the annual meeting to discuss research progress, the innovative data mining tool and preliminary results. The team engaged in formal and informal interactions, small group and full team discussion, as well as, a focus group to reflect on the on-going collaborative approach. Additional insights were provided through an anonymous evaluation survey of the meeting. Participant observation and reflections throughout the research process provide further data. All data were recorded and coded to identify and define the main components of the collaborative approach.

Results:

The findings describe preliminary deliberations of the ongoing iKT approach facilitators and barriers in the context of environmental health. Facilitators that contribute to the team strength and advancement of iKT include: mutual co-learning, mutual trust, built relationships, and the interdisciplinary aspect of the project. Challenges to the ongoing iKT include interdisciplinary issues (such as training, learning, keeping discipline credibility) unclear roles, difficulty in building consensus and developing knowledge translation in a sensitive context.

Conclusions:

Findings identified important components of the iKT process at present, which provide opportunities to address those during the ongoing DoMiNO research process. They also contribute to further understanding and learning of the collaborative process in this context in order to enable co-production and translation of new knowledge. As the DoMiNO project progresses, exploration of the collaborative process will continue, specifically related to interdisciplinary knowledge integration, building consensus and KT development.

Funded By: Graduate Studentship

Abstract #: 158
Presenter: Lisa Shulman
Supervisor: Yan Yuan
Title: Statistical methods for studying the relationships between body fat and weight changes during pregnancy
Authors: Lisa Shulman, Fatheema Subhan, Linglong Kong, Yan Yuan
Affiliations: University of Alberta
Research Activity: Maternal Research : Nutrition

Introduction

Normal physiological adaptations favour weight gain and fat accretion during pregnancy to support fetal growth, followed by postpartum weight loss and fat mobilization postpartum to meet increased maternal energy demands during lactation. It is well-known that the risk of poor maternal and fetal health outcomes increases when women gain either too little or too much weight during pregnancy. Recent studies indicate that, in developed countries, the majority of pregnant women gain more weight than recommended. Excessive weight gain during pregnancy followed by inadequate postpartum weight loss can contribute to maternal long-term obesity and associated sequelae including cardiovascular disease, hypertension, diabetes, and degenerative joint disease. In this study, we focus on the following questions: (1) What is the pattern of fat mass accretion during pregnancy among women with different pre-pregnancy BMI? (2) How does the postpartum fat loss and fat retention compare across different pre-pregnancy BMI groups? The answers to these questions provide important insights into fat accretion and mobilization during pregnancy and early postpartum, and suggest a framework for understanding the relationships between maternal body weight and composition.

Methods

Fat mass distribution during pregnancy and postpartum was studied in a large cohort (n~2200) of pregnant and postpartum women by examining changes in waist and hip circumference and changes in skinfold thickness at standard anatomical sites.

Results

We observe that the rate of fat mass accretion is higher during late pregnancy than in early pregnancy for women of all pre-pregnancy BMI categories. Our findings demonstrate that women with pre-pregnancy obesity gain less total fat between the first and third trimesters compared to women with normal and overweight pre-pregnancy BMI. We found that the mean fat loss between the third trimester and postpartum is significantly lower for obese women relative to women with underweight, normal, and overweight pre-pregnancy BMI. Furthermore, the fat retained between the first trimester and postpartum is greater, on average, for obese women than for women classified as normal or overweight before pregnancy.

Conclusions

Our results indicate that there are significant differences in fat mass accretion, postpartum fat loss, and fat retention between pre-pregnancy BMI categories. We have demonstrated that statistical modelling techniques can be employed to understand longitudinal fat accretion trajectories during pregnancy and early postpartum among different pre-pregnancy BMI categories.

Funded By: Summer Studentship

Abstract #:	159
Presenter:	Stephana Cherak
Supervisor:	Stephane Bourque
Title:	The effect of prenatal iron deficiency on fetal programming of body composition: Role of brown adipose tissue
Authors:	Stephana Cherak, Andrew Woodman, Sareh Panahi, Stephane Bourque
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition

Introduction: Fetal exposure to an adverse intrauterine environment can lead to altered growth and developmental trajectories, thereby increasing susceptibility to obesity and chronic disease in later life. Iron deficiency (ID) is the most common nutritional disorder in the world with pregnant women being the most susceptible subgroup. Prenatal iron deficiency reprograms offspring adipose tissue, resulting in changes in development and composition, predisposing offspring to fat accumulation. Brown adipose tissue (BAT) is highly metabolically active fat which generates heat in response to cold exposure to maintain core body temperature. The capacity of even small amounts of BAT to burn excess calories as heat makes it an attractive therapeutic target for obesity. We sought to determine whether prenatal ID precipitates an obese phenotype by chronically altering the thermogenic capacity of BAT, and thus whole body metabolism, in a sex-dependent manner.

Methods: Female Sprague Dawley rats were fed either a control or an iron-restricted diet prior to and throughout gestation. At birth, dams were given normal rat chow, and at 3wk of age offspring were weaned onto a high-fat Western diet. At 4wk of age, one male and female littermate were subjected to a chronic cold exposure protocol (4˚C, 12h/day, 5wk) to stimulate brown fat, and one male and female littermate were maintained at room temperature (22˚C). Metabolic parameters were analyzed *in vivo* via open-circuit indirect calorimetry. Maximal thermogenic capacity was assessed with pharmacological stimulation.

Results: Prenatal ID offspring exhibited lower body weights at 4wk of age. We observed sex-dependent effects such that female PID offspring didn't exhibit the same exaggerated body weight gain as was seen in the male PID offspring in response to the high-fat diet. Cold exposure was successful in increasing BAT mass in male and female offspring ($P=0.0042$, $P<0.001$, respectively). In all male offspring, chronic cold exposure increased thermogenic capacity ($P=<0.001$). A similar increase was seen in female control offspring ($P=0.0087$), but not in PID offspring ($P=0.63$). Cold exposure had minimal effects on control offspring body weight and body composition. However, cold exposure prevented body weight and fat mass gain ($P=0.05$) in male PID offspring, but not in female PID offspring ($P=0.88$).

Conclusions: In summary, prenatal iron deficiency causes sex-specific programming of growth trajectories, body composition and BAT function in the offspring. This work was supported by the Women and Children's Health Research Institute, the Canadian Institutes of Health Research and the Faculty of Medicine and Dentistry/Alberta Health Services.

Funded By: Start-up or Retention Funding, Innovation Grant and Graduate Studentship

Abstract #:	160
Presenter:	Meagan McLavish
Supervisor:	Donna Manca
Title:	A description of obstetric and neonatal outcomes for the Be Healthy in Pregnancy study
Authors:	Meagan McLavish, Laura Adam, Donna Manca, Rhonda Bell
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Nutrition

Introduction: Despite recommended weight gain guidelines, 49% of women in Alberta gain excess gestational weight. Excess gestational weight gain increases the risk for large-for-gestational-age infants (which secondarily can lead to increased risk of caesarean section and lacerations) and preterm birth. Weight gain in pregnancy is multifactorial and there is a need to better support women during pregnancy to gain weight within the guidelines. The Be Healthy in Pregnancy (BeHIP) study aims to understand if lifestyle support, such as discussions about healthy eating throughout pregnancy with a Registered Dietitian (RD), can help women achieve appropriate gestational weight gain. If interventions can help women gain weight within the guidelines, pregnancy-related complications can be reduced. The objective of this analysis is to explore the effect of different counselling approaches on obstetric and neonatal outcomes.

Methods: Eighty-four low-risk pregnant women were recruited <24 weeks gestation and they were divided into an intervention group (n=23), a control group (n=27) and a passive control group (n=34). Their obstetric charts were reviewed and obstetric outcomes (guideline-concordant weight gain, mode of delivery, rate of prematurity, induction of labour, and degree of laceration) and neonatal outcomes (birth weight and size-for-gestational age) were compared between groups. Differences between groups were analyzed using ANOVA and chi-square tests. Statistics were performed via Stata 14.2.

Results: There was no significant difference between the three groups in terms of mean birth weight, gestational age, birthweight for gestational age, induction rate, preterm rates and maternal guideline concordant weight gain. Mothers who gained weight above their respective guidelines gained weight at rate of 0.22 (±0.25) kg/week above those women who gained within the guidelines (p=0.012) and gave birth to babies 339.6 (±452.8) grams heavier than mothers who gained within the guidelines (p=0.011).

Conclusions: Women with gestational weight gain that exceeds guidelines gained weight at a greater weekly rate than those who gain within guidelines, and were more likely to give birth to babies with greater birth weights. BeHIP dietary counselling interventions did not result in significant changes in obstetric or neonatal outcomes between groups, however this may be attributable to the complex and multifactorial nature of gestational weight gain as well as the small sample size of this study.

Funded By: AIHS

Abstract #: 161
Presenter: Mette Madsen
Supervisor: Rhonda Bell
Title: Gestational weight gain in a cohort of women with standard prenatal care in Edmonton, Alberta
Authors: Mette Madsen, Laura M. Adam, Rhonda C. Bell
Affiliations: University of Alberta
Research Activity: Maternal Research : Nutrition

Introduction

Excessive weight gain in pregnancy can negatively influence the future health of mother and child. Supporting women to gain weight within Health Canada's recommendations can lead to the best health outcomes for mother and child in the short and long-term. Currently, it is unclear how best to support women to achieve appropriate gestational weight gain (GWG), and to this end, Adam and colleagues conducted a randomized controlled trial (RCT) to examine the impact of a supportive counselling intervention delivered by a Registered Dietitian. "Intervention" and "Active Control" groups were recruited to this RCT during pregnancy. The purpose of this sub-study was to recruit a "Passive Control" group to assess adherance to GWG recommendations for women with standard prenatal care, and to describe the support they received in regards to GWG.

Methods

Fifty-five postpartum women who received standard prenatal care for a low risk pregnancy (from a family doctor and/or Ob-GYN) in the last year, delivered in the Edmonton area, and did not see a Registered Dietitian were recruited to the "Passive Control" group. Recruitment occurred through Facebook (45% of participants), word of mouth (30%), previous studies (9%), farmer's markets (8%), and a local fitness group (8%). Participants were asked to complete an online survey that asked about their pre-pregnancy weight, total GWG, and GWG resources that were provided or discussed with them from their healthcare provider (HCP).

Results

The average age in the study was 32±4.1 years. Most women (67%) had a household income >$100,000, and 71% had a university degree. Prior to pregnancy, 1 woman was underweight, 36 were normal weight, 13 were overweight and 5 were obese. Based on self-reported weight gain, 43% of women gained in excess of GWG guidelines. With respect to prenatal care, 49% of women indicated they did not discuss GWG with their HCP, and 62% did not receive resources about GWG from their HCP. Almost half (49%) reported that resources they found themselves impacted their knowledge of healthy GWG the most.

Conclusion

Information gathered from postpartum women suggests that standard prenatal care in Edmonton, Alberta appears to include discussions and sharing of resources with ~40-50% of pregnant women. Health Canada suggests that these discussions should occur with all pregnant women to promote appropriate GWG. Thus, a more effective approach to discussing GWG and distributing resources is needed. Studies focusing on how to address these gaps in support of healthy GWG are needed.

Funded By: Summer Studentship

Abstract #:	162
Presenter:	Maryam Kebbe
Supervisor:	Geoff Ball
Title:	Perspectives of adolescents with obesity on nutrition, physical activity, sedentary behavior, and sleep habits: A scoping review
Authors:	Maryam Kebbe, Samah Damanhoury, Nadia Browne, Michele Dyson, Tara-Leigh McHugh, Geoff Ball
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Nutrition

Introduction: A key element to successful weight management is the adoption of a healthy lifestyle. Adolescents with obesity often struggle to achieve success in weight management, which may be linked with difficulties in attaining healthy nutrition, physical activity, sedentary behavior, and sleep habits. As such, the purpose of our study was to understand adolescents' perspectives in regards to the barriers to and enablers of making and maintaining healthy lifestyle behaviors.

Methods: Our scoping review was conducted according to expert recommendations. Six databases (CINAHL, EMBASE, MEDLINE, PsycINFO, ProQuest Dissertations and Theses, and Scopus) were searched for articles published in English and French from 1980 to June, 2016; references of articles meeting eligibility criteria were hand-searched as a further resource. We included articles with a focus on *(i)* 13 to 17 year olds, *(ii)* individuals with BMI ≥85th percentile, *(iii)* weight management programs, interventions, or services, and *(iv)* barriers to and/or enablers of achieving healthy lifestyle behaviorsinnutrition, physical activity, sedentary behavior, and/or sleep. Articles were excluded if adolescents presented with intellectual or developmental disabilities. Titles and abstracts, then full-text articles, were screened independently by two reviewers. Data from eligible studies were charted and study quality was appraised using the Mixed Methods Appraisal Tool. Findings were organized according to themes derived from the Social Ecological Model.

Results: A total of 2,594 articles were retrieved, out of which 17 were included in our review. Barriers and enablers were grouped at the individual (knowledge, attitudes, skills), interpersonal (social network), and organizational (environment, logistics) levels. Adolescents with obesity identified barriers (*e.g.,* mindless eating) and/or enablers (*e.g.,* motivation to prevent adverse health consequences) regarding healthy nutrition, physical, activity, and sedentary behavior habits in all of the aforementioned themes; however, none of the studies included sleep-related barriers and/or enablers. The most commonly cited barriers included limited pleasure in and lack of motivation towards physical activity, as well as availability of unhealthy foods; of enablers, support at the family-, social-, and professional-level was of highest recurrence.

Conclusions: Adolescents with obesity in pediatric weight management exhibit a diverse range of barriers to and enablers of making and maintaining healthy lifestyle behavior changes. These findings highlight the need for multi-level (home, clinic, school, community) interventions designed to minimize the impact of barriers and enhance the influence of enablers on adolescents' lifestyle habits.

Funded By: Graduate Studentship

Abstract #: 163
Presenter: Erin L. Faught
Supervisor: Paul J. Veugelers
Title: Disentangling the effects of food insecurity, household income, and diet on children's academic achievement in Nova Scotia, Canada
Authors: Erin L Faught, Patty L Williams, Mark Asbridge, Paul J Veugelers
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Nutrition

Introduction

Household food insecurity is an important issue on the rise in Canada. While food insecurity is known to have detrimental effects on childhood development and academic achievement, evidence evaluating the mechanisms of how these negative effects occur is incomplete. Understanding how food insecurity affects children's academic achievement is essential to developing effective interventions to support children's development and academic success when facing food insecurity. This study aimed to characterize the association between food insecurity and children's academic achievement independent of socioeconomic status and children's diet quality.

Methods

Grade 5 (10-11 years) students and their parents were invited to participate in a population-based survey in Nova Scotia, Canada, in 2011. Parents completed surveys containing the short-form Household Food Security Survey Module and questions about socioeconomic status. Children completed food frequency questionnaires to assess diet quality. These data were linked to children's performance on standardized exams in reading, writing, and mathematics written in grade 6, with complete data acquired for over 4,000 students. Mixed effect multiple logistic regression was employed to assess the relationship between food security and likelihood of meeting expectations on exams while adjusting for socioeconomic status, diet quality, and other relevant confounders.

Results

Food insecurity without hunger was reported by 9.2% of households, and food security with hunger was reported by 6.7% of households. Children who lived in households that reported experiencing food insecurity with hunger had 0.65 times the odds (OR: 0.65 [95%CI: 0.44, 0.96]) of meeting recommendations for reading performance and 0.62 times the odds (OR: 0.62 [95% CI: 0.45, 0.86]) of meeting recommendations for mathematics performance independent of all other covariates. Children who had the highest level of diet quality had 1.54-1.73 times the odds of meeting expectations in all subjects compared to those with the lowest. Children whose household income was >$60,000CAD had 1.85-2.02 times the odds of meeting recommendations in all subjects compared to those whose household income was <=$20,000CAD.

Conclusions

This study fills an important gap in knowledge about the mechanisms by which food insecurity affects children's academic achievement. This study provides support for interventions for the eradication of poverty and for school-based food programs, but also identifies the need to address the detrimental effects of food insecurity beyond the effects of income and diet.

Funded By: Graduate Studentship

Abstract #:	164
Presenter:	Daniel Fung
Supervisor:	Susan Gilmour
Title:	Pediatric liver transplant quality of life (PeLTQL) questionnaire to measure health related quality of life in the pediatric liver transplant populati
Authors:	Daniel Fung, Cheri Robert, Susan Gilmour
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Transplant

Introduction: Pediatric Liver transplant (PLTx) has become a successful treatment for children with end-stage liver disease and has lead to long-term survival. Yet the World Health Organization (WHO) defines health as a state of well-being and not merely the absence of disease. Health-related quality of life (HRQOL) has emerged as a multi-dimensional measure of the aspects of quality of life directly related to health. Studies have found short-term increase in HRQOL after PLTx along with low long-term outcomes (E.g. social functioning, school functioning) when compared with healthy children. The assessment of HRQOL in PLTx has previously been limited to generic tools, which have less sensitivity to clinical change. The Pediatric Liver Transplant Quality of Life (PeLTQL) questionnaire is a novel PLTx-specfic, validated tool for assessment of HRQOL in patients ages 8-18, and addresses PLTx specific issues and concerns. The present study aims to utilize the PeLTQL tool to measure the health related quality of life in the PLTx population at the Stollery Children's Hospital.

Methods: PLTx patients between the ages of 8-18 that had visited the Stollery Children's Hospital and had completed a PeLTQL questionnaire as part of their clinical assessment (between March, 2014, to April, 2016) were identified with a retrospective PeLTQL questionnaire and chart review. The PeLTQL questionnaire responses and scores along with patient demographics obtained from chart review were entered into a database. Further analysis with Microsoft Excel identified patient population composition and significant areas of HRQOL.

Results: In the PLTx population at the Stollery Children's Hospital 54% were diagnosed with biliary atresia for transplant, 49% were male, and in 91% of the patients only a single transplant was performed. The mean PeLTQL score for the population was 67.1(±13.3). The PeLTQL questions that had received the lowest and highest means scores were respectively, "Do you worry if you miss taking your medicine?" and, "How do you feel about taking medicine every day?"

Conclusion: For the Stollery Children's Hospital PLTx population, their domain and total PeLTQL questionnaire are most similar to a rank of 2 on the PeLTQL Likert Scale, which indicates the lack of larger and general deficit in HRQOL. Further studies to identify factors for low HRQOL can be performed. Identified areas of HRQOL for PLTx patients have the potential to be modified.

Funded By: Support services

Abstract #: 165
Presenter: Sarah Andrishak
Supervisor: Vivian Huang
Title: The impact inflammatory bowel disease has on breastfeeding patterns
Authors: Sarah Andrishak, Alisha Maonocha, Vivian Huang
Affiliations: University of Alberta
Research Activity: Women's Health : Infection, Inflammation, Immunology

Background:

Inflammatory Bowel Disease (IBD) is a disease characterized by inflammation of the digestive tract.Crohn's disease(CD) can affect any part from the esophagus to the anus,and Ulcerative Colitis (UC) only affects the large intestine.Factors that can contribute to the development of IBD include genetics, environment and microbiome. Breastmilk influences development of the neonatal microbiome and immune system. It is recommended that infants breastfeed until 12 months,to ensure nutritional and immunological development. Women with IBD have been reported to breastfeed less than healthy women.

Purpose:

To investigate the impact IBD has on breastfeeding patterns.

Methods:

Adult women with IBD attending the Pregnancy in IBD clinic were invited to fill out questionnaires regarding breastfeeding 2 or 3, 6, 9 and 12 months post partum (PP). They were asked if they were breastfeeding or not, and why not at each time points. Women were also asked about their clinical disease activity using Harvey Bradshaw index (HBI) for CD and Partial Mayo (pMayo) for UC.For subjects who are still in follow up (within the 12 months), we included any of their completed surveys up until July 2016. Incomplete or missing surveys were excluded from the analyses. SPSS 23.0 was used to analyze the data.

Results:

Fifty women completed surveys; 46% of patients had stopped breastfeeding by 12 months, while 36% of the patients (who completed all time points) breastfed through to 12 months. There was no significant pattern when breastfeeding stopped. The top three reasons reported for cessation of breastfeeding were insufficient milk, medications and sickness. Cessation of breastfeeding was not correlated to clinical disease activity.

Conclusion:

A majority of patients with IBD stopped breastfeeding by 12 months postpartum. Having IBD itself was not found to be associated with cessation of breastfeeding. Insufficient milk, medications, and fatigue were the top 3 reported reasons for cessation of breastfeeding. This is important as these may suggest that IBD may indirectly be related to insufficient milk production, cessation of breastfeeding due to concerns regarding IBD medication effect, and fatigue related to IBD - leading to early cessation of breastfeeding.

Funded By: University of Alberta

Abstract #:	166
Presenter:	Nicole Gehring
Supervisor:	Geoff Ball
Title:	Is there a role for home visits in managing pediatric obesity? Preliminary findings
Authors:	Nicole Gehring, Daniel Neuman, Laura Mercier, Nicholas Spence, Nicholas Holt, Geoff Ball, Mary Jetha
Affiliations:	University of Alberta
Research Activity:	Obesity Management

Introduction: Unfortunately, attrition for pediatric weight management programs is high and is an inefficient use of health care resources. Thus there is a need to improve accessibility and applicability of services to mitigate attrition, build trust, rapport and respect between family members and clinicians. Home-based approaches for managing chronic conditions have been used successfully in other areas of healthcare; however the potential of this service has been largely unexplored for managing pediatric obesity. Our objective was to determine families' interest in, and potential demand for, a home-based treatment option for pediatric weight management.

Methods: Participants included children (2–17 years old; BMI ≥85th percentile) and their parents who attend weight management appointments at the Pediatric Centre for Weight and Health (PCWH; Stollery Children's Hospital). From October 2015 to May 2016, we conducted breif in-person interviews with 38 families. Interviews were audio-recorded and transcribed verbatim. We used qualitative description as the methodological framework and manifest content analysis as the analytical strategy.

Results: Families provided insights on *(i)* perceived benefits, *(ii)* desired content, and *(iii)* perceived barriers for both families and clinicians regarding potential home visits. The most common benefits included convenience (described by 74% of families, n=28), focus on the home setting (66%, n=25), increased engagement (39%, n=15), and personalized service (37%, n=14). Healthcare provider support was most desired from a dietitian (42%, n=32) and exercise specialist (29%, n=22), preferably in the evenings (51%, n=19) for 30-60 minutes (62%, n=23). Nutrition counselling, including food assessment and meal preparation/ planning (74%, n=28) and advisement on physical activity within the home and community (66%, n=25) were the top areas of desired content of care. Although the majority of families (45%, n=17) reported that there were no barriers to home visits, minor barriers related to privacy, possible judgement, and obligation were expressed. Families also indicated barriers for clinicians including inconvenience to the clinical team, political concerns and expense of the program.

Conclusion: Families view home visits as an appropriate and convenient resource for managing pediatric obesity. The potential of this service can capitalize on the home environment by offering tailored, multi-disciplinary, family-centred care.

Funded By: Seed Grant

Abstract #:	167
Presenter:	Ambika Agrawal
Supervisor:	Karen Madsen
Title:	Breast milk from mothers with Inflammatory Bowel Disease elicits lower inflammatory responses than milk from healthy controls
Authors:	Ambika Agrawal, Vivian Huang, Heekuk Park, Naomi Hotte, Michael Laffin, Matt Emberg, Morgan Shipka, Amanpreet Gill
Affiliations:	University of Alberta
Research Activity:	Maternal Research : Infection, Inflammation, Immunology

Introduction: Inflammatory Bowel Disease (IBD) is a group of incurable intestinal diseases wherein changes to the gut microbiome are associated with gut inflammation in children and adults. Initial colonization of the infant gut begins at birth and is then influenced by environmental exposures and diet. Human breast milk contains bioactive factors (e.g. cytokines, immune cells, immunoglobulins, oligosaccharides, proteins) and bacteria that influence gut colonization and neonate immune development. Mothers with IBD may transmit increased levels of pro-inflammatory cytokines to their infants which may both alter microbial colonization and immune development in the infant. The hypothesis to be tested in this study was that breast milk from IBD mothers has different immune components compared to milk from healthy mothers.

Methods: Breast milk was obtained from healthy controls and IBD mothers and analyzed for cytokines by ELISA. In a second experiment, breast milk was placed onto cultured HT29 human colonic epithelial cells ± TNFa to determine if breast milk altered IL-8 secretion. Data was analyzed using student's t-test or ANOVA with either Welch's correction or via Kruskal-Wallis test.

Results: Breast milk was obtained from healthy controls (n=8) and from mothers with IBD (n=26). Breast milk from healthy mothers was found to have significantly lower levels of anti-inflammatory cytokine IL-10 compared to milk from IBD mothers (p-value 0.04). In addition, breast milk from healthy mothers induced significantly higher IL-8 secretion by cells treated with TNFa compared to those treated with IBD milk (p-value 0.05).

Conclusions: These results indicate that breast milk from mothers with IBD actually elicits a lower inflammatory response than healthy milk. Heightened immune response caused by healthy breast milk may serve protective function in early infancy.

Funded By: Summer Studentship

Abstract #:	168
Presenter:	Usha Rai
Supervisor:	Anita Kozyrskyj
Title:	Impact of duration of labor on infant gut microbiota composition at 3 months
Authors:	Usha Rai, Tedd Konya, David Guttman, Allan Becker, Piushkumar Mandhane, Stuart Turvey, Padmaja Subbarao, Malcolm Sears, James Scott, Radha Chari
Affiliations:	University of Alberta
Research Activity:	Infant gut microbiome and labor duration

INTRODUCTION

Pioneer microbial colonizers of the infant gut play a crucial role in the development of immune system. Evidence shows that infant gut dysbiosis is associated with childhood asthma, obesity and other disorders.Exposure to maternal vaginal and fecal microbes during vaginal birth provides important micorbial seeding opportunities for the newborn gut. Recent research has documented differential fecal microbiota profiles in infants born vaginally as compared to infants born after C-section. Although the new ACOG guidelines promote longer duration of labor to curb primary C-section rate, literature on the impact of duration of labor on infant gut microbiota is scarce.This study investigated differences in infant fecal microbial composition at 3 months based on duration of labor experienced by the mother.

METHODS

The study involved 426 vaginally delivered infants enrolled in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort from Edmonton, Winnipeg and Vancouver sites. Data on birth parameters were obtained from the hospital birth chart. At 3 months after delivery, infant fecal samples were collected and fecal microbiota were characterized by Illumina high-throughput sequencing of the hyper-variable V4 region of 16S rRNA gene. Microbiota taxon abundance and diversity were compared between infants whose mothers experienced normal duration of labor versus prolonged duration of labor, using Mann-Whitney U-test.

RESULTS

Nearly a quarter (n=83, 24.2 %) of all women delivering vaginally endured total labor duration longer than 12 hours; 26% of women experienced prolonged second stage (longer than 2 hours). Preliminary analysis showed that total duration of labor longer than 12 hours was associated with differential infant fecal abundance of Leuconostocaceae (p=0.003), Fructovacillus (0.003) and Clostridiaceae (p=0.004;) at family level, and Collinsella (p=0.006) at genus level. With prolonged second stage of labor, differential infant fecal abundance was observed for Prevotellaceae (p=0.007), Clostridiaceae (p=0.001) and Alcaligenaceace (p=0.004) at family level, and Megasphaera (p=0.001), Citrobacter (p=0.003) and Sutterella (p=0.004) at genus level.

CONCLUSION

Our findings provide evidence of association between duration of labor and changes to infant gut microbiota composition at 3 months of age; the resultant infant gut dysbiosis could contribute to aberrant immune programming and increase risk of childhood health disorders.

Funded By: CIHR (SyMBIOTA)

Abstract #: 169
Presenter: Jocelyn Shulhan
Supervisor: Lisa Hartling
Title: Effect of hydrolyzed formula and enteral nutrition infant products on the incidence of necrotizing enterocolitis in neonates: A systematic review
Authors: Jocelyn Shulhan, Kassi Shave, Lisa Hartling, Manoj Kumar, Allyson Jones, Bodil Larsen
Affiliations: University of Alberta
Research Activity: Child and Youth Development : Nutrition

Introduction

Premature and critically ill neonates with poor gut and immune functions are at an increased risk of necrotizing enterocolitis (NEC), a serious inflammatory disease of the gut. In Canada, 5.1% of babies born <33 weeks gestational age develop NEC. In the worst cases, damage to the gut may lead to surgery or death. The exact cause of NEC is not known. Researchers have found that cow's milk-based infant formulas may cause more babies to develop NEC compared to babies that are only fed human breast milk. Reasons for this finding are still unclear. A diet that only includes human milk may be better than standard infant formula, but it is a costly approach and does not prevent all cases of NEC. An area that has not been thoroughly explored is hydrolyzed formulas. These formulas facilitate digestion and absorption, which may reduce stress and pro-inflammatory processes in the gut. Our objective is to compare the effect of hydrolyzed formulas, cow's milk-based products and human breast milk products on the incidence of NEC in neonates (<30 days old).

Methods

Five databases, 2 proceedings, 3 regulatory agencies and 1 trial registry were searched. Screening was completed by two independent reviewers using a piloted form. Primary quantitative studies comparing different types of enteral infant nutrition products that reported on the incidence of NEC in term and preterm neonates were included. Methodological quality of eligible studies will be assessed using the Cochrane Risk of Bias Tool for randomized controlled trials, and the Newcastle Ottawa Scale for observational studies. Meta-analyses or a network meta-analysis will be completed for homogenous studies. Subgroup analyses will be performed based on birth weight categories and comorbidities (e.g. cardiac disorders). Sensitivity analysis will be performed to determine the influence of high versus low quality studies.

Results

A total of 8198 records from the database search were retrieved. No records were retrieved from the regulatory agency sites. After removal of duplicates, 4913 titles/abstracts were screened. Two-hundred and four records proceeded to full-text screening. Several challenges have been encountered during screening, particularly with respect to the intervention of interest.

Conclusions

This review will synthesize current evidence comparing hydrolyzed formulas, cow's milk-based products and human milk on the incidence of NEC. Clinicians will be able to use the SR to guide decisions on the type of nutrition used for neonates at risk of NEC. Progress and challenges of the review will be presented.

Funded By: Graduate Studentship

Abstract #:	170
Presenter:	Yesmine Elloumi
Supervisor:	Vivian Huang
Title:	Change in levels of inflammatory cytokines during pregnancy in women with IBD
Authors:	Yesmine Elloumi, Naomi Hotte, Lindsy Ambrosio, Kayla-Marie Smith, Karen Kroeker, Brendan Halloran, Levinus Dieleman, Richard Fedorak, Karen Madsen, Vivian Huang
Affiliations:	University of Alberta
Research Activity:	Women's Health : Infection, Inflammation, Immunology

Introduction

Inflammatory Bowel Disease (IBD) affects women in their reproductive years of life. Women with IBD are at increased risk for pre-term delivery, especially if they have active disease during pregnancy. Some women with IBD flare during pregnancy, while others stay in remission, and the reason for this difference in disease activity during pregnancy is unclear. The aim of this study is to characterize changes in the inflammatory cytokines during pregnancy in women with IBD.

METHODS

Adult (>18 years) women with Crohn's disease (CD) or ulcerative colitis (UC) were invited to participate by providing blood samples preconception (PC), and during pregnancy at each trimester (T[n]). Serum levels of IFN-g, INF-a, IL-6, IL-10, IL-17a, IL-12p40 and C-reactive protein (CRP) were analyzed using the MESO Scale V-Plex assays.

RESULTS

There were 21 women (8 CD, 13 UC) who provided both T2 and T3 blood samples. The T2 and T3 IFN-g and IL-6 levels were not significantly different between CD and UC patients. T2 and T3 TNF-a levels were slightly higher in UC patients. T2 and T3 CRP levels were significantly lower in UC patients compared to CD patients. T2 IL-10 levels were higher in UC patients with a trend downwards into T3. IL-17 levels decreased from T2 to T3 in both UC and CD patients. T2 IL-12p40 levels were higher in UC patients and significantly decreased into T3. Although the IL-17/IL-p40 ratios were not significantly different between UC and CD patients, the ratio was increased in T3 in UC patients.

CONCLUSION

There are differences in cytokine levels during pregnancy in women with ulcerative colitis compared to Crohn's Disease. These differences may be associated with disease activity during pregnancy in this study population of pregnant IBD patients.

Funded By: CEGIIR, AIHS

Abstract #:	171
Presenter:	Andre Isaac
Supervisor:	Hamdy El-Hakim
Title:	Predictors of failure of DISE-directed adenotonsillectomy in children with sleep disordered breathing
Authors:	Andre Isaac, Noura Alsufyani, Manisha Witmans, Paul Major, Hamdy El-Hakim
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Objective: To determine the predictors of failure of DISE-directed adenoidectomy and/or tonsillectomy (T±A) in otherwise healthy children with snoring/sleep disordered breathing (SDB).

Methods: We retrospectively reviewed a prospective database of children who presented with SDB. All patients underwent preoperative pulse oximetry (PO), followed by DISE with T±A, The variables documented included demographics, ethnicity, co-morbidities, family history, McGill Oximetry Score (MOS) on PO, as well as findings of collapse and or obstruction on DISE and symptom resolution based on modified Pediatric Sleep Questionnaire (PSQ). The primary outcome was the independent predictors of treatment failure based on multivariate binary logistic regression.

Results: 382 patients satisfied the inclusion criteria. Based on post-operative modified PSQ, SDB resolved in 259 patients (68%), whereas 123 (32%) had persistent symptoms. On bivariate analysis, neuropsychiatric diagnosis (r=0.286, p=0.042), history of sleepwalking or enuresis (r=0.103, p=0.044), MOS (r=0.123, p=0.033), presence of DNS (r=0.107, p=0.036), and presence of laryngomalacia (r=0.122, p=0.017) all positively correlated with treatment failure. Small tonsil size on DISE correlated with treatment failure (r=-0.180, p<0.001). Multivariate analysis identified age greater than 7 years (OR=1.799, [95% CI 1.040-3.139], p=0.039), obesity (OR=2.032, [95% CI 1.043-3.997], p=0.040), chronic rhinitis (OR=1.334, [95% CI 1.047-1.716], p=0.025), deviated nasal septum (OR=1.745, [95% CI 1.062-2.898], p=0.031) and tonsil size (OR=0.575, [95% CI 0.429-0.772], p<0.01) as independent predictors of treatment failure.

Conclusions: Obese, asthmatic, and children older than seven years are at increased risk of treatment failure after DISE-directed AT. Several DISE findings can independently predict AT failure, including tonsil size, degree of chronic rhinitis, and the presence of a deviated nasal septum, and can be addressed at a second stage. Further research is needed into the role of DISE in surgically naïve patients with SDB, and to compare DISE-directed surgery with the current standard of care.

Abstract #:	172
Presenter:	Atoosa Golfar
Supervisor:	Dr. Po-yin Cheung
Title:	The outcomes and predictors of INO on preterms with severe hypoxemic respiratory failure rescued with high frequency oscillatory ventillation
Authors:	Atoosa Golfar, Jagmeet Bhogal , Po-yin Cheung, Barb Kamstra, Ann Hudson-mason , Georg Schmölzer
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Lung Development

Background: Despite being an experimental therapy in preterm neonates, the use of Inhaled Nitric Oxide (INO) has increased as a rescue therapy when High Frequency Oscillatory Ventillation (HFOV) and other conventional therapies fail. **Objective**: We aimed to determine the effect of INO as a rescue therapy and the predictors of survival in preterm neonates with Hypoxemic Respiratory Failure (HRF).

Methods: We retrospectively reviewed all very preterm neonates (<33 weeks gestation) with birth weight <1500g who required HFOV and INO from Mar 2009-Apr 2014 at the Royal Alexandra Hospital (RAH). We collected demographic and clinical parameters, dosages, duration and response to INO, survival to NICU discharge, and major complications.

Results: During the study period,1168 preterm neonates were admitted to the RAH; 155 (13%) had HRF treated with HFOV, of which 47 (30%) received INO. There were 24 survivors (S) and 23 non-survivors (NS) who did not differ in baseline characteristics including oxygenation indices (OI) (median of 30.7 for S vs. 29.5 for NS). However, OI of S decreased as compared to NS starting at 6h of INO (mean OI as percentage from baseline of 33% for S vs. 61% for NS) (p=0.003). At 6h of INO treatment, 1(4%) S and 8(35%) NS were non-responders (<10% reduction in OI from baseline) with an 89% positive predictive value for non-survival. Causes of death were refractory hypoxemia (8), multi-organ failure (7), withdrawal complications (6) and others (2). Twenty-three S (96%) developed complications including: chronic lung disease (n=22, 92%), intraventricular hemorrhage (n=9, 38%), nosocomial infection (n=7, 29%), retinopathy of prematurity (n=6, 25%), and necrotizing enterocolitis (n=5, 21%).

Conclusions: In very preterm neonates with severe HRF despite HFOV, early response to rescue INO might predict non-survival. Further research is necessary to understand the clinical course and risk factors of adverse outcomes and to improve the management care of these critically ill neonates.

Funded By: The Dr ME Ledingham Memorial Summer Research Award, Neonatal Research Unit, Northern Alberta Neonatal Program

Abstract #:	173
Presenter:	Justin Haas
Supervisor:	Silvia Pagliardini
Title:	Determination of presynaptic connections to the parafacial respiratory group using viral constructs, optogenetics and immunohistochemistry
Authors:	Justin Haas, Annie Duan, Silvia Pagliardini
Affiliations:	University of Alberta
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Breathing in mammals is most fragile during REM sleep, and data from our laboratory suggest that recruitment of abdominal expiratory activity during REM may be critical in preventing breathing irregularities and strengthening inspiratory activity.

Acetylcholine, a neurotransmitter commonly released from the laterodorsal tegmentum (LDT) and pedunculo pontine tegmentum (PPT) during REM epochs, is able to activate an area of the brainstem responsible for the generation of expiratory activity (the parafacial respiratory group, pFRG). However, the presynaptic influences of the pFRG are not well established; therefore, we aimed to characterize these presynaptic networks anatomically and functionally, using a combination of retrograde viral and non-viral neuronal tracers, immunohistochemistry, and selective optogenetic stimulation of pontine projections to the pFRG. Our results indicate that multiple areas in the pons innervate the pFRG: these include the parabrachial nucleus, the periacqueductal grey, the LDT, the PPT, and the Kolliker Fuse nucleus. Our results further suggest that pontine neurons projecting to the pFRG are not cholinergic, and that optogenetic stimulation of these pathways did not elicit active expiration, although it did result in breathing rate depression and increased tidal volume. This suggests that the pons may send inhibitory projections to the pFRG, playing a role in its tonic inhibition at rest.

Funded By: NSERC

Abstract #:	174
Presenter:	Muna Kamal
Supervisor:	Piush Mandhane
Title:	Predictors of sleep disordered breathing trajectories at age 2 years: Analysis of data from the CHILD Edmonton study
Authors:	Muna Kamal, Lisa Smithson, Sukhpreet Tamana, Amanda Lau, CHILD study Investigators, Piush Mandhane
Affiliations:	Foreign Medical Student
Research Activity:	Child and Youth Development : Sleep and Breathing Disorders

Introduction: Childhood sleep disordered breathing (SDB), from snoring to obstructive sleep apnea syndrome (OSAS), may represent multiple overlapping phenotypes depending on a child's craniofacial anatomy, tonsil and adenoid growth, body habitus, and presence of rhinitis symptoms. The different SDB phenotypes may be distinguished by age of onset and duration of symptoms.

Method: Data from the Canadian Healthy Infant Longitudinal Study (CHILD) birth cohort study was used to determine patterns of SDB (SDB phenotypes) based on age of onset and duration of symptoms. The pediatric sleep questionnaire (PSQ) was completed by parents quarterly from three months to two years of age. Infants with a PSQ score greater than 0.33 were considered to have SDB at that quarterly assessment. We used the STATA Proc Traj extension to identify and assign SDB phenotypes to each child based on age of onset and duration between 3 months and 2 years of age. The optimal number of trajectories was selected based on the lowest Bayesian information criteria (BIC). Univariate linear regression was used to identify individual factors associated with for risk of each phenotype) each SDB phenotype.

Results: SDB symptoms, any PSQ positive, were prevalent in 11.1% (*n* =91/817) of children between 3 months to 2 years of age. Trajectory analysis identified four SDB phenotypes: children with no SDB symptoms (81.4%), early-onset SDB symptom (4.1%) with a peak onset at 9 months, late-onset SDB symptoms (12.8%) with peak symptoms at 21 months, and severe SDB symptoms (1.6%) with peak symptoms at 24 months. Ethnicity and socioeconomic factors (maternal education, family income) were not associated with developing SDB while maternal history of OSAS was significantly associated with developing all three SDB phenotypes. The risk of severe SDB was increased among children who had taken GERD medications at 1 year of age, (p=0.04) and among those with rhinitis symptoms. Increased maternal calcium intake during pregnancy (p<0.01) and increased total sugar ingested during pregnancy (p=0.02) increased the child's risk of early-onset SDB. An increased infant gestational age was associated with a decreased risk of developing late onset SDB (p=0.04) while an increasing number of URTIs at 2 years of age increased a child's risk of developing late onset SDB (p<0.001).

Conclusion: We have identified three separate SDB trajectories to two years of age using data from the CHILD Edmonton birth cohort. Each of the three trajectories was associated with unique pre-natal and post-natal risk factors in univariate analysis.

Funded By: Start-up or Retention Funding

Abstract #: 175
Presenter: Mahsa Alaee
Supervisor: Manijeh Pasdar
Title: Anti-tumor/metastasis activity of plakoglobin in invasive ovarian carcinoma cells
Authors: Mahsa Alaee, Manijeh Pasdar
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology

Introduction: Ovarian cancer (OVCA) is the leading cause of all female reproductive cancer deaths worldwide. The overall five-year survival rate of women diagnosed with OVCA is ~ 45%. Here, we have investigated the role of cell-cell adhesion protein plakoglobin (PG, g-catenin) in OVCA.

The epithelial cell adhesion receptor, E-cadherin and its cytoplasmic interacting proteins, b- catenin and PG form complexes that hold epithelial cells together and keep tissues intact. Disruption of cadherin-catenin complexes is a major contributing factor to tumorigenesis/metastasis. Furthermore, upon dissociation from E-cadherin, catenins can interact with other cellular proteins and regulate pathways involved in tumorigenesis/metastasis. In this context, β-catenin has oncogenic function, whereas PG acts as a tumor/metastasis suppressor. The oncogenic activation of β-catenin is well documented in OVCA. However, while the loss of heterozygosity of the PG gene has been reported in OVCA, little is known about how it acts as a tumor/metastasis suppressor in this neoplasm. One mechanism by which PG acts as a tumor/metastasis suppressor is by interacting with p53, a tumor suppressor that is mutated in >50% of OVCA. We have shown that PG interacts with both wild-type and a number of mutant p53s (mp53s) and its interaction with mp53s restores their tumor suppressor activities.

Methods: We investigated the *in vitro* tumor/metastasis suppressor effects of PG in epithelial OVCA cell lines with mp53 expression and different cadherin profiles. Mesenchymal cadherin (N-cadherin) expressing and E-cadherin and PG deficient OVCA cells (ES2) were transfected with constructs encoding E-cadherin or PG or with shRNAs to knock down N-cadherin expression. A combination of molecular and cell biological assays were used to assess expression, localization, protein interactions and *in vitro* growth, migratory and invasive properties of transfectants compared to normal ovarian epithelial cells (IOSE) and OVCA cells expressing PG and E-cadherin (OV90).

Results: Our data showed that PG interacted with and colocalized with cadherins in adhesion complexes. PG also interacted with mp53 in ES-2-PG transfectants. Consistent with these observations, we detected significant reduction in ES-2-PG and ES-2-shN-cad cells growth relative to ES-2 and ES-2-E-cad cells. The exogenous expression of PG or E-cadherin or knockdown of N-cadherin in ES-2 cells significantly reduced their migration and invasion.

Conclusions: Our data suggest that in the absence of E-cadherin, PG can induce growth/ metastasis inhibitory effects in cells expressing N-cadherin and mp53. This effect is likely due to PG interaction with and restoration of tumor suppressor activity of mp53, currently under investigation.

Funded By: CIBC, ACF, Cathy and Harold Roozen Entrance Scholarship

Abstract #:	176
Presenter:	Nicole Pitre
Supervisor:	
Title:	Living in the shadow of domestic violence: Mapping the experience of mothering in conditions of pervasive unpredictability and distrust
Authors:	Nicole Pitre, Kathleen Hegadoren, Gerri Lasiuk
Affiliations:	University of Alberta
Research Activity:	Women's Health : Mental Health

Introduction Mothering is complex and dynamic including interactions with self, personal history, others, and sociocultural expectations. Women's experiences of mothering and decision-making are not well documented as they negotiate the journey that precedes and follows the choice to leave an abusive relationship even if multiple interventions are organized to address and hopefully minimize potential long-term consequences to both women and their children. Little is also known about the power and influence that supportive and non-supportive interactions with service providers have on women's choices.

Method: Through a critical feminist narrative inquiry, we asked eight women to share stories of their experience of mothering, of trust and distrust in self and others, and of interactions with supportive/non-supportive service providers when living in a context of family violence. We also held 2 focus groups with women living similar experiences to confirm whether a broader group of women could see themselves mirrored in our interpretations. All women were further asked to volunteer suggestions for interventions to better meet their needs, and to help women living similar situations.

Results: Despite the wide range of experiences and variations found in women's trajectories, in-depth analysis of their stories revealed similar journeys involving five distinct themes. Women's mothering stories also were inseparable from the stories about the violence they encountered as they worked to free themselves and their children from these conditions. Access to available choices and opportunities ultimately was imbued with an overarching sense of unpredictability and often potentiated distrust of self and others.

Conclusions: Consistent with this research design's social advocacy agenda, women's voices are meant to be heard widely and to inform potential changes. The mapping of the complexities of mothering in interactions with self and others while contending with predominant unpredictability, self-doubt, guilt, and anticipation of harm (e.g., due to stigma, blame, societal views of mothering) will be discussed. Potential use of this map to facilitate and stimulate discussions and explorations toward social change will be reviewed. Specific attention will be given to strengths and challenges identified by women as facilitating or constraining their ability to free themselves and their children from domestic violence, as well as to conditions that contribute or lessen experiences of unpredictability.

Funded By: Innovation Grant

Abstract #: 177
Presenter: Rebecca Miyagishima
Supervisor: Sue Ross
Title: Developing and testing the validity of case definitions for pelvic floor disorders in women who consult family medicine practices in Canada
Authors: Sue Ross, Hilary Fast, Stephanie Garies, Deb Slade, Meghan Doraty, Rebecca Miyagishima, Tyler Williamson, Neil Drummond
Affiliations: University of Alberta
Research Activity: Women's Health : Urology/Gynecology

Introduction (Purpose)

Pelvic floor disorders are common among women, of whom as many as 40% are reported to be affected. This prevalence is expected to increase due to aging within the Canadian population and longer life span in women. The aim of this study was to create and validate case definitions for pelvic floor disorders to be used in the primary care setting. These case definitions would subsequently provide a prevalence estimate and may be applied to further study of pelvic floor disorders in Canadian women and associated workload in primary care. The Canadian Primary Care Sentinel Surveillance Network (CPCSSN) is a multi-disease surveillance system based on electronic medical records (EMR). This network developed and validated case definitions and case finding algorithms for a number of chronic diseases. This retrospective cross-sectional validation study replicated the methods from CPCSSN's previous validation study for pelvic floor disorders, specifically urinary incontinence, fecal incontinence, and pelvic organ prolapse.

Methods

The definition was developed and refined using the Southern Alberta Primary Care Network (SAPCReN), one of CPCSSN's primary care practice-based research networks. Six SAPCReN sites from Alberta participated in validating the EMR case finding algorithms. A random sample was reviewed, oversampling older patients and those with fecal incontinence, for a final sample of 985 charts. Charts were reviewed by trained research assistants and physicians who were blinded to the algorithmic diagnosis. Sensitivity, specificity, and positive and negative predictive values were calculated. Prevalence was estimated for each of the three case definitions.

Results

Sensitivity ranged from 39.8% (pelvic organ prolapse) to 62.5% (fecal incontinence); specificity ranged from 99% (fecal incontinence) to 99.1% (pelvic organ prolapse) positive predictive values ranged from 72.4% (urinary incontinence) to 82.2% (pelvic organ prolapse); all negative predictive values were above 88.4%. Prevalence was determined to be 19.0% for urinary incontinence, 5.7% for fecal incontinence and 9.4% for pelvic organ prolapse.

Conclusions

While the case definitions did not meet the acceptable minimum for sensitivity, they all performed with high specificity and predictive values. This study has also succeeded in generating prevalence estimates for pelvic floor disorders in community-dwelling women who speak to their family physician or nurse practitioner about their pelvic floor symptoms. Furthermore, this study is an important first step towards a better understanding of the impact of pelvic floor disorders in women in the primary care setting.

Funded By: Start-up or Retention Funding

Abstract #: 178
Presenter: Tho Tran
Supervisor: Lawrence Le
Title: A pilot study to measure ultrasonic velocity in human tibiae
Authors: Tho N.H.T. Tran, Mauricio Sacchi, Edmond Lou, Lawrence Le
Affiliations: University of Alberta
Research Activity: Women's Health : Mature Women's Health

Introduction: The use of ultrasound to study bone properties has been evolving for the last two decades. Particularly, axial transmission ultrasonography has shown great potential to be a non-invasive assessment tool to characterize cortical bone at multiple peripheral skeletal sites, e.g. radius and tibia, for assisting osteoporosis diagnosis. Osteoporosis is a widespread bone-weakening disease with significant morbidity and mortality affecting over two hundred million people throughout the world, especially the elderly and post-menopausal women. According to Osteoporosis Canada, at least one in three women will suffer from an osteoporotic fracture during their lifetime. The objectives of this study are to acquire and analyze the *in vivo* axially-transmitted ultrasound data from the human tibiae.

Methods: A TomoScan Focus LT™ phased array ultrasound system (Olympus NDT Inc., Canada) was used for the data acquisition. The left mid-tibia was chosen as the measured site for this clinical study. One hundred consented subjects, who had bone densitometry examinations, were recruited at a local Medical Imaging Consultant clinic in Edmonton. Each subject was scanned three times using different beam-steering configurations at a fixed transmitter-receiver distance.

Results: Ten subjects were assigned for this pilot study. For each dataset, the transit time of the first detectable signals at the receiving probes were measured. Since the ultrasound pathway was fixed, the midtibial ultrasound velocity could then be estimated by linear regression. The average speed was estimated from the three ultrasound records for each subject. The cortical speed of sound was found to decrease with age, i.e. sensitive to age- and osteoporosis-induced changes in bone.

Conclusions: This preliminary result will be used as a basis for the analysis of the remaining subjects' data to further examine the relationship between ultrasound parameters and skeletal health status. It is expected to provide a novel application of ultrasonic inspection technique in osteoporosis monitoring and diagnosis for aged women.

Funded By: Graduate Studentship

Abstract #:	179
Presenter:	Zelei Yang
Supervisor:	David Brindley
Title:	Role of autotaxin and inflamed mammary adipose tissue in the development of doxorubicin resistance in breast cancer
Authors:	Zelei Yang, Ganesh Venkatraman, Xiaoyun Tang, Matthew Benesch, Amadeo Parissenti, Todd McMullen, Denise Hemmings, David Brindley
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology

Introduction

The enzyme autotaxin and its production of a bioactive lipid lysophosphatidate (LPA) promotes breast tumor growth, metastasis and chemo-resistance. In breast tumor, breast cancer cell express low level of autotaxin, but its secretion of inflammatory cytokines stimulates autotaxin secretion from the adjacent adipose tissue. Autotaxin then produces LPA, which binds to its receptors on cancer cells to promote tumor growth and further inflammation, resulting in a vicious inflammatory cycle. This action of autotaxin and LPA is a part of the wound healing response, which is hijacked by tumors that are described as “wounds that do not heal”. We hypothesized that damage of breast tumors during doxorubicin therapy would also elicit a wound healing response. This would increase the secretion of autotaxin and inflammatory cytokines, thus enhancing the vicious cycle and leading to decreased efficacy of the therapy.

Methods

We treated human MCF-7 breast cancer cells or human adipose tissues with combinations of LPA and doxorubicin and then analyzed for the production of inflammatory mediators using qRT-PCR and at the protein level with multiplex ELISA. We also used a syngeneic mouse model with 4T1 breast cancer cell injection into the mammary fat pad to investigate the effect of doxorubicin therapy. Doxorubicin or PBS was injected every third day throughout tumor development. The expression of inflammatory mediators in adipose tissue adjacent to the tumor, the contralateral adipose tissue and the breast tumor were analyzed.

Results

MCF-7 cells selected as resistant to doxorubicin show higher expression of inflammatory cytokines. Treatment of MCF-7 cells with LPA amplified the doxorubicin-induced expression of inflammatory cytokines. In adipose tissue, autotaxin expression increases when treated with LPA in the presence of doxorubicin. Mice treated with doxorubicin show increased expression of autotaxin and inflammatory cytokines in the adipose tissue adjacent to the breast tumor, but not in the contralateral fat pad.

Conclusions

Our results support the hypothesis that damage caused by doxorubicin therapy establishes an inflammatory response involving increased production of inflammatory cytokines and autotaxin. This response was an attempt to heal the damage caused by chemotherapy and enhances the vicious inflammatory cycle that promotes tumor progression, therefore decreasing the efficacy of chemotherapy. This provides an additional understanding for the development of acquired chemo-resistance. For future study, we propose that by decreasing inflammatory responses through blocking autotaxin activity and LPA signaling could provide an effective strategy for increasing the efficacy of chemotherapy.

Funded By: Start-up or Retention Funding

Abstract #:	180
Presenter:	Xiaolu Han
Supervisor:	Yangxin Fu
Title:	Phosphorylation profiles in cisplatin-sensitive and -resistant epithelial ovarian cancer cells
Authors:	Xiaolu Han, Jiesi Zhou, Helen Steed, Lynne-Marie Postovit
Affiliations:	University of Alberta
Research Activity:	Women's Health : Oncology

Introduction: Ovarian cancer is the leading cause of death due to gynecologic malignancies and the fifth leading cause of cancer-related mortalities in women. Epithelial ovarian cancer (EOC) accounts for approximately 90% of all ovarian malignancies. Despite the initial positive response, acquired chemoresistance renders current chemotherapy regimens ineffective. There is an urgent need to better understand the molecular mechanisms of chemoresistance in EOC in order to develop more effective therapeutic strategies.

Methods: Carboplatin (the first-line chemotherapeutic agent to treat EOC) induces cell death by regulating multiple signaling pathways. To determine carboplatin-induced signaling events in cisplatin-sensitive EOC cell line A2780s versus its derivative cisplatin-resistant A2780cp cells, we performed a Proteome Profiler Human Phospho-Kinase Array experiment in these paired cell lines and validated the phosphorylation results by Western blotting. The effect of p38 and ERK inactivation by their respective inhibitors on carboplatin-induced cell death in A2780s and A2780cp cells as well as primary EOC cells was examined by the neutral red uptake assay and Western blotting.

Results: The Phospho-Kinase array revealed that multiple phosphorylation events were induced in both A2780s and A2780cp cells by carboplatin treatment. Interestingly, A2780s and A2780cp cells displayed different profiles in basal and carboplatin-induced phosphorylation. For example, the basal level of p38 and ERK phosphorylation was higher in A2780cp cells compared to A2780s cells, but the induction of p38 and ERK phosphorylation by carboplatin was more pronounced in A2780s cells than in A2780cp cells. Using specific p38 inhibitor, we showed that p38 phosphorylation was pro-apoptotic in both A2780s and A2780cp cells. Interestingly, inhibition of ERK showed different effects in A2780s and A2780cp cells; while the inhibitor sensitized A2780s cells, it rendered A2780cp cells more resistant to carboplatin. The effect of these inhibitors on carboplatin-induced apoptosis was confirmed by Western blotting using cleaved PARP as readout. Inhibition of p38 and ERK had variable effects on growth and carboplatin-induced cell death in primary EOC cells.

Conclusions: A2780s and A2780cp cells display different phosphorylation profiles at the basal level and after carboplatin treatment. Results in this study demonstrate a variable effect of p38 and ERK phosphorylation on cell growth and carboplatin-induced cell death in A2780s and A2780cp cells as well as primary EOC cells. Further characterization of the role of the phosphorylated molecules in carboplatin-induced cell death is warranted to better understand the mechanism of chemoresistance in EOC.

Funded By: Start-up or Retention Funding

Abstract #: 181
Presenter: Samuel Yang
Supervisor: Mark Glover
Title: Function of TopBP1 in ATR recruitment to sites of DNA damage
Authors: Samuel Yang
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology

Activation of Ataxia telangiectasia and Rad3 related (ATR) kinase is critical in maintaining genomic integrity and resisting DNA damage. In response to replication stress and persistent single-stranded DNA, ATR engages programs of apoptosis and senescence to prevent further mutagenic divisions. Recently, studies showed that the activation of ATR was mediated from contributions of conserved phospho-peptide binding BRCA1 C-terminal (BRCT) domains of Topoisomerase IIβ binding protein 1(TopBP1). BRCT domains play integral roles in the facilitation of protein-protein (PPI) and protein-DNA interactions in response to DNA damage -- they provide specificity to target different replication fork proteins. Here, we utilize fluorescence polarization assays (FP) and electrophoretic mobility shift assays (EMSA) with human TopBP1 to show the binding that takes place between the BRCT 5 domain and DNA. Previous studies showed that the fifth BRCT domain was integral for TopBP1 localization to stalled replication forks. However, the fourth and fifth domains exist as a tandem repeat where BRCT 5 interacts with multiple binding partners and BRCT 4 plays a suggestive role in stabilization. Our study corroborates the findings that the BRCT 5 domain play a contributing role in DNA interaction. Furthermore, from our binding assays involving various lengths of single-stranded DNA, results show that a minimum of 15 nucleotides are required for proper DNA interaction. These data provide insight into the domain specific interaction of TopBP1 regarding DNA damage and provide the basis for future functional and structural studies.

Funded By: AIHS

Abstract #: 182
Presenter: Jiesi Zhou
Supervisor: Yangxin Fu
Title: The RUNX family of transcription factors are oncogenes in granulosa cell tumors of the ovary
Authors: Jiesi Zhou, Abul Azad, Nidhi Gupta, Xiaolu Han
Affiliations: University of Alberta
Research Activity: Women's Health : Oncology

Introduction: Granulosa cell tumors of the ovary (GCTs), arising from sex cord-stromal cells, accounts for approximately 5% of all ovarian malignancies. Although the prognosis is more favorable than epithelial ovarian cancer, advanced or recurrent tumors show poor outcome. Surgery is the mainstay treatment to the tumors in the early stages. However, treatment options for advanced and recurrent GCTs are still limited. The molecular pathogenesis of GCTs remains poorly understood. The RUNX family of transcription factors are either oncogenes or tumor suppressors in a cancer-specific manner. It has been shown that all three RUNX proteins (RUNX1-3) and CBFβ (the common heterodimeric partner of RUNX proteins) are oncogenes in epithelial ovarian cancer. However, the role for RUNX1-3 in GCTs is unknown.

Methods: SVOG (immortalized granulosa cell line), KGN (adult GCT cell line) and COV434 (juvenile GCT cell line) are used. Expression of RUNX proteins in these cell lines was examined by Western blotting. Activity of RUNX1-3 was inhibited by a specific inhibitor or by CBFβ knockdown. RUNX3 was stably overexpressed in KGN cells and inactivated by a dominant negative form of RUNX3 (dnRUNX3) in COV434 cells. Cell growth, colony formation, and migration was measured by the neutral red uptake assay, the soft agar assay and the scratch assay, respectively. Western blotting and quantitative (q)RT-PCR was performed for molecular analysis. Expression of RUNX proteins in human adult GCT tissues was examined by Western blotting.

Results: Western blotting showed that RUNX1 was expressed in all three cell lines, whereas RUNX2 was expressed in KGN and SVOG, but not in COV434. RUNX3 was expressed at a high level in COV434 cells, but was not detected in SVOG and KGN cells. Inhibition ofRUNX1-3by the inhibitor or by CBFβ knockdown decreased growth of KGN cells. Overexpression of RUNX3 significantly increased growth, colony formation in soft agar and migration of KGN cells. By contrast, inactivation of RUNX3 by dnRUNX3 reduced growth of COV434 cells. Western blotting and qRT-PCR showed that RUNX3 downregulated p27, but increased cyclin D2 expression in KGN cells. Western blotting showed that RUNX1 and RUNX2 were expressed in human adult GCT tissues.

Conclusion: Our results suggest that RUNX proteins could be oncogenes in GCTs.Knockdown experiments are required to further investigate the role for each RUNX protein in GCTs.

Funded By: Start-up or Retention Funding

Abstract #: 183
Presenter: Ashley McCurdy
Supervisor: Margie Davenport
Title: The impact of exercise on postpartum depressive symptoms
Authors: Ashley McCurdy, Normand Boulé, Allison Sivak , Margie Davenport
Affiliations: University of Alberta
Research Activity: Maternal Research : Perinatal Mental Health

Introduction

Depressive symptoms during the postpartum period may adversely affect both maternal and infant health. Because conventional treatments, including anti-depressants and psychotherapy, are often not adhered to during postpartum period, alternative methods of treatment should be explored. Recent reviews have suggested that exercise is effective in reducing depressive symptoms in the general population, however, the effect has not been well studied in postpartum women. Therefore, we conducted a systematic review and meta-analysis examining the influence of exercise on depressive symptoms in women during the postpartum period.

Methods

A structured search of CINAHL, EMBASE, MEDLINE, Sport Discus, Ovid's All EBM Reviews, and ClinicalTrials.gov databases was performed up to June, 16, 2016. Studies were included if they were randomized controlled trials comparing exercise with no treatment for which outcomes measuring depressive symptoms were obtained. 15 papers met our inclusion criteria. Standardized mean differences (SMD) in post-intervention outcomes were pooled using a random effects model.

Results

Overall, post-intervention depressive symptoms were significantly lower in the exercise compared to control groups (SMD= -0.34, 95% Confidence Interval [95% CI] = -0.50, -0.19, I^2= 37 %). Depressive symptoms were found to be lower in women who were depressed at baseline (SMD= -0.47, 95% CI= -0.72, -0.22, I^2= 42%) when compared with women from the general postpartum population (SMD= -0.22, 95% CI= -0.36, -0.08, I^2= 2%), however these differences were not statistically significant (p= 0.08). Among women with depression pre-intervention, group exercise was associated with significantly lower post-intervention scores in depressive symptoms (SMD= -0.74, 95% CI= -1.07, 0.40, I^2= 27%) than individual exercise (SMD= -0.21, 95% CI= -0.45, 0.04, I^2= 0%). In trials examining the prevalence of depressive episodes following treatment, postpartum exercise was found to reduce the odds of experiencing a depressive episode by 54% among women who were depressed pre-intervention.

Conclusion

Our meta-analysis demonstrates that exercise during the postpartum period improves depressive symptomology and may decrease the likelihood of experiencing a depressive episode.

Notes

DISCLAIMER:
While the abstracts have been slightly modified for consistency, each abstract has been predominantly printed exactly as originally submitted.

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