Schulich School of Medicine & Dentistry

Western University

Department of Medicine

RESEARCH DAY

Friday, May 24, 2024

Best Western Lamplighter Inn

591 Wellington Road South

London, Ontario

This program has no commercial support.

CME INFORMATION

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by Continuing Professional Development, Schulich School of Medicine & Dentistry, Western University. You may claim a maximum of **3.75 hours** (credits are automatically calculated).

Each participant should claim only those hours of credit that he/she actually spent participating in the educational program.

25% of this program is dedicated to participant interaction.

Scan the QR code to complete the **Participant Evaluation** form online.

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Learning Objectives

By the end of this research day, participants will be able to:

- describe new research findings of relevance to Internal Medicine and related subspecialties.
- recognize all types of research conducted by trainees in the Department of Medicine.
- identify and promote research successes in the Department of Medicine.

Dr. Adrian Owen Learning Objectives:

1. To recognize the functional and behavioural differences between coma, vegetative state, minimally conscious state, and other disorders of consciousness.
2. To evaluate emerging diagnostic and prognostic neuroimaging methods for assessing residual cognition and covert awareness after severe brain injury.

Dr. Erin Spicer Learning Objectives:

1. To distinguish between outcome, process and balancing measures, and apply these to your QI project in a meaningful way.
2. To distinguish what data makes for meaningful metrics versus what is available in a timely manner.

Dr. Qasim Khan Learning Objectives:

1. To recognize the impact of obesity in chronic liver disease and in liver transplant recipients.
2. To identify current and upcoming strategies to manage obesity in liver transplant candidates and recipients.

Brief Biosketches for Keynote and Faulty Speakers

Keynote Speaker:

Dr. Adrian M. Owen OBE, PhD

Adrian M. Owen OBE, PhD is currently a Professor of Cognitive Neuroscience and Imaging in the Departments of Physiology & Pharmacology and Psychology at the University of Western Ontario, Canada. He also directs the Brain, Mind, and Consciousness program funded by the Canadian Institute for Advanced Research (CIFAR) and is on the Executive Committee of the CFREF funded initiative BrainsCAN at the University of Western Ontario, Canada. Dr. Owen was previously the Assistant Director of the Medical Research Council Cognition and Brain Sciences Unit at Cambridge University and the Canada Excellence Research Chair (CERC) in Cognitive Neuroscience and Imaging at Western University. His research combines structural and functional neuroimaging with neuropsychological studies of brain-injured patients and has been published in many of the world's leading scientific journals, including Science, Nature, The New England Journal of Medicine and Lancet. Dr. Owen has played multiple editorial roles, including 9 years as Deputy Editor of The European Journal of Neuroscience. He has published over 400 peer reviewed articles and chapters and a best-selling popular science book 'Into the Gray Zone: A Neuroscientist Explores the Border Between Life and Death. Dr. Owen was awarded Officer of the Most Excellent Order of the British Empire (OBE) in the Queen's Honors List, 2019, for services to scientific research. He was made a Fellow of the Royal Society of Canada in 2022 and a Fellow of the Canadian Academy of Health Sciences in 2023.

Faculty Speakers:

Dr. Erin Spicer MD, FRCPC, MSc. QIPS

Erin Spicer (MD, FRCPC, MSc. QIPS) is a Clinician-Researcher within the Division of General Internal Medicine at London Health Sciences Centre and Western University. Her research interests centre around quality of care and education on the clinical teaching unit, especially iatrogenic complications of inpatient admissions, including frailty and delirium. She is a member of the Centre for Quality Improvement, Innovation and Patient Safety (C-QuINS), co-leads the CTU Quality, Innovation and Education Research (C-QuIER) Hub, and is the local QI lead for the London branch of the General Medicine Quality Improvement Network (GeMQIN).

Dr. M. Qasim Khan, MBBS, MS, FRCPC

Dr. M. Qasim Khan is a clinical-researcher and Assistant Professor in the Department of Medicine, Division of Gastroenterology at Western University and its affiliated London Health Sciences Centre (LHSC) in London, ON, Canada. He is cross-appointed in the Department of Epidemiology and Biostatistics. As a transplant hepatologist, his clinical and research interests include metabolic dysfunction-associated steatotic liver disease (MASLD), portal hypertension, particularly as it pertains to MASLD, and the management of cardiometabolic disorders in the pre-, peri- and post-liver transplant settings. He is a past Steering Committee member of the Clinical Practice SIG of the American Association for the Study of Liver Diseases (AASLD), and a Vanguard Committee Member of the International Liver Transplant Society (ILTS), where he has played an instrumental role in developing educational content such as the ILTS Podcast by the Experts and Article of the Month Podcasts. In addition, he is a member of the Liver Transplant Special Interest Group of the Canadian Association for the Study of the Liver (CASL).

AGENDA

DoM Resident Research Day 2024

Friday, May 24, 2024

Best Western Lamplighter Inn

Schedule of Events			
Start	**End**		
8:00	8:30	**Breakfast**	**Poster Setup** (Crystal Ballroom South)
8:30	8:40	**Welcome & Opening Remarks by Dr. Vipul Jairath** (Crystal Ballroom North)	
8:40	9:40	**Trainee Oral Presentations – (4)** (Crystal Ballroom North) *10 min presentations, 5 min Q&A*	
9:40	10:25	**Keynote - Dr. Adrian Owen** **"Exploring Cognition at the Margins of Consciousness"** (Crystal Ballroom North) *35 min presentation, 10 min Q&A*	
10:30	11:30	**BREAK**	**Poster Presentation and Judging** (Crystal Ballroom South)
11:30	11:50	**Faculty Presentation - Dr. Erin Spicer** **"From Frontlines to Headlines: Using Meaningful Data to Drive Quality of Care"** (Crystal Ballroom North) *15 min presentation, 5 min Q&A*	
12:00	14:00	**LUNCH**	**Poster Presentation and Judging** (Crystal Ballroom South)
14:00	14:15	**GROUP PHOTO** **Everyone is invited to gather in the Crystal Ballroom North for a group photo**	
14:15	14:35	**Faculty Presentation - Dr. Qasim Khan** **"Obesity Management Pre- and Post-Liver Transplantation"** (Crystal Ballroom North) *15 min presentation, 5 min Q&A*	
14:35	15:50	**Trainee Oral Presentations – (5)** (Crystal Ballroom North) *10 min presentations, 5 min Q&A*	
15:50	16:00	**Presentation of Awards & Final Remarks** (Crystal Ballroom North)	

Trainee Oral Presentations

Morning

Time	Presenter	Level	Supervisor	Abstract Title	Page Number
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08:55	MacNeill, Michael	PGY-2	Dr. Joy Mangel	Assessment of Sarcopenia as a Measure of Frailty in Older Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma	35
09:10	Buckley, Gabrielle	Undergrad	Dr. Lillian Barra	Rheumatoid Arthritis Associated Proteins in An Animal Models	21
09:25	Natt, Navneet	PGY-4	Dr. Aze Wilson	Paradoxical Psoriasis following Anti-TNFα Therapy in Inflammatory Bowel Disease and Association with an IL-23 Receptor Variant: A Preliminary Report	40

Afternoon

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14:50	VanNynatten, Logan	PGY-4	Dr. Douglas D Fraser	Evaluation of Novel Plasma Liver Biomarkers in Critically Ill Sepsis Patients	56
15:05	Howarth, Nisha	PGY-5	Dr. Anouar Teriaky	Reducing inappropriate gamma-glutamyl transferase testing for inpatients: a quality improvement initiative in lab waste reduction applying the model for continuous improvement	27
15:20	Solitano, Virginia	Clinical Fellow	Dr. Vipul Jairath	Towards patient-centricity: why do patients with Inflammatory Bowel Disease Participate in Pharmaceutical Clinical Trials? A Mixed-Methods Exploration of Study Participants	50
15:35	Leung, Wayne	PGY-4	Dr. Reza Rahimi Shahmirzadi	Use of Dalbavancin in treatment of Acute Bacterial Skin and Skin Structure Infections: Prospective Case series from a Canadian Perspective	33

Trainee Poster Presentations

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List of All Submitted Abstracts (in alpha order)

Meisam AbdarEsfahani

High dose influenza vaccine for solid organ transplant patients. A Systematic review and meta-analysis

Meisam Abdar Esfahani, Rachel Couban, Michael Silverman, Mohammadreza Rahimi Shahmirzadi

Seasonal influenza can cause serious illness and even death, especially in people with immunocompromised like those who have had solid organ transplants (SOT). Early results from studies show that high dose (HD) intramuscular (IM) vaccine might help boost the body's immune in transplant patients. Given the uncertain benefits and harms associated with vaccine dose a synthetized appraisal of the evidence is warranted.Randomized controlled trials were included in this review. Studies with adults who underwent SOT and got IM influenza vaccine were included in this systematic review. We included trials that compared getting HD, IM influenza vaccine with standard dose.The outcomes of interests are seroconversion rate (SCR) for H1N1, SCR for H3N2, and graft rejection after vaccination. We searched MEDLINE, Embase, and Cochrane CENTRAL until Jan 2024. Screening, data extraction, risk of bias and certainty of evidence assessment were done by two reviewers. Pooling data from the 5 studies (1281 patients) shows moderate quality of evidence in the SCR towards using HD influenza vaccine in H1N1 type. (RR 1.87 (1.25 to 2.79))Analysis indicated high-quality evidence in the SCR (H3N2 type) in favour of HD influenza vaccine in patients with SOT. (RR 1.54 [1.31 to 1.80]) Analysis of five studies indicated that HD influenza vaccine likely results in no difference in graft rejection. (RR 0.73 [0.37 to 1.45]). Our systematic review indicates that HD influenza vaccine probably increase SCR in H1N1 and increase SCR in H3N2. Also, HD vaccine, probably does not increase graft rejection.

Romel Abou-Akl

Practice Variation Survey on Investigations and Management of Erythrocytosis: The Canadian Approach

Romel Abou-Akl, Jessica Liu, Aidan McKee, Michael MacNeil, Chai Phua, Benjamin Chin-Yee, Cyrus C. Hsia, Jenny Ho

Background: Erythrocytosis, defined by the World Health Organization as hemoglobin >165 g/L in men and > 160 in women, is present in 4% and 0.4% of the general population.The differential diagnosis of secondary erythrocytosis is extensive and standardized diagnostic and management guidelines are lacking, leading to variations in clinical practice. Methods: We developed a quick and effective survey which can be electronicallycompleted by internists, medical oncologists, and hematologists across Canada within 10minutes. Our survey aims to determine how practitioners incorporate diagnostic investigations to evaluate erythrocytosis and how they approach interventions in themanagement of secondary erythrocytosis. The survey was constructed in RedCap and will be distributed to approximately 400 Canadian specialists through email. Survey data willbe analyzed using descriptive analysis to identify trends, as well as differences betweenspecific groups of practitioners (e.g. community versus academic and hematologistsversus internists). The survey questions are designed to elicit responses along a spectrum rather than in a binary manner. Respondents are asked to provide

answers that reflect thecontinuum of options available in their clinical practice. Topics covered include routine laboratory investigations, bone marrow and molecular testing, imaging studies, treatment recommendations, and long-term follow-up strategies. Results: Our survey has been created and will be distributed following final REB approval. Conclusion: We have developed a cross-sectional survey that will provide insight oncurrent clinical approach to the evaluation and management of secondary erythrocytosis.This will guide future studies and development of guidelines.

Maud Ahmad

Laboratory reference ranges influence referral patterns for hemoglobin abnormalities in the Ontario virtual care system

Maud Ahmad, Benjamin Chin-Yee, Ian H. Chin-Yee, Ben Hedley, Cyrus C. Hsia

This retrospective cross-sectional study investigates the impact of laboratory-specific hemoglobin reference ranges on eConsult referral patterns for suspected anemia and elevated hemoglobin at a tertiary care center in London, Ontario that serves Southwestern Ontario. The study analyzed primary care referrals through the Ontario Telemedicine Network's eConsult platform for hemoglobin abnormalities, excluding patients under 18, between July 1, 2019, and June 30, 2023.The main outcome measures were influence of hemoglobin reference ranges on the referral patterns for suspected anemia and elevated hemoglobin, as well as the extent of pre-referral laboratory testing. Of the 619 eConsults reviewed, 251 referrals for suspected anemia and 93 for elevated hemoglobin were analyzed. Referral patterns showed significant variance in hemoglobin levels based on different laboratory thresholds. Referrals for suspected anemia in females from laboratories whose lower limit of normal was 120 g/L or greater had a hemoglobin concentration 7.5 g/L greater than referrals that used laboratories with a threshold lower than 120 g/L. The study also identified potential areas for improvement in pre-referral investigations; 44% of eConsults did not provide a ferritin level, 53% were missing a B12 level, and 81% were missing a reticulocyte count. In conclusion, laboratory reference ranges for hemoglobin significantly influence referral patterns for suspected hemoglobin abnormalities in Ontario's eConsult system. There is a need for standardized reference ranges and comprehensive pre-referral testing to avoid unnecessary medicalization and referrals. We propose an anemia management algorithm to guide primary care providers in the pre-referral investigation process.

Abdulaziz Alajmi

5-Aminosalicylates (5-ASA) for patients with active or quiescent Crohn's disease: An umbrella review of systematic reviews

Abdulaziz Alajmi, Yuhong Yuan, Vipul Jairath

Background: 5-ASAs (sulfasalazine and mesalamine) are commonly used in patients with mild to moderate Crohn's disease (CD). However, the evidence regarding its efficacy is mixed, with conflicting findings in systematic reviews (SRs). This umbrella review aims to consolidate existing knowledge by identifying, evaluating, and synthesizing findings from published SRs on the use of 5-ASA in patients with active or quiescent CD. Methods: We systematically searched major databases for relevant SRs

published in English until February 28, 2024, summarizing data on 5-ASA use in induction, maintenance, or withdrawal trials. Results: Of 795 screened references, 8 SRs met our inclusion criteria. Only Cochrane reviews assessed the level of certainty of evidence. The latest NMA in 2017, including 22 RCTs for induction, suggested high-dose mesalamine was more effective than placebo, ranking higher than low-dose budesonide and sulfasalazine, though lower than corticosteroid and high-dose budesonide. Conversely, the latest Cochrane review in 2016, including 12 RCTs for maintenance, concluded no evidence supporting oral 5-ASAs over placebo for maintaining medically induced remission. Only the NMA conducted a sensitivity analysis related to baseline disease activity, indicating high-dose mesalamine's significant superiority to placebo when restricted to RCTs with enrolment CDAI between 150 and 450. Conclusion: High-dose mesalamine may be considered for induction of remission in mild-moderate CD; however, evidence does not support 5-ASA efficacy in maintaining medically induced remission. Updating systematic reviews with new evidence is imperative to provide guidance on the subset of patients who may benefit from 5-ASA use or withdrawal.

Ranya AlJumaily

Authorship Gender Diversity in Allergy and Immunology: A Decadal Analysis of High-Impact Journals

Ranya Al Jumaily, Natalie DeGruse, Samira Jeimy

Background: Gender diversity in authorship is essential for equitable scientific advancement, yet disparities persist in various fields, including Allergy and Immunology. High-impact journals serve as influential platforms for research dissemination, but the extent of gender diversity within their authorship remains underexplored. Aim: This study investigates authorship gender diversity within Allergy and Immunology by analyzing articles published in the top high-impact journals over a 10-year period (2013-2023). It aims to assess trends and patterns in gender composition. Method: A comprehensive methodology categorizes authors by gender using journal databases and supplementary sources. Quantitative analysis examines gender representation, authorship positions, geographical distribution, and institutional affiliations. Statistical analysis identifies correlations between gender diversity and publication metrics. Results: Data analysis is currently underway. This section will be updated once that is complete. Our hypothesis is an increase in women first author publications over time. Conclusion: The study provides insights into authorship gender diversity in Allergy and Immunology. These findings will contribute to diversity, equity, and inclusion efforts in academia, informing initiatives for a more inclusive scientific community.

Ranya AlJumaily

Anaphylaxis to Bivalent Omicron COVID-19 Vaccine: A Case Report in a 59-Year-Old Female

Ranya Al Jumaily, Mark Kuprowski

Background: Anaphylactic reactions to COVID-19 vaccines are rare but have been reported. We present a case of a 59-year-old female, with no previous history of vaccine reactions, who experienced anaphylaxis following her fourth dose of the Bivalent Omicron vaccine. Case Description: Our patient is a 59 year old female who developed diffuse diaphoresis, chest tightness, neck angioedema, and

presyncope within 5 minutes of vaccine administration. No hives, facial angioedema, or respiratory symptoms were noted. Immediate epinephrine administration, antihistamines, and steroids led to resolution within 2-3 hours. Intradermal skin testing done at St Joseph's Allergy & Immunology clinic revealed positive reactions to the Pfizer Comirnaty vaccine, confirming a true allergy. Discussion: This case underscores the importance of recognizing and managing anaphylactic reactions. Despite previous vaccinations, this was her first such reaction. Positive skin test did confirm a true allergy. Future retesting and administration of alternative vaccines may be considered if required. Conclusion: Anaphylaxis to COVID-19 vaccines, though rare, can occur even in individuals with no prior history of allergic reactions. Clinicians should be vigilant in identifying and managing such cases, emphasizing the importance of thorough evaluation and appropriate follow-up care. Keywords: COVID-19 vaccine, anaphylaxis, allergy, skin testing, case report.

Ala Almanaseer

Sensitivity, specificity and positive predictive value of leukoerythroblastosis as a predictor of clinically significant myelofibrosis or myelophthisic anemia

Ala Almanaseer, Jonathan Keow, Ben Chin-Yee, Ben Hedley, Ian Chin-Yee, Cyrus Hsia

Leukoerythroblastosis, marked by the appearance of immature erythroid and myeloid cells in the peripheral blood, has been recognized as a potential indicator of pathological conditions in the bone marrow that include myelofibrosis and other infiltrative disorders, called myelophthisis. The primary objective of this study was to investigate the association between leukoerythroblastosis and myelofibrosis and myelophthisis, focusing on the predictive value of leukoerythroblastosis in these conditions.We aim to complete a retrospective chart review of all adult patients, age 18 years and above, who underwent a bone marrow biopsy with available peripheral blood films at the London Health Sciences Centre (LHSC) between Jan 1, 2018 to Dec 31, 2019. The sample size includes 1762 patients that are currently being assessed for markers of leukoerythroblastosis, including presence of teardrop red blood cells, immature granulocytes, and/or nucleated erythrocytes as well as presence of myelofibrosis and myelophthisis on bone marrow biopsy. 217 pediatric patients were excluded prior to chart review. Medical histories and laboratory reports will be assessed. The bone marrow biopsy reports will be examined for presence of myelofibrosis, defined as MF-2 or higher, and other infiltrative disorders. Statistical analysis will include a Cox univariate analysis of predictive power for leukoerythroblastosis as a marker of myelofibrosis or myelophthisis and a Cox multivariate analysis of predictive power for nucleated erythrocytes, immature granulocytes, and teardrop erythrocytes. Through this study, we aim to provide valuable insights into the diagnostic utility of leukoerythroblastosis and potentially refine its clinical interpretation.

Elnaz Assadpour

Early Discharge Pathway in Patients with Stemi: Initial Experience of a New Clinical Pathway at London Health Sciences Centre

Elnaz Assadpour, Vinay Jayachandiran, Sofia Babapulle, Ryan Davey, Nicole Adams, Ashlay Huitema, Nikolaos Tzemos, Sabe De, Daniel Durocher, Sonia Mota, Adam Lucas, Rodrigo Bagur, Sarah Blissett

Background London Health Sciences Centre (LHSC) implemented a new clinical pathway in January 2023 to facilitate early hospital discharge (EHD) within 48 hours for low-risk ST Elevation Myocardial Infarction (STEMI) patients. This study characterizes the common exclusion criteria, barriers, safety profile and patient satisfaction of EHD. Methods/Results Patients presenting with STEMI between January 9th, 2023, and March 31st, 2024 were prospectively identified, and a patient satisfaction survey was conducted 4-8 weeks post-discharge. Those discharged ≤48hours were defined as the EHD-cohort (EHDC), and those after 48hours the non-EHD-cohort (non-EHDC). Of 433 patients with STEMIs, 65% (n=282) were ineligible for EHD (revascularization considerations 19% and infarct-related complications 57%). The remaining 35% (n=151) were eligible for EHD of which 72% (n=109) were in the EHDC and 28%(n=42) in the non-EDHC. We found that 82% of patients admitted in the afternoon were discharged early versus 61% of patients admitted in the morning or night (odds ratio=3.5; 95% confidence interval 1.565-7.828; p=.002). Fewer 30-day readmissions (EHDC 0% vs. non-EHDC 7%, p=.007) were noted. Overall satisfaction (96% vs. 95%, p=.841), perception of length of stay (91 vs. 82%, p=.149), and intention to attend cardiac rehabilitation (63% vs. 67%, p=.727) were similar in both EHDC and non-EHDC. Conclusion Common reasons for exclusion from EHD pertain to coronary anatomy and infarct-related complications. Morning or evening admission times were identified as a potentially modifiable barrier for EHD. Notably, fewer 30-day readmissions were observed, and patients were highly satisfied following an EHD pathway.

Esraa Babaeer

A Case Report of Long-standing Profound Neutropenia with Uncertain Etiology and Concomitant Cutaneous Fungal Infection

Esraa Babaeer, Lili Ataie, Danielle Ouellette, Sameer Elsayed, Lise Bondy, Megan Devlin, Huma Saeed, Mahshid Mohammadi, Michael Silverman, Sarah Shalhoub, Lalit K.Saini, Reza Rahimi Shahmirzadi

Background: To discuss a significance of considering cutaneous fungal infections in assessing patients with chronic cutaneous ulcers unresponsive to antibacterial therapy and long-standing neutropenia. Case: 64-year-old man who was being investigated for chronic neutropenia sought evaluation for a soft tissue ulcer in the right shin as result of trauma. Despite multiple courses of intravenous and oral antibiotics for possible cellulitis, he exhibited minimal response to treatment. Pancytopenia, with a critically low neutrophil count of 0.0, were noted, raising concerns about a potential peripheral consumptive process. Further investigations, including an autoimmune workup, revealed a strongly positive antineutrophil antibody (ANA) at a titre of 1:5120, positive anti-double stranded DNA (anti-DS DNA) at 130, and positive rheumatoid factor at 228, with wound cultures growing Fusarium solani. Based on culture results and immunocompromise, he received liposomal amphotericin B and Full body computed tomography ruled out invasive disease, after which he was transitioned to oral voriconazole. The skin biopsy had grown Fusarium solani, reinforcing the fungal nature of his infection. Surgical management was deemed to be a challenge due to the patient's comorbidities and anticoagulation therapy. Consultation with Hematology for long-standing neutropenia lead to the diagnosis of a peripheral consumption process, based on bone marrow examination. After over six months of anti-fungal treatment, a complete clinical and microbiologic response was achieved. Discussion: Localized cutaneous Fusariosis should be considered in chronic unresponsive ulcers and associated profound neutropenia in patients with possible autoimmune processes

Alyssa Ball

The effectiveness of calcium supplementation in adult trauma patients: a systematic review

Raquel Oleksin, Alyssa Ball, Mohammad Hmidan Simsam, Alla Iansavitchene, Ian Ball, Colin Laverty

Post-traumatic hemorrhage remains one of the leading causes of preventable death among trauma patients. Historically, management of severe hemorrhage has focused on hemorrhage control followed by management of the lethal triad: acidosis, hypothermia, and coagulopathy. However, emerging evidence supports a fourth component: hypocalcemia, thus forming the lethal diamond. This systematic review investigates calcium supplementation and its association with adult trauma patient outcomes, more specifically, its effects on transfusion requirements and mortality. A systematic search of Embase, MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) electronic databases was conducted for eligible studies from their inception to June 2023. ClinicalTrials.gov. Screening for studies and data extraction was conducted independently and in duplicate with PRISMA compliance maintained. Prospero registration number #CRD42023415133. Out of 1139 studies screened, 20 were assessed for full-text eligibility, with 5 retrospective analyses included in the final analysis. Among the 1008 patients studied, 40% received intravenous calcium supplementation (treatment group), while 60% did not (non-treatment group). Ionized hypocalcemia was defined as serum iCa <1.12 mmol/L, and severe ionized hypocalcemia as serum iCa <0.9 mmol/L. Data collected included demographics, admission vitals, laboratory values, injury details, and trauma severity scores.The data indicates that calcium supplementation may lower hypocalcemia risk but often inadequately corrects it. Moreover, most studies remain inconclusive regarding calcium's impact on patient outcomes, including mortality. The current evidence is retrospective and lacks clarity on calcium's benefits for trauma patients, necessitating further prospective randomized controlled trials to assess its efficacy in this population.

Tayyaba Bhatti

Sex, Gender, and Racial Differences in Uptake of Genetic Testing in Chronic Kidney Disease

Tayyaba Bhatti, Dervla Connaughton

Background: Chronic Kidney Disease (CKD) has an estimated prevalence of 10% and is one of the leading causes of death worldwide. Genetic testing for CKD is an expanding field. Genetic testing can identify mutations in genes associated with polycystic kidney disease, Alport syndrome, cystinuria, renal ciliopathies, and focal segmental glomerulonephrosis. Certain mutations in the PKD1 gene are associated with more severe disease and earlier progression to renal failure. Furthermore, genetic testing can identify patients with PKD who are more likely to benefit from tolvaptan therapy. Despite these advances, there is limited uptake from patients in genetic testing. Proposed barriers to genetic testing include poor health literacy, distrust of the healthcare system, and differential access to genetic testing. Our aim is to determine whether there are sex, gender, and racial disparities in uptake of genetic testing in CKD in Ontario. Methods: We used data from a provincial registry of genetic kidney disease testing. The data analysis is currently underway. Results: We had a total of 566 patients, of which 279 were male and 286 were female. 171 (30.2%) patients were European, 14 (2.5%) were Asian, 14 (2.5%) were Hispanic, 14 (2.5%) were Native American, 9 (1.6%) were East Indian, 7 (1.2%) were African, and 5 (0.9%) were African American. Conclusion: Based on our findings so far, there is no

difference in gender distribution. However, there is significant variation in ethnicity uptake, with the biggest proportion being European, followed by Asian and Hispanic, then Native American, and lowest being African and African American.

Garth Blackler

Pain and Synovial Fibroblast Subsets in Osteoarthritis

Garth Blackler, Holly T. Philpott, Joseph Klapak, Easton Farrell, Tristan Maerz, Cheryle Séguin, C. Thomas Appleton

Fibroblasts that line the synovium (lining fibroblasts) are critical for joint health. They produce hyaluronan and lubricin, which are necessary for resisting impact and lubrication. Previous research has shown synovial fibroblast subsets are altered in osteoarthritis (OA). However, the role of fibroblast subsets in mediating OA pain remains unclear. This study aimed to identify the association of synovial fibroblast subsets with pain, how these subsets arise, regulatory mechanisms, and their potential function. A human knee OA synovial tissue single-cell RNA-sequencing dataset was analyzed to identify synovial fibroblast subsets associated with worse pain, their differentiation trajectories, and regulatory transcription factors. Mineralization is associated with worse pain in OA; therefore, synovial fibroblasts were exposed to mineralization media with or without synovial fluid (to mimic the harsh joint environment) and TGFβ1 (a growth factor increased in OA). Lining fibroblasts were strikingly reduced in patients experiencing worse pain while LRRC15+, senescent-like, and progenitor fibroblasts were enriched. Trajectory analysis suggested that lining fibroblasts arise from progenitor fibroblasts by differentiating through the LRRC15+ subset. The transcription factors CEBPβ, ETS2, and FOXO1 were identified as regulators of senescent, lining, and LRRC15+ subsets, respectively. LRRC15+ fibroblasts express pro-mineralization genes while lining fibroblasts express mineralization inhibitors. When exposed to TGFβ1 and synovial fluid, synovial fibroblasts from 3/6 patients produced mineral. The loss of synovial lining fibroblasts may contribute to poor outcomes including worse pain and mineralization. Understanding the mechanisms that lead to and maintain lining fibroblasts may help identify novel avenues to promote joint health in OA.

Samantha Bruzzese

The effect of prolactin-secreting pituitary adenomas on bone health: A systematic review

Samantha Bruzzese, T. Birk, A. Yusuf Ibrahim, S. Van Uum, K. Clemens

Background: Although a relationship between prolactinoma and bone health has been well described, we have little understanding of whether treatment of prolactinoma improves bone health outcomes. Methods:We conducted a systematic review of published studies that investigated the relationship between prolactinoma and its treatment on the bone health of adults aged 18 years and older (MEDLINE, EMBASE, and Web of Science). Outcomes of interest included bone density, fractures, and/or markers of bone turnover. Results:We identified 18 relevant studies of 897 participants. Studies described a relationship between prolactin secreting adenomas and reduced bone mineral density, particularly at the lumbar spine, as well as an increased risk of vertebral fractures across the sexes. Risk

factors for fractures included older age, longer duration of disease, male sex, lower bone density score, and lack of dopamine agonist therapy. There did not appear to be a difference in fracture risk between patients with hypogonadism vs. eugonadism. Upon normalization of prolactin levels and reversal of hypogonadism, the literature to date does not suggest that bone density returns to baseline. Treatment does appear to halt further progression of bone loss and may be protective against vertebral fractures. Conclusions: In patients with prolactin secreting adenoma, there is an increased risk of osteopenia/osteoporosis at the lumbar spine as well as vertebral fracture. Bone loss does not appear to be completely reversible with appropriate treatment to normalize prolactin. Further research on use of bone protective medications in this population could inform clinical practice on fracture risk reduction.

Gabrielle Buckley

Presence of Citrullinated and Homocitrullinated Proteins in the Joints of Collagen-Induced Arthritic Mice

Gabrielle Buckley, Jaspreet Kaur, Ewa Cairns, Lillian Barra

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease primarily affecting synovial joints. In RA, synovial joint proteins that have been modified through citrullination and homocitrullination, post-translational modifications of arginine and lysine, respectively, are targeted by immune responses, leading to joint histopathology. Studies involving RA frequently employ the collagen-induced arthritis (CIA) mouse model due to similar disease manifestations; however, the literature lacks characterization of citrullinated and homocitrullinated protein levels in the joints. Objective: To determine whether joint damage and inflammation will associate with the presence of citrullinated and homocitrullinated proteins in CIA mice. Methods: CIA was induced in mice by immunizing with bovine type II collagen (N=12) and compared to naïve (N=2) and phosphate-buffered saline (PBS) immunized (N=2) mouse controls. Joint sections were stained with hematoxylin and eosin to examine joint structures and infiltration or toluidine blue to assess cartilage health. Joint citrullinated and homocitrullinated protein levels were characterized through immunofluorescent microscopy. Results: CIA mice exhibited synovial thickening, pannus formation, intra-articular exudate, and cartilage erosion in the metatarsophalangeal and tibiotalar joints, unlike the controls. Citrullinated and homocitrullinated proteins were found in all animal group joints. Unexpectedly, citrullinated protein levels in the metatarsophalangeal joint were significantly greater in the PBS mice compared to CIA and naïve. No other significant differences were observed. Significance: This research shows that citrullinated and homocitrullinated proteins can be found in the joints of both arthritic and non-arthritic mice. The role of these modified proteins in the CIA animal model requires further study.

Gabrielle Buckley

Rheumatoid Arthritis Associated Proteins in An Animal Models

Gabrielle B, Jaspreet Kaur, Ewa Cairns, Lillian Barra

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease that primarily affects synovial joints. In RA, synovial joint proteins that have been modified through citrullination and

homocitrullination, post-translational modifications of arginine and lysine, respectively, are targeted by immune responses, leading to the joint histopathology. Investigations involving RA frequently employ the collagen-induced arthritis (CIA) mouse model due to similar disease manifestations; however, literature lacks characterization of citrullinated and homocitrullinated protein levels in these mice. Hypothesis: Histopathological damage will positively associate with the presence of citrullinated and homocitrullinated proteins in the joints. Methods: CIA was induced in mice using two immunization concentrations (N = 6 for each). Joint sections were stained with hematoxylin and eosin to examine joint structures and infiltration or toluidine blue to assess cartilage health. Joint citrullinated and homocitrullinated protein levels were characterized through immunofluorescence microscopy. Results: The low-dose immunization induced greater histopathology than the high dose. However, greater levels of citrulline and homocitrulline were detected in the joint synovium of high-dose compared to low-dose mice. Additionally, high-dose mice had higher levels of homocitrulline in the bone marrow. Significance: While additional work is required to increase sample size, this research suggests that citrullinated and homocitrullinated proteins are found in CIA joints. Further investigation regarding their presence and role in the CIA model will aid the advancement of RA research.

Sarah Cocco

Assessing the use of a National Early Warning Score (NEWS) for pre-hospital refusal of service (ROS) calls in a pediatric population.

Sarah Cocco, Matthew Davis, Kristine Van Aarsen

Background ROS is a common occurrence; it occurs when patients refuse transport after paramedical arrival on scene. In 2020, the Middlesex London Paramedic Service (MLPS) introduced the use of a NEWS tool to identify ROS patients at high risk of adverse events and a protocol of escalating interventions to aid with patients making informed decisions regarding transportation. The NEWS has been validated in prehospital settings for patients >16yrs to assess 48hr and 30-day mortality and ICU admission risk. Currently, the NEWS is being applied to patients <16yrs, for which it is not validated. The objective of this study was to compare the NEWS to a pediatric equivalent score for MLPS ROS calls. Methods Ambulance call records (ACRs) were reviewed for ROS pediatric calls (age <16yrs) from Feb 2021 to Jan 2022. Vitals were given a score based on a Pediatric Early Warning Score (PEWS). Scores were compared to their assigned risk based on their NEWS and paramedic documentation. Results 231 ACRs were reviewed. 7.8% were “moderate” and 3.5% were “high” risk based on their NEWS. When a PEWS was applied, 4.8% were “moderate” risk and 0% were “high” risk. 84.8% of calls were risk-congruent and 15.2% were risk-incongruent. The NEWS score resulted in over-estimation of risk in 10.4% and under-estimation in 4.8%. Conclusion This QI project identified an incorrect application of a validated score. Pediatric patients had an incorrect risk calculated in 15.2% of calls. Next steps include introduction of a PEWS and revaluation of outcomes after this intervention.

Bianca DeBenedictis

Femoral Vein Doppler as a Non-Invasive Screening Tool for Venous Congestion and Right Ventricular Dysfunction in Septic Shock

Bianca De Benedictis, Rachael Houlton, Ross Prager, Nicolas Orozco, Robert Arntfield, John Basmaji

Background: Venous congestion and right ventricular (RV) dysfunction are associated with adverse patient outcomes in septic shock. Echocardiographic and VEXUS ultrasound protocols to quantify these phenotypes require specialized expertise and can be time consuming. This pilot study evaluates femoral vein doppler (FVD) as a screening tool to provide rapid assessment of venous congestion and RV dysfunction. Methods: We performed a prospective, observational study of adult patients with septic shock at two intensive care units. FVD was performed within 24 hours of admission. FVD with pulsatility or reversal were considered positive tests. VEXUS (Grade 2/3) was used to identify venous congestion. ECHO was used to identify RV dysfunction. Results: Seventy patients were enrolled from January 2022 to 2023. FVD pulsatility had 100% sensitivity (95% CI of 73.5 to 100.0) and 22.6% specificity (12.3 to 36.2) for detecting venous congestion, whereas FV reversal demonstrated 46.2% sensitivity (19.2 to 74.9) and 80.7% specificity (68.1 to 90.0) for venous congestion. For detecting RV dysfunction, pulsatile FVD was 87% sensitive (66.4 to 97.2) and 21.4% specific (10.3 to 36.8). The sensitivity and specificity of FV reversal for RV dysfunction was 54.2% (32.8 to 74.5) and 91.3% (79.2 to 97.6), respectively. Conclusion: FVD has excellent (100%) sensitivity in identifying venous congestion when using pulsatility as a threshold and could be an effective triage test. FV flow reversal is more specific for both venous congestion and RV dysfunction, and this finding should prompt echocardiographic investigation.

Jane Ding

Percent predicted vs. absolute six-minute walk distance as predictors of lung transplant-free survival in fibrosing interstitial lung diseases: a multicenter study

Jane Ding, Fabrizio Luppi, Umberto Zanini, Karina Kaur, Niccolò Anzani, Giovanni Franco, Giovanni Ferrara, Meena Kalluri, Marco Mura

In fibrosing interstitial lung diseases(ILDs), reliable indicators of prognosis and disease progression are necessary to optimize treatment and timing for lung transplant(LTx). Longitudinal changes of six-minute walk distance(6MWD) are known predictors of survival in idiopathic pulmonary fibrosis(IPF) and other fibrosing ILDs. Equations for percent predicted 6MWD(6MWD%) may even better predict function and disease trajectory by accounting for age, sex, height, and weight. We conducted a retrospective study comparing the ability of 6MWD-m vs. 6MWD% to predict LTx-free survival in fibrosing ILDs. We identified a discovery cohort of 211 patients with fibrosing ILD from London, Canada, and a validation cohort of 260 patients from Edmonton, Canada and Monza, Italy. Clinical and functional data were collected on initial consultation, and longitudinal data at 1 year±3 months. The endpoint was 3-year LTx-free survival. Receiver operating characteristic analysis identified optimal cutoff values for 6MWD-m and 6MWD% for outcome prediction, and competing risk regression analysis(Fine-Gray method) identified the significance of variables in endpoint prediction. In the discovery cohort, baseline 6MWD-m and 6MWD% were both significant predictors of LTx-free survival, 6MWD% slightly more significant. Longitudinal decline in 6MWD% was also a slightly stronger predictor of transplant-free survival compared to 6MWD-m. Kaplan-Meier survival analysis grouped by 6MWD% showed significant discriminatory power towards LTx-free mortality, slightly superior to 6MWD-m. Results were confirmed in the validation cohort. Overall, 6MWD% offers only a very small advantage over 6MWD-m in

predicting survival in fibrosing ILDs, highlighting a need for more accurate reference equations for predicting 6MWD.

Melissa Fowler

Unmasking Complexity: Navigating the Diagnostic Challenge of a False Positive Cryptococcal Antigen in Chronic Meningitis with Suspected Indolent CNS B-Cell Lymphoproliferative Neoplasm

Melissa Fowler, Lise Bondy, Seth Climans, Jonathan Lau, Eric To, Yiannis Iordanous, Marilyn Phung, Jeffrey Fuller, Michael Silverman, Reza Rahimi Shahmirzadi

Objectives: Chronic meningitis is a diagnostic challenge with a broad differential diagnosis. Herein, we describe a patient with chronic meningitis and an initial positive cerebrospinal fluid (CSF) cryptococcal antigen (CrAg) who was later found to have a possible central nervous system B-cell lymphoproliferative neoplasm. Causes of false-positive CrAg were also reviewed. Case Summary: A 47-year-old woman presented with a two-year history of visual symptoms and worsening headache. A lumbar puncture (LP) demonstrated a lymphocytic pleocytosis with nucleated cell count of 22, lymphocyte percentage 86%, protein 514mg/L, glucose 3.2mmol/L, and CrAg 1:256. Her history included multiple instances of meningitis, apparent Guillain-Barré syndrome, and migraine headaches. She was not immunosuppressed and denied any travel history. CSF fungal culture, serum CrAg, and repeat CSF CrAg results were negative. She had an extensive negative infectious workup. She was started on liposomal amphotericin B and flucytosine followed by fluconazole for fifteen months. Her symptoms persisted, and her CSF parameters remained unchanged. CSF flow cytometry revealed a monoclonal B-cell population suspicious for a B-cell lymphoproliferative neoplasm. MRI head was unremarkable, and a full body positron emission tomography scan did not reveal any visible lymphoproliferative disease. Given the persistent presence of a monoclonal B-cell population, she was thought to have a true indolent process. Ultimately, she underwent insertion of a VP shunt for symptom management. Discussion: This case explores additional causes of false-positive CrAg and emphasizes the importance of interpreting test results in the complete clinical context, especially with a challenging diagnosis such as chronic meningitis.

Shany Gertzbein

How Do We Identify Hearing Impaired Patients Admitted to the Geriatric Rehabilitation Unit at Parkwood Hospital Based on Review of Medical Records?

Shany Gertzbein, Margaret Taabazuing

Background: With advanced age, most people develop mild hearing loss characterized by difficulty hearing and understanding others in noisy environments. Strategies to address hearing loss as part of routine clinical care are pertinent because unaddressed hearing loss often leads to a breakdown in patient communication. Purpose: Our aim was to assess how patients with hearing impairment are being identified. Methods: Data was manually abstracted from electronic medical records of inpatients on the Geriatric Rehabilitation Unit at Parkwood Hospital during a three-month period between the dates July 18, 2022 to October 20, 2022. Results: A total of seventy-two charts were reviewed

corresponding to 72 admissions. Twenty-nine patients (40.3%) were identified as hearing impaired, twenty-two (30.6%) were without hearing impairment. For twenty-one patients (29.1%) hearing status was not documented. For those identified as hearing impaired, twenty-six patients (89%) were captured on the physician admission note and nine patients (31%) were captured on the nursing adult admission note. Two patients (0.06%) captured on the nursing adult rehab system assessment form and one patient (0.03%) was captured on an allied health initial assessment form. Discussion: Overall, hearing status was documented in 70% of admitted patients. This number suggests that there are many clinical interactions that are occurring with suboptimal communication. This audit helped inform process mapping and implementation of a rapid cycle change aiming for a performance measurement of 85% or greater.

Sarah Ghnaim

Clerkship on the Clinical Teaching Units: Designing a Better Experience for Novice Clerks

Sarah Ghnaim, Bonnie Liu, Rahman Ladak, Albert Huynh

Background: Transitioning from a didactic pre-clerkship to a clinical clerkship introduces students to the reality of clinical practice, while also laying the foundation for future patient interactions. However, this transition is a source of stress negatively impacting learning. Third-year medical students at Western University must complete a 6-week Internal Medicine (IM) rotation on a Clinical Teaching Unit (CTU). This project aims to improve the CTU experience for novice clinical clerks. Methods: Third-year medical students at Western University starting their CTU rotations were invited to engage in a co-design process, whereby end-users actively engage in an iterative design process. This ensures usable results that meet their needs. We utilized the five-stage design thinking model proposed by Stanford d. school: Empathize, Define, Ideate, Prototype, and Test. Results: Insights derived during the 'Empathize' stage were reframed as opportunities. The most important challenge was 'Defined' as: How might we impart the skills needed to complete effective daily assessments on the CTU using an IM approach? 'Pain points' identified include how to: efficiently review a patient record; conduct focused but accurate histories and physical exams; and write good notes. Students then 'Ideated' creative solutions to address this challenge. Discussion: Third-year medical students complete daily assessments on patients admitted to the CTU. However, they struggle with an active-issue-based IM approach, resulting in feelings of unpreparedness. Further, explicit guidance on how to improve these skills is lacking, determined using a human-centered, co-design process. Next steps include prioritizing brainstormed solutions with top ideas iteratively 'Prototyped' and 'Tested'.

Yasaman Hajiesmaeili

Risk Factors Associated with the Incidence of Cardiovascular Disease among Aging Patients with Rheumatoid Arthritis

Yasaman Hajiesmaeili, Saverio Stranges, Lillian Barra, Osvaldo Espin-Garcia

Background: Rheumatoid arthritis (RA) is an autoimmune inflammatory arthritis associated with a higher risk of cardiovascular disease (CVD). This study examined incidence of CVD in individuals with and

without RA and assessed the role of potential risk factors in this association. Methods: This study used data from the Canadian Longitudinal Study on Aging (CLSA) database. Incidence rate ratio (IRR) for CVD was calculated to compare the CVD incidence among RA and non-RA individuals and Cox proportional hazard regression models were used to examine potential risk factors for CVD incidence in these populations. Stratification based on sex and education levels were conducted. Results: The study population was 54% females and had a mean age of 60.9 (± 9.4) years. RA patients experienced significantly higher CVD incidence, compared to the non-RA individuals (IRR = 1.69, 95% CI: 1.34 – 2.11). By multivariable analysis, elevated C-reactive protein (CRP) level, disease-modifying antirheumatic drugs (DMARDs) other than methotrexate, male sex, older age, low physical activity, smoking, dissatisfaction with sleep quality, diabetes, hypertension and mood disorder were associated with higher CVD incidence. Sex-stratified analysis revealed that RA was only a risk factor for CVD among females, while DMARDs other than methotrexate were only found to increase the CVD risk in males. Lastly, RA was found to be associated with higher CVD incidence only among individuals with lower education level. Conclusion: This study identified potential risk factors for CVD in RA patients. Monitoring and managing these risk factors may mitigate the burden of CVD among people living with RA.

Yasaman Hajiesmaeili

Factors Associated with Incident Cardiovascular Disease in Patients with Rheumatoid Arthritis: A Scoping Review

Yasaman Hajiesmaeili, Preeti Tamhankar, Saverio Stranges, Lillian Barra

Introduction: Rheumatoid arthritis (RA) is an autoimmune inflammatory arthritis and is associated with various comorbidities including cardiovascular disease (CVD). This scoping review summarizes the current evidence on longitudinal cohort studies assessing factors associated with the incidence of cardiovascular events in RA patients. Methods: Scopus, PubMed, Ovid MEDLINE and Cochrane databases were used to identify longitudinal cohort studies investigating the incidence of CVD among RA patients. Using predetermined inclusion and exclusion criteria, two reviewers screened and extracted the relevant studies independently to map the existing literature on this topic. The extracted data included study characteristics, demographics, comorbidities, behavioural and RA-related factors. Results: Thirty-three research papers were included with a mean follow-up duration of 7.8 years. The sample size of the studies ranged from 182 to 4,311,022 subjects, the mean age from 46.1 to 72.3 years, and on average, 34.6% of the participants were male. The following factors were reported to be associated with a higher incidence of CVD in RA patients: older age, male sex, co-morbid hypertension, diabetes, and/or dyslipidemia, the presence of rheumatoid factor and/or acute phase reactants. Among RA treatments, glucocorticoids were shown to increase CVD incidence while DMARDs, especially methotrexate, were associated with a lower incidence of CVD. Conclusion: This review summarizes the current literature highlighting important modifiable risk factors for CVD incidence among RA patients. Future research should focus on the less studied behavioural factors, including physical inactivity, alcohol consumption and sleep habits as well as some RA-related factors such as anti-citrullinated protein antibodies and functional impairment.

Emma Holjak

The Effect Of The Covid-19 Pandemic On Cardiac Rehabilitation

EJB Holjak, TC Hartley, A Huitema, R McKelvie, P Prior, K Unsworth, NG Suskin

Introduction: The COVID-19 pandemic challenged the healthcare system's ability to deliver patient care, including cardiac rehabilitation (CR). The SJHC CR Program delivered most care virtually. The pandemic may have impacted patients' willingness to attend hospital visits or adhere to CR programming and impacted the ability of CR professionals to deliver care. We investigated whether the pandemic impacted time from CR referral to intake, intake attendance (enrollment), or program completion. Methods: Data was retrospectively extracted from the CR program's electronic medical record. Two different cohorts of patients post percutaneous coronary interventions (i.e., PCI) were compared: those enrolled in CR before the pandemic (PRE; March 2017 to February 2019), vs. those enrolled in CR during the pandemic (PAN; March 2020 to February 2022). Results: The PRE-group consisted of 706 patients, the PAN-group consisted of 514 patients. Enrollment in CR was decreased by 27.5% in the PAN group vs PRE group. Median wait-time from CR referral to intake improved during the pandemic (PRE: 59 days vs PAN: 46 days; $p < 0.05$). Rates of program completion were similar in PRE and PAN (PRE: 72.4%, PAN: 71.3%). Conclusion: During the pandemic, CR completion rates post-PCI were similar to pre-pandemic rates, however, there was a reduction in the total number of patients enrolled in CR. Wait times from patient referral to enrollment into CR improved during vs. pre pandemic. The decreased wait times for CR enrollment may be attributable to the virtual nature of CR delivery during the pandemic but requires further study.

Nisha Howarth

Reducing Inappropriate Gamma-Glutamyl Transferase Testing For Inpatients: A Quality Improvement Initiative In Lab Waste Reduction Applying The Model For Continuous Improvement

Nisha Howarth, Gurpreet Malhi, Tamoor Afzaal, Raaed Alramdan, Hasan Bualbanat, David Hudson, Ian Chin-Yee, Anouar Teriaky

Background: Roughly 30% of inpatient laboratory testing is inappropriately repeated. Laboratory overutilization increases healthcare costs and can lead to overdiagnosis, overtreatment and negative health outcomes. Indications for repeat Gamma Glutamyl Transferase (GGT) testing in adults are limited, particularly within the same admission. Purpose: We aimed to reduce ordering of repeat inpatient GGTs by 25% at LHSC over one year. Methods: An interprofessional team was created to engage stakeholders, collect data, and assess the indications for GGT testing. Root cause analysis tools (Ishikawa diagram, Pareto chart) were utilized to identify factors contributing to the overutilization of GGT. After prioritizing potential solutions, intervention bundles were developed, and Plan-Do-Study-Act (PDSA) cycles were created to target correctable factors. In PDSA cycle #1, we eliminated GGT as a laboratory testing option in the three most used admission order care sets. PDSA cycle #2 implemented a computerized Clinical Decision Support (CDS) system to restrict the reordering of GGT tests within 72 hours of the same admission. Results: Baseline data showed that in 2022, 56,086 GGT tests were ordered, approximately 4,670 orders per month. Of these, 16.4% were ordered through admission order care sets, and ~25% of GGT tests were repeated within 72 hours of admission. PDSA cycle #1 yielded no

significant reduction in GGT testing. PDSA cycle #2 reduced the total number of GGT tests by 21%, leading to an estimated annualized cost savings of $60,480. Conclusions: CDS systems are effective in reducing laboratory overutilization and emphasize the potential for cost-effective CDS development in contemporary healthcare.

Marly Isen

Indigenous health education in Canadian medical residency: A needs assessment

Marly Isen, Joyla A Furlano, Laura Diachun, Jaspreet Bhangu

Background Indigenous health has become a mandatory component of postgraduate medical education (PGME) in Canada in an effort to address stark health inequities and racism faced by Indigenous populations. Our study assesses postgraduate medical trainees' knowledge of Indigenous health and confidence in providing culturally safe and appropriate care. Methods We recruited from all postgraduate medical and surgical residency programs at Schulich School of Medicine and Dentistry, a leading Canadian medical school. Participants (n=52) completed an online mixed methods anonymous survey. ResultsSixty-five percent had formal education about Indigenous health during undergraduate medical education and only 42% during PGME. While 96% felt they had fair to very good knowledge about health disparities experienced by Indigenous peoples, fewer felt they had knowledge about historical colonial events (77%) and how these link to current barriers and disparities faced by Indigenous peoples (50%). Seventy-one percent felt neutral to not confident at all about providing culturally safe and appropriate care to Indigenous patients. Online modules were perceived to be the least effective educational modality. Discussion Though physicians-in-training seem knowledgeable about Indigenous health disparities, knowledge gaps remain with respect to understanding the social, economic and political determinants of health. There is a lack of training, particularly at the postgraduate level, for how physicians can address these disparities in a culturally safe and appropriate way in everyday practice. Conclusion To improve healthcare for Indigenous peoples, Canadian universities should focus on developing cultural safety and trauma-informed care training to PGME curricula in interactive, in-person formats.

Faramarz Jabbari-Zadeh

Evaluating the role of Thrombopoietin Receptor Agonists in the Treatment of Acquired Amegakaryocytic Thrombocytopenia: A Retrospective Multi-Center Case Series

Faramarz Jabbari-Zadeh, Mujtaba M. Basharat, Cyrus Hsia

BackgroundAcquired amegakaryocytic thrombocytopenia (AAMT) is a rare condition in which the levels of platelets are low due to absent or significantly reduced megakaryocytes. To our knowledge, there have been only 15 cases reported in the literature where thrombopoietin receptor agonists (TPO-RAs) were utilized for the treatment of AAMT. We sought to examine the natural history of AAMT when treated with TPO-RAs.MethodsWe will perform a retrospective multi-center case series investigating the treatment of AAMT with TPO-RAs. We will conduct an online survey from March 2024-May 2024 that we will send to the researchers who reported the 15 aforementioned cases and include local case(s).

The survey includes questions regarding patient demographics, comorbidities, dosing of TPO-RAs, type of response observed, adverse drug effects, and outcomes. Descriptive analysis of these will be performed.ResultsWe are in the process of data collection. Results will include data about demographics, comorbidities, dosing of TPO-RAs, type of response observed, medication effects, and outcomes.DiscussionTo our knowledge, this is the largest multi-center case series examining the role of TPO-RAs in treating AAMT. Ultimately, we believe that investigating specific treatment options for AAMT on an international level will lead to the development of more effective treatment regimens in the future and improve patient outcomes for this rare condition

Seonho Jang

Takotsubo Cardiomyopathy after Stroke

Seonho Jang, Amir Geressu, Yun-Hee Choi, Rodrigo Bagur

BACKGROUND: There have been studies suggesting Takotsubo cardiomyopathy (TCM) as a potential complication following cerebrovascular accident (CVA), but the association, contributing factors, and prognosis significance have not been well-characterized. OBJECTIVES: 1) Assess the incidence, factors and prognosis associated with TCM-complicated CVA and, 2) Determine the 30-day unplanned readmission rates for TCM after discharge for CVA. METHODS: The U.S. Nationwide Readmission Database was queried using ICD-codes to gather information on discharges with diagnosis of CVA between January 2010 and November 2020. Incidence and factors associated with TCM-complicated CVA and 30-day readmissions with diagnosis of TCM were assessed. RESULTS: Of 3,696,202 patients hospitalized with primary diagnosis of CVA, 5,526 (0.15%) patients developed TCM during the admission. Patients with TCM were more likely to be women (80% vs. 52%, P<0.001) and had a higher comorbidity burden. Mortality rate was significantly higher among those with TCM vs no-TCM (20% vs. 6.4%, P<0.001). Of 3,690,676 patients who did not experience TCM during index-admission for CVA, 255,947 (6.9%) patients were readmitted within 30 days of discharge, and 250 (0.1%) with a primary diagnosis of TCM. These individuals were more likely women (78% vs. 51%, P<0.001) and had a higher mortality rate (12% vs. 5.7%, P=0.009) during readmission. CONCLUSIONS: Although rare, TCM-complicated CVA can be highly fatal. It tends to occur more in women and pre-existing health conditions. Readmission for TCM after discharge for CVA is also uncommon and carries a significantly elevated risk of mortality.

Hanyu Jiang

Lysophosphatidylcholine and synovial microvasculature dysfunction in knee osteoarthritis

Hanyu Jiang, Tom Appleton

Mechanisms leading to knee osteoarthritis (OA) is not well understood. Synovium microvessels supply nutrients to the joint but is damaged in OA patients. We discovered that pain in patients is associated with histopathological features of synovial microvascular dysfunction (MVD) and with higher levels of lysophosphatidylcholines (LPC) in synovial fluid. Others have shown that the LPC metabolite lysophosphatidic acid (LPA) is increased in the OA synovium, suggesting that LPC might be converted to LPA. LPA signals through GPCRs such as LPA receptors (LPAR) and are known to induce pain, synovitis,

and endothelial cell dysfunction. We aim to study LPA's impact on synovial MVD in knee OA and hypothesize that LPA signaling via LPAR impairs synovial microvascular endothelial cell function and the microvascular barrier, promoting synovial MVD.We will characterize LPAR expression profile (scRNAseq, IF) in synovial cells. Then, effects of OA patient synovial fluid (SF) and selective inhibitors of LPAR on human microvascular endothelial cells (HMEC-1) will be explored. Finally, we will explore the effects of LPA and LPAR inhibitors in healthy rat knee synovial microvasculature.scRNAseq shows synovial endothelial cells express LPAR6, while intimal and perivascular fibroblasts express LPAR1 and 6. IF supports this finding. We expect an increased dysfunctional endothelial barrier phenotype in SF-treated HMEC-1s. LPAR1/6 inhibitors will confirm which receptors mediate these effects and if they can alleviate the dysfunctional phenotype in SF-treated HMEC-1s and rat knee microvessel pathology injected with LPA. LPA pathways shows promise as targets to control and reduce pain in knee OA.

Jaspreet Kaur

Do Rheumatoid Arthritis-Specific Immune Responses Relate to Joint Pathology in an Animal Model?

Jaspreet Kaur, Sofya Ulanova, Ewa Cairns, Lillian Barra

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by progressive joint pain and destruction. These disease manifestations are driven by aberrant immune responses that target modified joint proteins containing citrulline (CitP) or homocitrulline (HomoCitP). These responses include T cell proliferation and RA-specific autoantibody production. Problem: Collagen-induced arthritis (CIA) mice are commonly used to study RA, despite a lack of consensus on how well this model represents the human disease. Objective: To determine whether RA-specific immune responses develop in CIA and if they relate to joint pathology. Methods: Mice were injected with type II collagen (CIA; N = 17) or PBS (negative control; N = 6). Pain-like behaviour was assessed using the von Frey method. Joints were imaged using MicroCT. T cell proliferation was measured using flow cytometry and antibody concentrations were determined via ELISA. Results: CIA mice, but not PBS mice, developed arthritis with symptoms such as joint swelling and a reduced pain withdrawal threshold. Imaging showed a decrease in bone mineral content and density, indicative of osteopenia, as well as bony erosions in CIA joints. T cell proliferation was higher in CIA vs. PBS mice when stimulated with collagen or HomoCitP, but not CitP. In CIA, T cell responses to HomoCitP were correlated with lower bone mineral density. CIA mice developed antibodies against collagen; however, RA-specific antibodies were not higher compared to controls. Significance: While immune responses to CitP require further investigation, T cell responses to HomoCitP may be related to joint destruction in CIA.

Seung Kim

Spatially resolved gene expression profiles of fibrosing interstitial lung diseases

Seung Kim, Matthew Cecchini, Elissa Woo, Nathashi Jayawardena, Daniel Passos, Frederick Dick, Marco Mura

Fibrosing interstitial lung diseases (ILDs) encompass a diverse range of scarring disorders that lead to progressive lung failure. Previous gene expression profiling studies focused on idiopathic pulmonary

fibrosis (IPF) and bulk tissue samples. We employed digital spatial profiling to gain new insights into the spatial resolution of gene expression across distinct lung microenvironments (LMEs) in IPF, chronic hypersensitivity pneumonitis (CHP) and non-specific interstitial pneumonia (NSIP). We identified differentially expressed genes between LMEs within each condition, and across histologically similar regions between conditions. Uninvolved regions in IPF and CHP were remarkably distinct from normal controls, and displayed potential therapeutic targets. Hallmarks LMEs of each condition retained distinct gene signatures, but these could not be reproduced in matched lung tissue samples. Based on these gene expression signatures and unsupervised clustering, we grouped previously unclassified ILD cases into NSIP or CHP. Lastly, we characterized a gene expression pattern associated with poor outcome . Overall, our work uniquely dissects gene expression profiles between LMEs within and across different types of fibrosing ILDs. This new spatial transcriptomics approach has the potential to reclassify unclassifiable cases, to qualify the transcriptional relevance of smaller biopsies for clinical use, and to predict outcome at the time of diagnosis.

Alexandre Le-Nguyen

Role of Azathioprine in the Management of Immune Thrombocytopenia (ITP): A Single Centre Retrospective Study

Alexandre Le-Nguyen, Shamim Mortuza, Cyrus C. Hsia

Background: Immune thrombocytopenia (ITP) is an autoimmune disease associated with low platelets and risk of bleeding. Management may include steroids, intravenous immunoglobulins, immunosuppressive agents, splenectomy, and the novel thrombopoietin-receptor agonists (TPO-RA). We investigated the role of azathioprine in relapsed/refractory ITP patients to determine its efficacy and safety in the era of TPO-RAs. Methods: We retrospectively reviewed 706 adult patients, age 18 years and older, who were worked up for ITP between January 2009 and March 2024 at a single tertiary care centre in Ontario, Canada. We included all ITP patients who received azathioprine. Results: There were 92 ITP patients who received azathioprine, mean age 55.6 ± 22.3 years, 53 females and 39 males, with 64 having primary ITP. The overall response rate (ORR) was 47.8% (44/92), with 35 patients achieving complete response (CR), and median time to response was 6 weeks. Fourteen patients (31.8%) relapsed with an average duration of response of 28 weeks. A total of 32 patients had no response (NR) and 16 were intolerant. Most patients (73.9%) had documented side effects, with nausea/vomiting, infections and myelosuppression being the most common. The majority of patients received azathioprine as 3rd line and 11 patients were post-TPO-RA. In those 11, the ORR was 36.4% (4/11), with 3 patients achieving CR. Conclusion: This is the largest retrospective study conducted on the use of azathioprine in ITP demonstrating benefit in relapsed/refractory ITP with efficacy in both pre and post-TPO-RA (p=0.71). Azathioprine remains a viable option for relapsed/refractory ITP in the era post-TPO-RA.

Wayne Leung

BYOCP - Build Your Own Care Program: Using Design Thinking Methodology to Develop a Monthly Injectable Cabotegravir/Rilpivirine Program for Vulnerable Patients Living with HIV in London, Ontario

Wayne Leung, Wayne Leung, Dawn-Marie Harris, Janhavi Malhotra, Michael McGregor, Kelly Muhsin, Megan Devlin

In London, Ontario, people living with HIV who experience housing instability and have substance use disorders have challenges with daily antiretroviral medication adherence. Monthly injectable antiretroviral medication offers a possible solution; however, safe delivery of this medication requires a comprehensive care program. Design thinking methodology provides a framework to create an innovative model of care that centers this population's needs and utilizes the local resources available in this setting. We describe the design thinking-informed process used for the inspiration and ideation phase of care program design. During the inspiration and ideation phase, we engaged stakeholders to build off of pre-existing care structures and brainstorm new care pathways. Interviews for end-users were performed with participants enrolled in our pre-existing HIV care programs. Engaged stakeholders include primary care serving vulnerable patients, physicians and outreach workers from the local public health unit, an outpatient pharmacy, psychiatry outpatient teams (ACT), and the local jail.Eleven interviews were conducted with participants enrolled in our pre-existing HIV care program. Themes generated include dissatisfaction with their current daily antiretroviral regimen, while reasons cited include forgetting to take or losing their medications, having them stolen, and that picking up their medications disrupts their lives. Participants were interested in enrolling in a program, though anticipated barriers include attending regular appointments, or concurrent competing social factors including lack of housing. Design thinking methodology was useful in the early phases in the creation of a care program to safely deliver injectable HIV medication to vulnerable patients.

Wayne Leung

Navigating the challenges: Managing mold, mycobacterial, and viral infections in a hematopoietic stem cell transplant recipient

Wayne Leung, Michael Silverman, Huma Saeed, Sarah Shalhoub, Reza Rahimi Shahmirzadi

Objective: To discuss the challenges in concurrently managing mold, mycobacterial, and viral infections in a hematopoietic stem cell transplant recipient. Case summary: We discuss a 39-year old female who underwent a hematopoietic stem cell transplant in 2017 for high risk acute myeloid leukemia. In May 2023, she presented to our tertiary care hospital in London, Ontario with shortness of breath, and a computed-tomography scan of her chest revealed a 1.5 cm cavitary lesion in her right upper lobe. Mycobacterium chimaera was cultured from her bronchoscopy and she was initiated on intravenous amikacin, azithromycin, ethambutol, and rifampicin. Subsequently, Microascus spp. was cultured from the same bronchoscopy and voriconazole and inhaled liposomal amphotericin B were added to her regimen. She had a history of bilateral retinal disc atrophy and ophthalmology consultation recommended to discontinue ethambutol, which was substituted for moxifloxacin. Her course was complicated by transaminitis related to rifampicin and voriconazole and both were discontinued; voriconazole was re-initiated upon resolution of transaminitis. In August, susceptibilities for Mycobacterium chimaera returned resistant to moxifloxacin and indeterminate to linezolid. Moxifloxacin was substituted for clofazimine, and rifabutin was introduced, which was chosen over rifampicin due to lower theoretical risk of hepatotoxicity. In total for her Microascus spp. invasive fungal infection, voriconazole and inhaled amphotericin B was continued for twelve weeks total. For her

Mycobacterium chimaera pulmonary disease, she was given twelve weeks of intravenous amikacin, and will receive at least twelve months total of three additional active agents, including azithromycin, rifabutin, and clofazimine.

Wayne Leung

Use of Dalbavancin in treatment of Acute Bacterial Skin and Skin Structure Infections:Prospective Case series from a Canadian Perspective

Wayne Leung, Janhavi Malhotra, Lili Ataie, Sameer Elsayed, Lise Bondy, Megan Devlin, Sarah Shalhoub, Huma Saeed, Mahshid Mohammadi,Michael Silverman, Reza Rahimi Shahmirzadi

Background: Treatment of acute bacterial skin and skin structure infections (ABSSSIs) with parenteral antibiotics is difficult in marginalized populations including PWID due to challenges with homelessness necessitating prolonged hospitalization for IV therapy, and frequent accessing of IV lines for drug use. Dalbavancin which is a novel lipoglycopeptide antibiotic with activity against gram-positive organisms with a duration of action of 7-14 days may be an ideal antibiotic in patients in whom administering parenteral antibiotics may be difficult. Methods: Prospective cohort study consisting of 19 patients who were referred to the Cellulitis Clinic at London, Ontario, Canada who were referred for ABSSSI between February 1st and July 30th, 2023. Patients were treated as outpatients with one dose of IV dalbavancin. Patients had social factors which precluded administration of outpatient parenteral antibiotics in a traditional setting, such as injection drug use, severe psychiatric comorbidities, or unstable housing. Results: The median age of patients enrolled was 43 (range 36 to 56), were predominantly male (74%), unemployed (90%), and with unstable housing (58%). Treatment with dalbavancin was successful in 13/19 (68%); indeterminate (presumed success as could not be reached for follow-up but were not admitted to any institution within our catchment area) 3/19 (16%); Failure (needed further antibiotics following dalbavancin) 3/19 (16%). Conclusions: Administering dalbavancin through a single IV infusion eliminates the need for indwelling IV access and may enhance treatment of ABSSSI without the need for hospital admission, in those with challenging socioeconomic factors who may have difficulty with adherence to outpatient antibiotic therapy.

Jessica Liu

Diagnosis, management, and outcomes of secondary erythrocytosis: A systematic review

Jessica Liu, Aidan McKee, Romel Abou-Akl, Benjamin Chin-Yee, Jenny Ho, Alla Iansavitchene, Cyrus C. Hsia

Background: Secondary erythrocytosis (SE) refers to an elevation in hemoglobin > 160 g/L in women or > 165 g/L in men that is not due to an underlying myeloproliferative neoplasm. Common causes include chronic hypoxia, medications such as testosterone and sodium-glucose cotransporter-2 inhibitors, erythropoietin-secreting tumours, and post-transplantation erythrocytosis. Current guidelines on the diagnosis and management of SE are limited. There is a lack of evidence on the role of phlebotomy, cytoreduction, antiplatelet agents, and anticoagulation. Furthermore, the risks of thromboembolism, bleeding, and mortality in SE have yet to be fully described. We therefore conducted a systematic

review to inform the clinical management of SE and its subgroups. Methods: Following PRISMA guidelines, we performed a systematic literature search in MEDLINE, EMBASE, CENTRAL (all via Ovid), and Google Scholar. We included adult patients, age 18 years and older, and studies analyzing five or more subjects published from 2005, the year of JAK2 discovery, to February 2024. Two reviewers independently screened titles and abstracts of studies, with disagreements resolved by a third party. Data was extracted on variables pertaining to the diagnosis, management, and outcomes of SE and its subgroups, and will be synthesized using descriptive analysis. (PROSPERO CRD42024508643) Results: Our systematic search identified 2,037 studies for screening. Data extraction is underway, and results are currently pending. Conclusion: SE is a heterogeneous condition for which there is no clear consensus among clinicians about the diagnosis and management of the various underlying causes. Pending the results of this systematic review, full conclusions will be drawn.

Tony Liu

A Rare Case Of Non-Islet Cell Tumour Hypoglycemia From A Solitary Fibrous Lung Tumour

Tony Liu, Anna LiuHernan, Franco Lopez

Background: Non-islet-cell tumour hypoglycemia (NICTH) is a rare paraneoplastic syndrome caused by high molecular weight (“big”) IGF-II production from tumours. NICTH is important to identify because treatment differs from other causes of hypoglycemia. We highlight the clinical presentation, pathophysiology, and treatment of NICTH caused by a solitary fibrous tumour, also called Doege-Potter syndrome. Case: An 89-year-old woman, recently diagnosed with a 13 cm biopsy-proven fibrous tumour, complained of fatigue, nausea, and diaphoresis associated with point-of-care hypoglycemia (2.3-3.3 mmol/L), which resolved with correction of hypoglycemia. Bloodwork showed glucose 2.1 (4-10 mmol/L), C-peptide 67 (370-1470 pmol/L), insulin <7 (18-173 pmol/L), beta-hydroxybutyrate <0.1 mmol/L, and IGF-I 35 (17-167 mcg/L). Glucagon administration increased glucose from 2.9 to 4.0 mmol/L (>1.4 mmol/L). The IGF-II assay is unavailable at our center (n.b. ratio of IGF-II:IGF-I >3:1 is suggestive of NICTH). She was diagnosed with Doege-Potter syndrome. Results: Her hypoglycemia resolved with dexamethasone 6mg daily. She was not a surgical candidate. She was discharged on dexamethasone and prn intranasal glucagon. Discussion: Recognizing NICTH is important for management of hypoglycemia. NICTH from Doege-Potter syndrome is associated with the NAB2-STAT6 fusion gene, which drives big IGF-II production causing hypoglycemia through activating IGF-I, IGF-II, and insulin receptors to reduce growth hormone, increase glucose uptake, and suppress gluconeogenesis, glycogenolysis, and glucagon. Definitive treatment is tumour resection. Medical therapy may be required for bridging to surgery and non-surgical candidates. Our case aligns with previous reports demonstrating high dose steroids equivalent to prednisone >20mg is effective at resolving hypoglycemia.

Michael MacNeill

Risk Factors and Clinical Management of Post-Renal Transplant Erythrocytosis: A Regional Transplant Centre Retrospective Review

Michael MacNeill, Chai Phua, Ian Chin-Yee, Benjamin Chin-Yee, Dervla M. Connaughton, Corinne Weernink, Cyrus Hsia, Jenny Ho

Introduction: Post-transplant erythrocytosis (PTE) is a condition of elevated hematocrit and hemoglobin typically presenting within 8-24 months after kidney transplants. PTE has been estimated to have an incidence of around 10-15%. PTE is associated with a variety of symptoms, including plethora, headache, dizziness, and lethargy, as well as significant complications, including hyperviscosity syndrome, thromboembolic events, and cardiovascular disease. Therefore, early recognition and management of PTE is important in the post-renal transplant population. Management options include angiotensin-converting enzyme inhibitors (ACEis), angiotensin II receptor blockers (ARBs), and phlebotomy. We aimed to assess the donor-recipient risk factors predisposing to PTE development as well as efficacy on the various PTE management strategies on clinical outcomes. Methods: We conducted a retrospective observation study of post-renal transplant patients ≥18 years of age diagnosed with PTE, defined as a hematocrit >51% or hemoglobin >170 g/L for >1 month within the first 24 months post-transplant, at London Health Sciences Centre between January 1, 2000 to August 31, 2020. Patients with alternative explanations for erythrocytosis were excluded. Renal donor and recipient data were collected. PTE groups were categorized by their initial treatment choice and sub-grouped by subsequent treatments. Relevant adverse events and clinical outcomes were assessed, including thromboembolisms, hyper viscosity syndrome, and renal graft function. Results: Data extraction is underway, and results are currently pending. Conclusion: We will evaluate PTE treatment efficacy and outcomes such as thromboembolism, symptoms associated with hyperviscosity, and renal graft function.

Michael MacNeill

Assessment of Sarcopenia as a Measure of Frailty in Older Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma

Jodi Chiu, Michael MacNeill, Chai Phua, Andy Kin On Wong, Joy Mangel

Introduction: Diffuse large B cell lymphoma (DLBCL) is an aggressive lymphoma that occurs primarily in older adults. The challenge in treating older patients is accurately identifying frailty, which confers increased vulnerability to adverse treatment outcomes. Sarcopenia, the loss of muscle mass, is independently associated with an increased risk of all-cause mortality and may correlate with frailty. We aimed to assess the prevalence of baseline sarcopenia in older patients with relapsed/refractory (R/R) DLBCL, its evolution throughout treatment, and its correlation with clinical outcomes. This group also serves as a historical control for our concurrent prospective study incorporating both clinical frailty and sarcopenia assessments. Methods: We conducted a retrospective cohort study of patients >60 years of age with R/R DLBCL treated over the past 5 years at London Regional Cancer Centre, with PET-CTs suitable for sarcopenia assessment. Sarcopenia measurements via skeletal muscle index, standardized uptake value, and skeletal muscle density, were measured at the level of L3 vertebra and mid-thigh on baseline pre-treatment PET-CT and scans throughout their treatment course. Adverse events and clinical outcomes data was also collected. Results: 62 patients (41M/21F) with a median age of 66 (range 59 – 88) at relapse were included. They received a median of 6 cycles of chemotherapy (range 1 – 8) with 60% of cycles requiring dose reduction. Adverse events included 28 infections, 21 episodes of febrile neutropenia, and 9 bleeding events. Overall response rate was 39%. Median progression-free survival was 200 days (range 18 – 1081). Conclusion: Preliminary conclusions will be presented at research day.

Gurpreet Malhi

Examining The Impact Of Inflammatory Bowel Disease In Primary Sclerosing Cholangitis Patients Post Liver Transplantation

Gurpreet Malhi, Luis Antonio Diaz, Gopika Punchhi, Rokhsana Mortuza, Mohammad Qasim Khan, Mayur Brahmania, Vipul Jairath, Juan Pablo Arab

Background: Primary sclerosing cholangitis (PSC) is an immune-mediated disease that is characterized by biliaryinflammation and fibrosis. It is associated with IBD in 80% of cases To date, theimpact of IBD in liver transplantation (LT) recipients is not completely understood. Aims: To assess the impact of IBD in individuals with PSC who underwent liver transplantation (LT) in terms of graftsurvival, infections, and mortality. Methods: This was a retrospective cohort study that included individuals with PSC who received a LT between1999–2021. Statistical analysis included Kaplan-Meier survival curves, a binary logistic regression to estimateinfection risk, and a competing-risk analysis to estimate post-LT mortality. Results: 122 LT recipients were included. Mean age at LT was 44.9±12.6 years old. The median MELD-Na at LT was22 [17–28]. Estimated graft survival was 93.2% (95%CI: 86.9%–96.6%) at 1 year and 81.3% (95%CI: 72.5%–87.6%) at 5 years. An adjusted competing-risk model demonstratedthat increasing age (sHR 1.05, 95%CI: 1.01–1.10; p=0.018), baseline MELD-Na (sHR 1.07, 95%CI: 1.02–1.12;p=0.005), and ERCP requirements before LT (sHR 6.33; 95%CI: 1.63–24.65; p=0.008) were associated with higherpost-LT mortality, while IBD was not associated with post-LT mortality (sHR 1.02, 95%CI: 0.38–2.70; p=0.962). Theincidence of infections after LT was 50.8% at 30 days. Conclusions: Based on this retrospective review, an older age, higher MELD-Na at LT and prior ERCP requirementswere independently associated with a higher mortality post-LT in PSC patients.

Aminmohamed Manji

The role of aging on pulmonary microvascular endothelial barrier function during mechanical ventilation

Aminmohamed Manji, Sanjay Mehta, Lefeng Wang, Cynthia M. Pape, Lynda McCaig, Ruud Veldhuizen, Sean E. Gill

Elderly individuals have substantially elevated mortality following pulmonary insult and often require mechanical ventilation (MV) to sustain respiratory function. MV is associated with injury to pulmonary microvascular endothelial cells (PMVEC), leading to a compromised vascular barrier, and fluid and protein leakage within the lungs. However, the precise impact that age has on the vascular endothelium during MV is unknown. We hypothesized that aging augments PMVEC barrier dysfunction during MV. To address this, young and aged mice were ventilated at a tidal volume of 20 mL/kg for 3 hours. Microvascular permeability was assessed by measuring abundance of the serum protein, immunoglobulin M, in lung lavage fluid. Lungs were used for single-cell RNA sequencing (scRNAseq) analysis to give insight into the role of specific cells, particularly PMVEC. To directly assess molecular mechanisms, PMVEC were isolated from separate cohorts of young and aged mice and cultured to confluency in vitro. Barrier integrity was assessed by measuring albumin leak across monolayers and immunofluorescence staining of cell junctions.Compared to young, aged-ventilated animals had significantly greater immunoglobulin M in their lavage fluid, suggesting augmented vascular barrier

dysfunction. ScRNAseq analysis revealed increased signaling pathways associated with cell adhesion that were enriched in aged animals following MV, potentially in a compensatory manner. Endothelial monolayers from aged animals in vitro exhibited significantly elevated albumin flux, which was associated with poor adherens and tight junction formation. These findings may highlight molecular pathways involved in predisposing aged individuals to worsened outcomes during MV, which can aid in developing targeted therapeutics.

Karl Maxemous

A Rare Case of Acquired Angioedema Treated with Lanadelumab

Karl Maxemous, Rongbo Zhu

Acquired angioedema (AAE) is a rare cause of bradykinin mediated angioedema. It is non-hereditary, presents later in life, associated with lymphoproliferative disorders and autoimmunity. No established guidelines exist on the treatment of this condition. We describe a case of a patient who developed AAE and was successfully treated with lanadelumab.A 66-year-old male with CLL was referred for new onset episodes of angioedema. He had several episodes of angioedema which is described in detail in our case report. He went to ED, where he was prescribed diphenhydramine, prednisone, and epinephrine, with resolution 48 hours later. Initial investigations showed a low C4 with a normal C1 inhibitor level and function. In subsequent months, following a dental procedure, the patient had significant laryngeal swelling requiring ICU admission. C4 and C1 inhibitor level drawn during this episode were both low. The patient had repeat blood work in clinic, demonstrating persistently low levels of C4 and C1 inhibitor level. Subsequent C1q performed was undetectable. The patient was diagnosed with AAE and with collaborative decision-making was put on lanadelumab as long term prophylaxis and icatibant for acute therapy. Following initiation, the patient had improvement of his angioedema episodes and overall quality of life.This case highlights a rare cause of angioedema and encompasses the need to perform sequential testing, especially during acute attacks. Currently, treatment options for AAE are limited to case series. Overall, this case underscores the importance of creating guidelines surrounding AAE, similar to current guidelines for hereditary angioedema.

Christopher McChesney

Investigating Glucocorticoid Use in Admitted Patients with Alcohol-Associated Hepatitis

Christopher McChesney, Poojitha Pai, Gurpreet Malhi, Rokhsana Mortuza, David Hudson, Juan Pablo Arab

INTRODUCTION: Alcohol-associated hepatitis is a severe clinical presentation characterized by the abrupt onset of jaundice, malaise, decompensated liver disease and coagulopathy. In Ontario, alcohol-associated liver disease is the 2nd most common etiology of cirrhosis and is increasing in incidence among younger adults. The Maddrey discriminant function (MDF) score is commonly used to determine whether glucocorticoids would provide a benefit in Alcohol-associated hepatitis patients. METHODS: This study was a retrospective cohort study which examined a subset of individuals with alcohol-associated hepatitis who were admitted to London Health Sciences Centre (LHSC) from 2010-2023. The

objective was to determine whether glucocorticoids were appropriately administered to patients based on the calculation of their MDF score. RESULTS: 143 patients admitted with alcohol-associated hepatitis were identified. The number of cases where glucocorticoids were indicated based on a MDF score > 32 was 91, however, glucocorticoids were given in only 60 (65.9%) of these cases. When removing those with steroid contraindications, a substantial portion of steroid eligible patients (42.3%) did not receive this therapy. Furthermore, of the 43 cases where the MDF score was noted to be < 32, 7 (16.3%) were given steroids. CONCLUSION: Based on the MDF score, a significant number of patients did not receive glucocorticoid therapy appropriately. As steroids can play both a supportive and negative role in therapy, it is interesting to note this variation in use. Possible explanations include inability to calculate MDF score due to missing investigations, patient behaviours, lack of education, and clinician hesitancy to start immunosuppressive therapy.

Aidan McKee

Describing a cohort of secondary erythrocytosis patients at London Health Sciences Centre: population characteristics, clinical outcomes, and management practices

Aidan McKee, Jessica Liu, Romel About-Akl, Jenny Ho, Alejandro Lazo-Langner, Lalit Saini, Arvand Barghi, Michael Kovacs, Ian Chin-Yee, Pratibha Bhai, Laila Schenkel, Bekim Sadikovic, Cyrus Hsia, Benjamin Chin-Yee

Background Secondary erythrocytosis (SE) refers to elevated hemoglobin, > 160 g/L in women, > 165 g/L in men, in the absence of a diagnosis of any myeloproliferative neoplasm. The clinical course and appropriate management of SE are not well described. We aimed to characterize patients with SE at London Health Sciences Centre (LHSC), and to measure thrombosis and bleeding outcomes, as well as use of phlebotomy, antiplatelet medications, and cytoreduction in this population.MethodsWe reviewed all adult patients at LHSC with erythrocytosis who underwent next generation sequencing (NGS) between January 2018 and December 2019 inclusive. SE was defined as absence of JAK2 mutation or any other mutation characteristic of a myeloproliferative neoplasm.Results We identified 227 patients with SE. Average age was 56 years; average hemoglobin was 177 g/L (average hematocrit 0.52). The most prevalent risk factors for SE were: smoking history (48.9%), obstructive sleep apnea (42.3%), chronic obstructive pulmonary disease (15.9%), SGLT2i use (12.8%), and androgen use (12.8%). Management practices included antiplatelet medications for thrombosis prevention (42.3%) (though many patients had other notable indications for antiplatelets), phlebotomy (14.1%) (with varying hematocrit targets), and cytoreduction (0.9%). Rates of arterial and venous thrombosis occurring at any time in the patients' lives were 15.9% and 9.3%, respectively. Rate of bleeding episodes was 10.6%, though only 1.8% experienced a major bleed per ISTH criteria. Interpretation This retrospective cohort study sheds light on the population characteristics, clinical outcomes, and management practices for patients with SE at LHSC.

Shamim Mortuza

Myelodysplastic Neoplasms (MDS) with Ring Sideroblasts or SF3B1 Mutations: The Improved Clinical Utility of World Health Organization and International Consensus Classification 2022 Definitions, A Single Centre Retrospective Chart Review

Shamim Mortuza, Benjamin Chin-Yee, Tyler E. James, Ian H. Chin-Yee, Benjamin D. Hedley, Jenny M. Ho, Lalit Saini, Alejandro Lazo-Langner, Laila Schenkel, Pratibha Bhai, Bekim Sadikovic, Jonathan Keow, Nikhil Sangle, Cyrus C. Hsia.

Background: Myelodysplastic neoplasms (MDS) with ring sideroblasts (RS) is diagnosed on bone marrow aspirate in the presence of either i) ≥15% RS or ii) 5-14% RS and an SF3B1 mutation. Based on the evidence from recent randomized clinical trials, lower risk MDS-RS patients demonstrated decreased transfusion dependency with luspatercept. Thus, MDS patients with <15% RS with SF3B1 mutations may still benefit from luspatercept. We performed a retrospective study to identify and to estimate the proportion of patients with SF3B1 defined MDS-RS who would be excluded based on morphologic criteria alone. Methods: A total of 6817 patients with suspected hematologic malignancy underwent molecular testing using a next generation sequencing based genetic assay and 395 MDS patients seen at our centre from January 1, 2018 to May 31, 2023 were reviewed. Results and Discussion: There were 39 lower risk MDS with SF3B1 mutations, 20 (51.3%) males and 19 (48.7%) females, with median age 77 years (range 57-92). Nineteen (48.7%) patients had an isolated SF3B1 mutation with mean variant allele frequency 35.2% +/- 8.1% ranging from 7.4% to 46.0%. There were 29 (74.4%) patients with ≥15% RS, 6 (15.4%) with 5 to 14% RS, one (2.6%) with 1% RS, and 3 (7.7%) with no RS. Our study suggests that approximately 25% of patients would be missed based on morphologic criterion of ≥15% RS only and support the revised 2022 World Health Organization (WHO) and International Consensus Classification (ICC) definitions which shift toward this molecularly defined subtype of MDS and appropriate testing.

Shamim Mortuza

Utility of azathioprine in immune thrombocytopenia (ITP): a systematic review

Shamim Mortuza, Alexandre Le-Nguyen, Cyrus C. Hsia.

Background: ITP is an autoimmune disorder characterized by low platelets with an increased risk of bleeding. Frontline therapies include corticosteroids and IVIG. Newer agents such as rituximab, thrombopoietin receptor agonist, Syk inhibitors, and neonatal Fc receptor inhibitors are currently in use as subsequent lines. However, access to these therapies is limited and patients are often limited to options such as splenectomy and immunosuppressive medications. Although, these older immunosuppressive medications have been available for some time, their utilization in ITP is not well studied in the literature. Methods: Following PRISMA guidelines, we performed a systematic literature search in Cochrane Library, MEDLINE, CINAHL, EMBASE and clinical trial registries. We included only studies with adult patients, age 18 years and older and with five or more subjects. No restrictions will be placed on language or date of publication. Non-English articles will be translated where necessary. The primary outcome of interest will be efficacy of azathioprine as per the individual reporting study. Secondary outcomes will include timing in the sequence of treatment, dosing and safety.PROSPERO registration No. CRD42023493791 Discussion: A systematic review is needed to collate and analyze this

evidence in the era of novel ITP treatments given the lack of access to these agents. Findings of this systematic review will help guide future areas of clinical studies and treating physicians managing patients with ITP. Recommendations on the utilization of azathioprine for future studies and treating physicians are outlined.

Prathana Nathan

Antibody Drug Conjugates in Treatment of Genitourinary Cancers: An Updated Review of Data

Prathana Nathan, Adnan Rajeh, Meh Noor, Gabriel Boldt, Ricardo Fernandes

The treatment landscape of genitourinary (GU) cancers has significantly evolved over the past few years. Recent advancements have produced new targeted therapies, particularly antibody drug conjugates (ADCs). ADCs function as a 'drug delivery into the tumor' system. They are composed of an antigen-directed antibody linked to a cytotoxic drug that releases cytotoxic components after binding to tumor cell's surface antigen. ADCs have been proven to be extremely promising in the treatment of several cancer types. In this study, we thoroughly reviewed the current literature and summarized preclinical studies, clinical trials and retrospective studies that evaluated utility, activity, and toxicity of ADCs in GU cancers, prospects of ADC development, and ongoing clinical trials. In particular, enfortumab vedotin (EV), sacituzumab govitecan, and trastuzumab deruxtecan have shown promise. For instance, enfortumab vedotin has shown high response rates in patients with metastatic urothelial cancer (mUC), even those who have undergone previous therapies. Several trials (EV-101, EV-201, and EV-301) have established its effectiveness, with manageable side effects. A phase III trial (EV-302/KEYNOTE-A39) combined EV with pembrolizumab and demonstrated significant improvements in progression-free survival (PFS) and overall survival (OS), suggesting its use as a first-line treatment for mUC. Trastuzumab deruxtecan's (T-DXd) efficacy has been observed in advanced HER2-expressing urothelial carcinoma. Sacituzumab govitecan (SG) has shown notable efficacy in mUC after progression on other treatments, as demonstrated in the TROPHY-U-01 trial. This review emphasizes the potential that ADCs have in changing the treatment of GU cancers.

Navneet Natt

Paradoxical Psoriasis following Anti-TNFα Therapy in Inflammatory Bowel Disease and Association with an IL-23 Receptor Variant: A Preliminary Report

Navneet Natt, Aze Wilson

Background: Patients with inflammatory bowel disease (IBD) receiving anti-tumour necrosis factor (TNF)-α therapy are at risk for paradoxical psoriasis (PP). No tools are validated for identifying high-risk individuals susceptible to this drug reaction. Variation in the IL-23 receptor (IL23R) gene has been linked to psoriasis and may be implicated in PP. Aims: To evaluate the frequency of the IL23R variant (IL23R1142G>A) in anti-TNFα exposed IBD patients who develop PP versus those who do not, and clinical variables associated with PP. Methods: A retrospective cohort study is ongoing, including anti-TNFα-exposed adult IBD patients. Charts were reviewed from the time of anti-TNFα exposure until therapy discontinuation for development of PP, demographic variables, and disease characteristics. All

participants were genotyped for the IL23R1142G>A variant. Results: To date, we have included 59 IBD patients with anti-TNFα exposure. 11 patients developed PP after a median treatment duration of three months. Six patients had >50% body surface area (BSA) involvement and nine participants discontinued therapy due to PP. PP patients were similar to controls with respect to baseline characteristics. The variant genotype occurred more frequently in PP patients than controls (54.5% vs. 4.2%, OR 27.6, 95%CI 4.3-145.4). Conclusion: In this preliminary analysis, there was an increased frequency of the IL23R1142G>A variant in patients who developed PP following anti-TNFα exposure compared to controls. We did not identify any other clinical variables associated with development of PP. Completion of this study may help clarify the association between PP and the IL23R gene.

Anton Nikouline

Prophylactic Non-Invasive Ventilation for Patients High Risk for Extubation Failure: A Quality Improvement Initiative

Anton Nikouline, Hira Raheel, Madison Burella, Karina Nabieva, Paul Cameron, Ian Ball

Prophylactic Non-Invasive Ventilation for Patients High Risk for Extubation Failure: A Quality Improvement Initiative Non-invasive ventilation (NIV) and high flow nasal cannula (HFNC) has demonstrated benefit in both mortality and reducing reintubation of patients when applied prophylactically for correctly selected patients. Despite the benefit in patient outcomes, prophylactic application of these devices remains an underutilized strategy.A chart audit from July 1, 2023 to Dec 31, 2023 at London Health Sciences Centre demonstrated the application of NIV or HFNC for patients meeting criteria for high extubations was 30%. We conducted a nonrandomized, prospective, quality improvement (QI) study from January 1st, 2024 to December 31st, 2024 based on the Model for Improvement. Root cause analysis was performed, and plan-do-study-act PDSA cycles were developed according to change concepts identified. Our objective was to increase the prophylactic application of NIV or HFNC post-extubation in patients meeting high risk criteria to more than 80%. Time series analysis demonstrated a run in NIV or HFNC application following intervention. Within 3 months of project initiation, we have met our target of >80% of prophylactic application in high risk extubations. There has been no increase in aspiration events or skin complications. Current PDSA cycles are targeting sustainability of the results and data collection is ongoing. Conclusion We were able to demonstrate a successful QI project in improving the evidence based practice of prophylactic post-extubation NIV or HFNC in high risk patients.

Meh Noor

Association between immune-related side effects (irAEs) and Clinical Outcomes in patients with advanced renal cell carcinoma (RCC) treated with immunotherapy

Meh Noor, Prathana Nathan, Adnan Rajeh, Gabriel Boldt, Ricardo Fernandes

Background: Immunotherapy with the use of immune checkpoint inhibition (ICI) has evolved the treatment landscape of advanced renal cell carcinoma (RCC). However, ICIs may affect peripheral tolerance to autoantigens, resulting in autoantibody formation, which could be associated with immune-

related adverse events (irAEs). The aim of this study is to to determine whether the incidence of irAEs after the use ICIs is associated with clinical outcomes in patients with RCC treated with immunotherapy in a real-world setting. Methods: This was a retrospective study of patients treated in the London regional Cancer Program (LRCP) in London, Ontario, Canada. Eligible patients had metastatic or advanced RCC and were treated with immunotherapy. Demographic data was collected and used to generate descriptive statistics.(Data analysis is currently underway).

Mateen Noori

Obesity Management for Kidney Transplant: A qualitative study (OK TRANSPLANT 1)

Mateen Noori, Rutvi Brahmbhatt, Kristen Clemens, Louise Moist

Background: Obesity represents a significant barrier to kidney transplantation for approximately 25% of Canadians with end-stage renal disease (ESRD), necessitating an exploration of effective weight loss strategies for these patients. Despite the critical importance of transplantation and the known difficulties imposed by obesity, limited research exists on safe and effective weight loss methods within this population, complicated by the dietary and physical constraints of ESRD and its treatments. Objective: This study employs a qualitative, phenomenological approach to understand the unique challenges, facilitators, and intervention opportunities for weight loss among ESRD patients with obesity in Southwestern Ontario Methods: Through semi-structured interviews with 12 patients, we aim to uncover the individual, social and systemic factors influencing their weight loss experiences. Results: Preliminary analysis reveals motivation and the management of hope and expectations, facilitated by healthcare provider discussions, as pivotal elements. While dietary interventions and medications are recognized as primary weight control methods, there exists a notable gap in awareness and utilization of community supports. Upon completion of data analysis, our findings seek to illuminate strategies that can effectively address these barriers, enhancing the feasibility and success of weight loss regimens recommended by Canadian kidney transplant centers. Impact: This research not only contributes to the scarce literature on this topic but also proposes practical interventions to improve transplant eligibility and outcomes for this vulnerable population.

Abdelhady Osman

Patient Perceptions of Telemedicine in Nephrology Clinics during COVID-19: A Qualitative Study

Abdelhady Osman, Seung Heyck Lee , Mateen Noori , Melissa Al-Jaishi , Kerri Gallo, Louise Moist

Background: The COVID-19 pandemic had a significant impact on delivering care for patients with chronic kidney disease (CKD) requiring an accelerated transition to alternative models of care such as telemedicine. The aim of this study was to understand patient perceptions of their experiences with telemedicine in nephrology clinics at LHSC. Methods: Participants were recruited from the general nephrology clinic and the multidisciplinary kidney clinic at LHSC. Interviews were conducted using a predetermined interview guide. Transcripts were independently reviewed line-by-line by three reviewers using a directed content analysis approach. The most common themes were identified. Results: Twelve participants were interviewed (Mean age: 66). Most participants (11/12) appreciated

the convenience of using telemedicine to access care during the pandemic particularly with saving time and costs. They also found that the level of care received from their nephrologist was the same in telemedicine as in-person visits. Most participants (11/12) felt that they were more able to establish a personal connection with their nephrologist in-person than over the phone. A majority (8/12) would request in-person care if they believed there is a deterioration in their condition. Going forward, most participants expressed a preference for a combination of in-person and virtual care with the majority preferring video over telemedicine. Discussion: The use of virtual care including telemedicine and video-based platforms in CKD care will continue in future. The shared experiences of patients documented in our research must be integrated into future virtual care models to assist in delivery of excellent patient care.

Poojitha Pai

High Rate of In-Hospital Complications and Mortality in Patients Admitted with Alcohol-associated Hepatitis

Poojitha Pai, Christopher McChesney, Gurpreet Malhi, Rokhsana Mortuza, David Hudson, Juan Pablo Arab

INTRODUCTION: Alcohol-associated Hepatitis (AH) is a severe syndrome related to alcohol use disorder, and is characterized by the abrupt onset of jaundice, malaise, tender hepatomegaly, and coagulopathy. While it is known that AH is associated with infectious complications, gastrointestinal bleeding (GIB), and high short-term mortality, the impact of patient demographic variables on their rates is less understood. AIM: To identify demographic characteristics of patients admitted with AH and its effect on infectious complications, liver transplantation, and mortality. METHODS: A retrospective chart review was performed on all patient encounters with a diagnosis of AH and were admitted to the inpatient wards at London Health Sciences Centre from January 2010 to June 2023. Data on patients' demographic characteristics, in-hospital infectious complications, liver transplantation, and mortality was collected. RESULTS: 143 patient encounters (mean age 48.8 ± 12.6 years, 60.1% male, 29.4% with cirrhosis, mean MELD-Na on admission 24.7±8.3) from 135 unique patients were included. Complications during admission included acute kidney injury (AKI) (30.8%), GIB (30.1%), and infections (29.4%) and 67 (46.9%) patients were treated with steroids. 29 (20.2%) patients were readmitted within 30 days and 5 (3.7%) patients received a liver transplant. The overall mortality rate was 33.5% (n=48), including 19 (13.3%) patients that died during admission. CONCLUSION: AH patients are prone to developing several in-hospital complications, most notably, infection, AKI, and GIB during admission. AH patients also had a high mortality rate, with a majority occurring within the first 30 days. Further studies examining the global impact of AH are currently underway.

Hayley Patrick

Informing Equity, Diversity, and Inclusion Initiatives for the Department of Medicine: A National & Intersectional Lens

Jasmine Badesha, Liam McAlister, Hayley Patrick, Ava Pourtousi, Tisha R. Joy

BACKGROUND The Department of Medicine (DOM) at Schulich School of Medicine & Dentistry serves a large and diverse patient population across Southwestern Ontario through two major affiliated teaching hospitals. Incorporating equity, diversity, and inclusion (EDI) values and educational materials could improve the quality of care by addressing the unique and intersectional factors influencing health. Given the existence of hospital-based teams for Indigenous, Black Health, and Accessibility locally, we primarily focused on identifying gap areas and creating intersectional-based educational materials for patients and providers within DOM. METHODS: A cross-sectional analysis of all 570 Canadian hospital websites was performed to inform key EDI-related initiatives relevant to local DOM context. Specific information was gathered on individual hospital demographics, EDI-based statements/plans, and available materials. Clinical observerships within multidisciplinary team settings were conducted within one Division to identify relevant areas for EDI incorporation in outpatient care. RESULTS: Three main themes were identified from the cross-sectional analysis: (1) There was minimal availability of specific EDI-related initiatives and resources; (2) Urban and teaching hospitals were more likely to publicize EDI-related content than their rural or non-teaching counterparts; and (3) Available EDI-related materials were evidence-based and/or community-group informed. Educational materials were created in three main areas: (1) gender-inclusive care; (2) patient orientation to clinic visits and to the Canadian health care system; and (3) health advocacy. An intersectional-based clinic poster was also developed. CONCLUSIONS: Intersectional-based educational initiatives are minimally available currently. Incorporating these into patient-centred care may help foster inclusion, improve patient-provider relationships, and ultimately enhance health outcomes.

Victor Pope

Baseline assessment of diagnosis and referral pathway for lymphoma patients referred to London Regional Cancer Program

Victor Pope, Arvand Barghi

Delays in diagnosis and treatment of lymphoma patients lead to adverse outcomes including clinical deterioration of the patient due to progression of lymphoma, and patient and caregiver anxiety. Delays in care are multifactorial. We hypothesize that outpatient referral triage performance is a significant contributor to delays.A retrospective audit of all referrals received at London Regional Cancer Program (LRCP) lymphoma group between October 31 to December 15, 2023, was undertaken. Time points between first presentation to medical attention until first appointment with a hematologist were recorded. A process map from patient presentation, to imaging, to biopsy, to hematologist appointment, was derived, and intervals between each event were calculated. Pareto charts were used to identify areas of significant delay. The average delay was 62.2 days from first documented medical contact until first appointment with a hematologist. The largest delays were seen during imaging (10.4 days from order until completed, 17.2 days after result for a biopsy or referral), waiting for an LRCP appointment (16.7 days from referral), and obtaining a biopsy result (9.4 days from order until completed, 10.9 days in pathology).The delay from referral to first appointment at LRCP accounted for 27% of the total delay. To combat this, we created a triage algorithm using a Delphi method to identify patients who can be safety deferred, and those who need to be seen urgently. We aim to better utilize the limited space in the LRCP and improve access to care using this tool in a subsequent quality improvement project.

Gabrielle Pundaky

A comparative observational study evaluating alternative dosing regimens of consolidative durvalumab treatment post chemoradiotherapy in patients with Stage III Non-Small Cell Lung Cancer.

Gabrielle Pundaky, Jonathan Moroniti, Sarah Ma, Eric McArthur, Nawar Tarafdar, Robin Sachdeva, Saritha Surapaneni, Sara Kuruvilla

Background: Objectives:The COVID-19 pandemic impacted delivery of care for patients with Stage III Non-Small Cell Lung Cancer-NSCLC. To optimize consolidative care of patients treated with radical chemoradiation while minimizing patient exposure to health facilities, Cancer Care Ontario-Ontario Health- approved extending dosing interval of durvalumab from 10mg/kg every 2weeks-Durvalumab-Q2w- to 20mg/m2 every 4weeks-Durvalumab-Q4w- administered for a year. Southwestern Ontario-SWO- serves a demographically distinct population and uncertainty remains regarding the impact of this modification. We aimed to evaluate differences in tolerability and effectiveness between these regimens in our region. Methods: Retrospective chart review of adult patients serially diagnosed with Stage III NSCLC, 01/01/2018-01/05/2023, treated with chemoradiation at London Health Sciences Centre-SWO regional center- following Institutional Research Ethics Board Review. Descriptive statistics applied to demographic, treatment-related and clinico-pathologic characteristics. Overall survival-OS- and real-world progression free survival-rwPFS- analysis evaluated using Kaplan-Meier curves and Cox proportional hazard models. Results: Discussion: Amongst 196 patients, median age 70years, majority male-53%, current/former smokers>90%, ECOG-PS 0-1(89%). 45% patients had adenocarcinoma versus <30% squamous cell carcinoma. EGFR and ALK+ mutations<10% of sample and 30% PDL1≥50%. 66% received carboplatin versus cisplatin-36% and consolidative Durvalumab-Q4w-63% versus Durvalumab-Q2w-27% (10% no durvalumab use). In the Durvalumb-Q2w versus Durvalumab-Q4w groups, risk of death-HR:0.70;95%CI:0.42-1.14;p=0.15-, and risk of progression-HR:0.77;95%CI:0.52-1.14;p=0.19- were not significantly different. Conclusions: Despite regional focus, this study identified comparable effectiveness of consolidative durvalumab administered every 4weeks to every 2weeks and supports further investigation of its use post pandemic.

Yashasavi Sachar

Epidemiology, Treatment Pattern, And Survival In Canadian Patients With Chronic Hepatitis B-Related Hepatocellular Carcinoma

Yashasavi Sachar, Carla Coffin, Abdel-Aziz Shaheen, Alnoor Ramji, Sheikh Rahman, John Talia, Dave K. H. Wong, Scott Fung, Curtis Cooper, Mang Ma, Robert Bailey, Gerald Minuk, Alexander Wong, Karen E. Doucette, Magdy Elkhashab, Mayur Brahmania

Introduction: This study evaluates the existing trends in patient diagnosis of HCC amongst mono-infected CHBpatients, and observes long-term follow-up. Method: Data was collected from January 1, 2012, to December 31, 2022, from a cross-sectional cohort of subjectsmono-infected with CHB and HCC from the Canadian HBV Network. Descriptive analysis and Chi-squaremodeling used for statistical outcomes. Results: Of the 6711 CHB patients who met inclusion criteria, 232 (3.5%) developed HCC. The median age for theHCC cohort was 65 years (IQR 57-73), 80% male and 71% SEA patients. The CHB-HCC cohort had a higher proportion of male (80% vs 55%; p<0001) and SEA patients (71% vs 55%; p<0001).

92% of HCC patients had advanced liver disease (minimum Fibrosis Stage 3). HCC patients were followed for a median 41 months (IQR 19-87) post-diagnosis. 53% of patients were diagnosed with HCC as part of surveillance protocols. The median lesion number was 1(IQR 1-1), with a median lesion size of 2.5cm (IQR 1.7-4.0). Most HCC diagnoses were early-stage BCLC 0-A (81%). There was an 84% survival rate post-HCC diagnosis during follow-up, the only variable significantly associated with survival in follow-up was diagnosis through surveillance. Overall, 38% of patients received ablation, 16% received TACE, 25% underwent resection, 17% underwent a liver transplant, 8% required systemic therapy, and 6% received palliative therapy. Conclusion(s): In this CHB-HCC cohort, majority of patients were detected with early-stage HCC and received treatment with curative intent, resulting in excellent survival rates.

Yashasavi Sachar

Impact Of Distance From Liver Transplant Centre On Waitlist Mortality: A Population-Based Cohort Study

Yashasavi Sachar, Bhati, Piali; Onizuka, Kristyne; Tang, Ephraim; Teriaky, Anouar; Arab, Juan Pablo; Khan, Mohammad Qasim; Skaro, Anton; Qumosani, Karim; Rahman, Adam; Brahmania, Mayur

Introduction:Liver transplantation (LT) is a lifesaving treatment, however, accessibility can impact equitable care. The primary objective of this study was to determine the effect of distance from the LT center on waitlist mortality. Methods:Patients included were on waitlist or had received LT between January 1st, 2012, and December 31st, 2020. Linked databases with ICES generated to establish relevant demographics and healthcare utilization outcomes. Patients were stratified for comparison using a 150km cutoff for distance and impact on waitlist mortality was assessed using the Cox proportional hazards model. Results:Of 585 patients identified, 413 underwent LT. Overall population was predominantly male (70%), with median age of 59 years (IQR: 51-64), and median distance 110 km (IQR: 59-191) away from LT center. Patients in >150km and <150km cohorts had similar median NaMELD (17 vs 19, p>0.05) and indicators of SES, including rural (16% vs 24%, p>0.05) and low-income zip codes (23% vs 20%, p>0.05). ALD was most common primary diagnosis in both cohorts (31 vs 32%). Patients living >150km had more frequent ER visits (3.01 vs 4.68, p<0.05) and hospitalizations (1.75 vs 2.20, p<0.05). After adjusting for the etiology of liver disease, age, sex, and BMI, distance >150km had no significant impact on time to LT or waitlist mortality. The NaMELD score was the only significant driver of waitlist mortality and time to LT. Conclusion:Distance from the LT center did not have a significant impact on LT waitlist mortality or time to LT.

Clara Schott

Utility of Genetic Testing in Adults with Chronic Kidney Disease: A Systematic Review and Meta-analysis

Clara Schott, Victoria Lebedeva, Cambrie Taylor, Saeed Abumelha, Pavel Roshanov, Dervla M. Connaughton

Background: Chronic kidney disease (CKD) is a prevalent global problem affecting 11 to 13% of the adult population globally. We now predict that 10-20% of adults with CKD have a genetic cause for their

disease. At present, there is wide variation in the reported diagnostic yields after genetic testing in CKD, and data specific to adults can be difficult to decipher across the studies. In this systematic review, we aim to determine the utility of genetic testing in adults with CKD by determining the overall diagnostic yield, which patients should be tested, what testing strategies are most optimal, and the clinical impact of a positive result. Methods: We searched published literature using PubMed and Embase including those published between January 2005 to December 2023. Studies that reported diagnostic rate as a proportion of solved patients (with pathogenic or likely pathogenic variants) in the whole tested CKD cohort, and had data on adults (>18) were included. Results: In total, 60 studies with 10,107 patients were included. The overall diagnostic yield was 40% [95% CI: 33 to 47%]. A positive family history of CKD was positively associated with diagnostic yield (p=0.01). Additionally, subgroup analysis showed the following diagnostic yields; 61% for cystic kidney disease, 28% for glomerulopathies, 34% for tubulointerstitial kidney disease, and 21% for CKD of unknown aetiology. Conclusions: This systematic review provides data to support clinical expectations of genetic diagnoses per phenotypic group, and testing type, and informs the importance of genetic testing in adult patients.

Clara Schott

Vascular Calcification

Clara Schott, Allison A. Dilliott, Jian Wang, Adam D. McIntyre, Surim Son, Samantha Colaiacovo, Cadence Baker, Lakshman Gunaratnam, Andrew A. House, Shih-Han Susan Huang, Hariharan Iyer, John Johnson, Khaled Lotfy, Mario Masellis, Douglas P. Munoz, Faisal Rehman, Pavel

Background: Vascular calcification is prevalent in chronic kidney disease (CKD). Genetic causes of CKD account for 10-20% of adult-onset disease. Despite the high prevalence of vascular calcification in CKD, no single gene cause has been described. We hypothesised that variants in vascular calcification genes may contribute to disease pathogenesis in CKD, particularly in families who exhibit a predominant vascular calcification phenotype. Methods: We developed a list of eight genes that are hypothesised to play a role in vascular calcification: ABCC6, ALPL, ANK1, ENPP1, NT5E, SLC29A1, SLC20A2, and S100A12. With this, we assessed exome data from 77 CKD patients, who remained unsolved following evaluation for all known monogenic causes of CKD. We also analysed an independent cohort (Ontario Neurodegenerative Disease Research Initiative (ONDRI), n=520) who were screened for variants in ABCC6 and compared this to a control cohort of healthy adults (n=52). Results: We identified two CKD families with heterozygous pathogenic variants (R1141X and A667fs) in ABCC6. Patients from both families have severe vascular calcification, and through reverse phenotyping we found the phenotype to be indicative of Pseudoxanthoma Elasticum, caused by variants in ABCC6. Additionally, we identified 10 participants from the ONDRI cohort with heterozygous pathogenic or likely pathogenic variant in ABCC6. Replication in a healthy control cohort did not reveal any variants. Conclusions: Our study provides preliminary data supporting the hypothesis that ABCC6 may play a role in vascular calcification in CKD.

Ayesh Seneviratne

Microglia Morphology Characterization in Aging

Seneviratne AK, Myers SJ, Carrese C, Nikolik A, Bayona C, Whitehead SN

Introduction: Chronic inflammation is a hallmark of aging, manifesting in the brain as neuroinflammation (López-Otín et al., 2023). Chronically activated microglia drive inflammation in the brain by releasing pro-inflammatory cytokines, chemokines, and reactive oxygen species (Hanisch and Kettenmann, 2007). These processes make the brain more vulnerable to dementias such as Alzheimer's disease (Asai et al., 2015). Activated microglia have a more ameboid, less branched morphology, making it a potential marker of brain vulnerability (Vidal-Itriago et al., 2022). However, the relationship between microglia morphology and cognitive deficits has been poorly characterized. This study aimed to understand if microglia morphology changes as brain function declines with age. Methods:Brain cross-sections from male and female 3-, 9-, and 15-month-old Fisher 344 rats were stained with the microglial marker Iba1. Both 9- and 15-month-old rats had known cognitive deficits. MatLab based 3DMorph software (York et al., 2018) was first validated and then used to characterize microglia morphology from the prefrontal cortex, orbitofrontal cortex, CA1 hippocampus, striatum, and corpus callosum using a double-blinded study design. Results: Ramification index and cellular branching metrics indicate age- and brain region-dependent changes in microglia morphology. Discussion and Conclusions:In Summary, using 3DMorph, we can accurately quantify the morphology of microglia in Iba1-stained rat brain cross-sections. Now, we are better poised to 1) accurately characterize microglia morphology from different brain regions, 2) understand the relationship between microglia morphology and neuroinflammation, and 3) determine if microglia morphology can be used as a marker of cognitive decline.

Zack Singer

Driving Restrictions and Incapacitation Vulnerability Evaluation after ST Elevation Myocardial Infarction

Zachary Singer, Harindra Wijeysundera, Feng Qiu, Jiming Fang, Ragavie Manoragavan, Chris Simpson, Luiz Ybarra

Background: After STEMI, a 2-4 week restriction for private driving is recommended, depending on the LVEF. This duration is based on the incidence of sudden cardiac death early after MI, but does not consider other causes of sudden incapacitation. Driving restrictions impose a significant societal and economic burden and empiric data is limited to inform recommendations. Methods: This cohort study using Ontario health administrative data followed patients with a STEMI between 2017 and 2021 for one year. The primary endpoint was the composite of death, cardiac arrest, syncope, MI, stroke, or hospitalization/ED visit for any arrhythmia. Results: Over the study period, 24,890 patients completed follow-up. The risk of sudden incapacitation was highest at 0-15 days (2.6%) and decreased over time as reflected by incidence rate per person-year (0.65 at 0-15 days (95% CI, 0.60-0.70), 0.28 at 16-30 days (95% CI, 0.24-0.31), 0.14 at 31-90 days (95% CI, 0.13-0.15), and 0.07 at 91-365 days (95% CI, 0.07-0.08) (P for each pairwise comparison < 0.001)). After heart failure, age > 65 was the next strongest predictor of sudden incapacitation in a Cox multivariate regression (HR 1.84, 90% CI 1.69 to 2.01; P < 0.001). When stratified by age ≤ 65 or > 65 years, 6.7% vs 16.8% of patients had an event (P < 0.001). Using the Canadian Cardiovascular Society Risk of Harm equation, optimal driving restrictions were determined based on the observed sudden incapacitation rate. The data support a one month restriction overall, and a two week restriction in age ≤ 65.

Emily Sodhi

The role of serum urate in the relationship between pain and synovitis in knee OA

Emily Sodhi, Trevor Birmingham, Tom Appleton

Purpose: Since there is no cure for knee osteoarthritis (OA), early disease intervention is key in preventing pain and suffering. Serum urate was identified as a potential therapeutic target, as higher serum urate concentrations are associated with presence of synovitis, worse pain, and OA progression, but metabolic syndrome (MetS) confounds this relationship. Serum urate levels are often elevated in patients with MetS, and MetS is a risk factor for knee OA and worse outcomes. It remains unknown whether MetS drives the relationship between serum urate and worse pain in early-stage disease.

Methods: Patients with knee OA contributed serum samples, US images for synovitis measurement, x-ray images for disease staging, and Knee Osteoarthritis Outcome Scores for pain measurement. Multivariable linear regression modelling assessed disease stage-dependent relationships between pain and serum urate in knee OA and clarified any confounding effect of MetS. Secondary analyses assessed the confounding effects of individual MetS sub-components.

Results: 581 knees with OA were included, with there being 336 early-stage and 239 late-stage. A 1 umol/L increase in serum urate was associated with a 0.033 decrease in Knee Osteoarthritis Outcome Scores in early-stage knees (p= 0.025), but this relationship became non-significant when adjusting for MetS. Of all MetS sub-components, obesity and hypertriglyceridemia were key confounders in the relationship between serum urate and pain in early-stage OA. There was no association between serum urate levels and pain in late-stage knees.

Conclusion: A 300 umol/L increase in serum urate levels was associated with a clinically significant increase in pain in early-stage knee OA, and this association was driven by obesity and hypertriglyceridemia. Future studies should explore whether treating-to-target MetS can prevent or delay progression of early-stage knee OA.

Virginia Solitano

Management of Complications in Patients with an ileostomy: an umbrella review of systematic reviews

Virginia Solitano, Sudheer Kumar Vuyyuru, Yuhong Yuang, Vipul Jairath

Ileostomies, whether temporary or permanent, may be required in patients with Crohn’s Disease (CD) due to medically refractory disease or penetrating complications. Standardized clinical care processes for patients with CD and a permanent ileostomy (PI) are lacking. This umbrella review sought to consolidate existing knowledge by identifying, evaluating, and synthesizing findings from published systematic reviews on various aspects of clinical care for ileostomy patients.Following Cochrane guidelines for Overviews of Reviews and adhering to Preferred Reporting Items for Overviews of Reviews (PRIOR), we systematically searched major databases for relevant systematic reviews (SRs) or scoping reviews (ScR) published in English until January 5, 2024. Out of 1379 screened papers, we selected 24 reviews, including 22 SRs (8 with meta-analysis) and 2 ScRs, However, none exclusively focused on PI. Furthermore, ten reviews did not mention inflammatory bowel disease (IBD) patients.

The identified reviews covered 12 types of interventions, including ostomy care pathways, clinical management of high-output stoma, peristomal skin care, dietary management, nurse specialists, post-discharge continuous care, telemedicine, technology-based interventions, patient education, self-management interventions, management of parastomal varices, and chewing gum for postoperative ileus. Notably, none of the reviews examined stoma appliances and adhesive, behavioral interventions, or mental health exclusively.Evidence for best practice interventions to help quality of life for patients living with an ileostomy is limited and heterogeneous. Systematic reviews have largely overlooked interventions for patients with PI. There is an urgent need for standardized clinical care processes and pathways tailored to the unique needs of this patient population.

Virginia Solitano

Performance of bowel preparation quality scales in patients with Crohn's disease

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The performance of bowel preparation (BP) in patients with Crohn's disease (CD) is unknown and may be suboptimal due to the presence of mucosal inflammation, strictures, pseudopolyps and bowel resection. We evaluated the reliability and validity of available BP scales in patients with CD.Bowel preparation, in colonoscopy videos (N=50) from patients with CD (N=40) was independently rated twice, separated by at least 2 weeks, by 3 central readers using the Boston Bowel Preparation Score (BBPS), modified BBPS, Harefield Cleansing Scale (HCS), FDA bowel cleansing assessment scale (FDA BCAS), and a 100-mm VAS of bowel cleanliness. Endoscopic activity was assessed with the SES-CD. Reliability of BP assessment was quantified using the intraclass correlation coefficient (ICC). Correlation between BP quality and SES-SD scores by location was assessed using Spearman's rho.Substantial (ICC ≥0.61) inter-rater reliability was observed for all BP scales and the VAS during insertion and withdrawal, except for the FDA BCAS, which had moderate (ICC ≥0.41) inter-rater reliability on insertion. Intra-rater reliability was similarly substantial for all BP scales and almost perfect (ICC ≥0.81) for the VAS during insertion and withdrawal. BP and endoscopic disease activity were negatively correlated in the colon, particularly in the left colon, suggesting that lower BP scores in this segment may result in higher SES-CD scores. Existing scales are reliable for the assessment of BP in patients with CD. These results provide a framework for scoring of BP quality in both trials and clinical practice for CD.

Virginia Solitano

Towards patient-centricity: why do patients with Inflammatory Bowel Disease Participate in Pharmaceutical Clinical Trials? A Mixed-Methods Exploration of Study Participants

Virginia Solitano, Heather Prins, Meagan Archer, Leonardo Guizzetti, Vipul Jairath

A better understanding of motivations to participate and recommendations to reduce barriers to enrolment may assist in design of future clinical trials.We developed a 32-item electronic questionnaire to explore motivations, experiences, and recommendations of inflammatory bowel disease (IBD) patients, who have participated in pharmaceutical clinical trials in a tertiary center in Canada over the

last decade. We employed a mixed-methods approach that integrates both quantitative and qualitative research methods.We distributed a total of 69 e-mails with surveys and received 46 responses (66.6% response rate). Study participants were mostly male (27/46, 58.7%), non-Hispanic white (43/46, 93.5%), with a mean age of 45.5 years (SD 10.9). Most decided to participate in a clinical trial to benefit future patients (29/46, 63.0%). Half of participants (23/46, 50.0%) reported they were worried about the possibility of receiving placebo, although the majority (29/46, 63.0%) understood they could improve on placebo. The most challenging aspect reported was the number and length of questionnaires (15/46, 32.6%), as well of the number of colonoscopies (14/46, 30.4%). Strategies recommended to increase enrollment were reduction of the chance of receiving placebo (20/46, 43.5%), facilitating inclusion of patients who have failed multiple therapies (20/46, 43.5%), allowing virtual visits (18/46, 39.1%), including subtypes of disease traditionally excluded from trials (16/46, 34.8%) and improving outreach to underrepresented populations (13/46, 28.3%). The vast majority (37/46, 80.4%) reported their experience of participation to be better than expected.These results should help inform the design of future clinical trials with a focus on patient centricity.

Emily Stephenson

A Case of Breast Cancer Metastasis Masquerading as Signet Ring Cell Carcinoma of The Stomach

Emily Stephenson, Cady Zeman-Pocrnich, Michael Sey

This case study explores the challenge of diagnosing and managing patients when metastatic lesions mimic primary gastric cancer, as seen in this case of breast cancer metastasis resembling signet ring cell carcinoma of the stomach. A 68-year-old woman with a history of breast cancer with bone metastasis, had been well controlled for the past five years. The patient underwent gastroscopy for nausea and vomiting, which was grossly unremarkable. Random biopsies for Helicobacter pylori identified a single focus of signet ring cell adenocarcinoma. Subsequent chromoendoscopy identified an area of subtle mucosal abnormality, for which the patient declined surgery and was instead managed by endoscopic submucosal dissection (ESD), which surprisingly yielded no dysplasia. Random biopsies on a subsequent gastroscopy again identified a minute focus of adenocarcinoma with signet ring cell morphology. Given the unusual presentation of apparent signet ring cell adenocarcinoma in two distinct areas in the stomach without any visible endoscopic abnormality, an in-depth pathological analysis was conducted with immunohistochemistry staining being positive for estrogen receptor, GATA3 and CK7 but negative for CK20 and CDX2, in keeping with minute multifocal breast cancer metastases to the stomach from hematogenous spread.In this case, repeated endoscopic investigations and immunohistochemical staining revealed minute multifocal breast cancer metastases to the stomach. Conventional tumor staging methods often cannot identify microscopic metastases, potentially impacting disease progression and patient care. A high level of suspicion for metastatic breast cancer and a detailed pathological analysis allowed for the correct diagnosis in this patient.

Julia Steriopoulos

The Molecular Mechanism of TLR3 Initiated Cell Death

Julia Steriopoulos, ZhuXu Zhang

Background: Endothelial cells (ECs) are one of the first defences of the innate immune system. One of their unique characteristics is surface level expression of TLR3, a double stranded RNA (dsRNA) sensing toll-like receptor which can only signal through TIR domain-containing adaptor molecule inducing interferon-β (TRIF). TLR3 can commence molecular cascades resulting in different forms of cell death, including apoptosis and necroptosis. While apoptosis is non-inflammatory, necroptosis involves cellular contents leaking into the extracellular space, making it inflammatory. It is known that TRIF can bind receptor tyrosine kinases 1 and 3 (RIPK1 and RIPK3), which form a macromolecular complex necessary to necroptosis known as the necrosome. The subsequent molecules leading to mitochondrial damage in this pathway remain unknown, and are the subject of our study. Methods: Cell death in ECs stimulated with synthetic dsRNA under several conditions was measured. Treated ECs are used for protein binding analysis through co-immunoprecipitation and western blotting. Identified proteins in the cascade will be silenced to examine the effect on TLR3 initiated cell death. Results: ECs stimulated with synthetic dsRNA (P(I:C)) will die, even when treated with a caspase 8 inhibitor. TLR3-/- cells will not die when stimulated with P(I:C). Inhibiting RIPK1 will prevent TLR3 initiated cell death in ECs. Discussion: This indicates TLR3 can cause apoptotic and non-apoptotic cell death in ECs, and that RIPK1 is involved in both forms of cell death. Further investigation will attempt to determine molecules in the cascade leading to mitochondrial damage and cell death.

MargaretMan-Ger Sun

Single cell RNA sequencing analysis of human osteoarthritis synovial tissue in response to PPARδ agonist

Margaret Man-Ger Sun, Garth Blackler, Joseph Klapak, Matthew Grol, Jan Tuckermann, Frank Beier, C. Thomas Appleton

Osteoarthritis (OA) is the most common type of arthritis, causing significant disability worldwide. OA affects tissues of the whole joint, and synovial tissue function is critical to restore joint homeostasis. Peroxisome proliferator-activated receptor delta (PPARδ) is a nuclear receptor known to exacerbate cartilage damage in post-traumatic OA, but its role in synovial tissue dysfunction is less understood. Our study investigated the effect of PPARδ agonism on human OA synovial tissue using single-cell RNA sequencing (scRNA-Seq) to assess changes in cell subsets and gene expression profiles.Synovial tissues were collected from patients with late-stage knee OA undergoing arthroplasty and treated with vehicle control or a PPARδ agonist (GW501516) for 24 hours before scRNA-Seq. Cell cluster analysis and annotation were performed using Seurat in RStudio, and twelve molecularly defined cell clusters were identified including fibroblasts, macrophages, endothelial cells, T-cells, mural cells, B-cells, and mast cells. Examination of cell cluster proportion in GW501516 treated cells showed macrophages, lining fibroblasts, and T-cells to be more proportionally abundant. Differential gene expression analysis of synovial fibroblasts showed GW501516 treatment increased gene expression involved in fatty acid oxidation (ACADVL, ACAA2), cellular respiration (MT-ND3, MT-CO3), and stress response to metal ions (MT2A, MT1E), and decreased expression of genes involved in cell adhesion (COL6A3, COL6A2, ACTG1, CCN5, SPOCK1).Our results suggest that PPARδ agonism dysregulates genes involved in oxidative stress, mitochondrial function, and extracellular matrix regulation in synovial fibroblasts. This provides insight into the potential mechanisms by which PPARδ mediates synovial tissue dysfunction to worsen OA outcomes.

Salman Surangiwala

Improving Osteoporosis Treatment in Patients Admitted with Fragility Fractures to the Clinical Teaching Units at London Health Sciences Centre

Salman Surangiwala, Jenny Thain, Kristin K Clemens, Tayyab S. Khan

Effective screening and treatment of osteoporosis can reduce morbidity, mortality, and healthcare utilization. However, numerous studies demonstrate inadequate osteoporosis management in patients admitted for fragility fractures, partly due to clinical workloads and knowledge gaps on clinical guidelines. Our project aimed to assess the proportion of patients who received osteoporosis treatment during an admission to the Clinical Teaching Units (CTUs) at University Hospital, London Health Sciences Centre (LHSC) for fragility fracture. We hypothesized that a minority of patients would receive treatment prior to discharge.We screened 3518 health records of patients admitted to the CTUs for a fragility fracture from January 1st, 2023, to December 31st, 2023. Among the 35 patients admitted with fragility fractures, with a mean age of 84 +/- 9 years, vertebral fractures were most common, followed by pelvic fractures. Nine patients (26%) were already using an antiresorptive drug at admission. Only 5/26 (19%) patients without osteoporosis treatment at admission received on during their stay and 7/21 (33%) patients were discharged without such treatment in their hospital discharge summary. All patients already on an antiresorptive drug at admission were advised for reassessment by their family physician or specialist.These findings align with existing data, indicating that most patients admitted with fragility fracture to the CTUs at LHSC do not receive adequate osteoporosis treatment. To address this, we will explore root causes and potential tests of change to improve treatment. Strategies may include establishing an in-patient post-fracture service and educating CTU physicians about osteoporosis treatment options and referral protocols.

Kathryn Taberner

Optimizing the CTU Day – A Gap Analysis

Kathryn Taberner, Erin Spicer, Mark Goldszmidt

Background: The CTU (clinical teaching unit) rotation can be challenging - the days are long, and are highly variable in regards to tasks and patient acuity. However, the day-to-day activities for a resident on CTU can consist of underlying “waste”. This “waste” can refer to wasted effort, energy, and time. To reduce this “waste” or inefficiencies for CTU residents, we must first identify what inefficiencies currently exist. There have been no studies looking at factors that contribute to these inefficiencies. The purpose of this study was to identify the inefficiencies experienced by residents while on CTU that interfere with providing quality healthcare and receiving educational opportunities through an observational approach. Methods: Mixed methods study involving direct observation and focus groups. All three teaching CTU teams at University Hospital were directly observed over 4 weeks, with a focus on transition days. Once data collection was completed, a focus group was held with internal medicine residents at various levels of training. Results: Six main themes emerged: 1) ordering of non-routine tasks 2) tasks that require more nursing involvement, 3) communication and collaboration, 4) Paging, 5) clinical and educational workflow, and 6) implementation of best practices. Conclusions: Our findings suggest that there are several key areas that could be targeted for improvement. Next steps will involve

future QI studies addressing these areas for improvement primarily through PDSA cycles, which will hopefully ultimately lead to optimization of CTU

Cheng-Chun Tai

Stool Hemoglobin for Older Patients Polyps Surveillance (The SHOPPS Study)

Cheng-Chun Tai, James Gregor

INTRODUCTIONWith the Canadian population aged over 75 set to double, there's a conflict between colorectal cancer (CRC) screening guidelines and the reality of CRC mortality in this group. Current practices don't recommend screening past 75, yet the prevalence of advanced adenomatous polyps and CRC is higher for these individuals. Data is scarce on the post-polypectomy surveillance in the older population, particularly weighing the benefits of fecal immunochemical test (FIT). This study examines the utility of the FIT as a non-invasive alternative to colonoscopy for post-polypectomy surveillance in this age group.OBJECTIVESThe study aims to determine the effectiveness of FIT for 75-84-year-olds post-polypectomy, assessing its correlation with colonoscopy in detecting advanced adenomas and CRC. The negative predictive value (NPV) of FIT will be a primary measure, alongside secondary outcomes like colonoscopy complications and patient surveillance preferences.METHODSA cohort of 75-84-year-olds with prior polypectomies will undergo FIT followed by colonoscopy. The goal is to enroll 417 subjects to achieve a margin of error under 5%.ANTICIPATED RESULTSAn NPV of at least 95% for FIT is expected, which could justify eliminating the need for further colonoscopies in patients with negative FIT results. We wish to propose an amendment to the current guideline, suggesting that patients aged 75-84 with previous polypectomy should undergo at least one FIT. CONCLUSIONThe study's implications could be significant, offering a safer, more efficient screening method for an at-risk population, aligning cancer prevention strategies with the demographic realities of an aging society.

Alexandra Troitskaya

Impact of aging on septic response

Alexandra Troitskaya, Sean Gill, Ruud Veldhuizen

Sepsis is characterized by life-threatening organ dysfunction caused by dysregulated systemic infection. Clinically, sepsis remains one of the major causes of mortality worldwide specifically in elderly hospitalized patients. Unfortunately, most pre-clinical research studies have used young animals to evaluate septic responses and potential therapies. To address this issue, as a part of the National Pre-Clinical Sepsis Platform (NPSP) of Sepsis Canada, our laboratory compared the severity of sepsis in young and aged mice. We hypothesized that aged animals would have a more overwhelming inflammatory response. Methods: Young (2-3 months) and aged (22-23 months) mice were randomized to an intraperitoneal injection of either cecal slurry to induce sepsis or a dextrose solution as our sham control. Animals were monitored using an established mouse sepsis scoring assessment. Lung tissue was collected post-euthanasia and will be assessed for markers of inflammation using RT-qPCR.Results: In response to the injection of cecal slurry all animals showed a septic response whereas animals in the sham control group did not. A comparison of the mouse sepsis scores demonstrated significantly higher

scores in aged septic animals as compared to the young septic animals. It is anticipated that our assessment of inflammation will show higher inflammatory mediators in aged septic mice as compared to young septic mice. Discussion: These findings emphasize the importance of using age-appropriate models for pre-clinical studies. To help mitigate age-related changes in response to sepsis, future studies can utilize this model to identify clinically relevant mechanisms responsible for poorer outcomes in the aging population.

Claire Vannelli

Exploration of postgraduate trainees' perspectives and experiences with competency-based medical education

Claire Vannelli, Jenny Thain, Alishya Burrell, Laura Diachun, SheriLynn Kane

Background: In the past six years, competency-based medical education (CBME) has been implemented in Royal College accredited residency training programs across Canada. Though there is a strong theoretical basis for providing constant and actionable feedback, there is a current paucity of literature regarding its real-world impact on trainees. This study aims to explore the lived experience of trainees and their perceptions on the implementation of CBME. Methods: A thematic analysis methodology was applied to seek to understand the trainee experience. Semi-structured interviews with trainees in non-surgical specialties at a single academic institution in Ontario were conducted to explore key themes. The initial interviews were coded line by line and reviewed by the core research team to ensure consensus followed by an iterative process of constant comparison to refine codes and identify themes in subsequent interviews. Data collection continued until data sufficiency was reached. Results: Ten interviews were conducted involving residents from six specialties. Analysis has identified several key themes and shared experiences amongst residents of different programs. Firstly, the pervasive nature of trainees learning to play the game, pre-filling EPAs and strategically deciding when to trigger EPAs. Secondly, the institutional culture and hidden curriculum of CBME enactment is not reaching its stated goals. And finally, the residents' lived experience includes a negative impact on wellness. Conclusion: This research will provide valuable insight into the trainee lived experience and illuminate factors both intended and unintended in the real-world implementation of CBME.

Logan VanNynatten

A Novel Multiplex Biomarker Panel for Profiling Human Acute and Chronic Kidney Disease

Logan R. Van Nynatten, Michael R. Miller, Maitray A. Patel, Mark Daley, Guido Filler, Sigrun Badrnya, Markus Miholits, Brian Webb, Christopher W. McIntyre, Douglas D. Fraser

Acute and chronic kidney disease continues to confer significant morbidity and mortality in the clinical setting. We utilized a novel kidney multiplex panel to measure 21 proteins in plasma and urine to characterize the spectrum of biomarker profiles in kidney disease. Blood and urine samples were obtained from age-/sex-matched healthy control subjects (HC), critically-ill COVID-19 patients with acute kidney injury (AKI), and patients with chronic or end-stage kidney disease (CKD/ESKD). Biomarkers were measured with a kidney multiplex panel, and results analyzed with conventional statistics and machine

learning. Correlations were examined between biomarkers and patient clinical and laboratory variables. Median AKI subject age was 65.5 (IQR 58.5–73.0) and median CKD/ESKD age was 65.0 (IQR 50.0–71.5). In plasma, 19 proteins were significantly different in titre between the HC versus AKI versus CKD/ESKD groups, while NAG and RBP4 were unchanged. TIMP-1 (PPV 1.0, NPV 1.0), best distinguished AKI from HC, and TFF3 (PPV 0.99, NPV 0.89) best distinguished CKD/ESKD from HC. In urine, 18 proteins were significantly different between groups except Calbindin, Osteopontin and TIMP-1. Osteoactivin (PPV 0.95, NPV 0.95) best distinguished AKI from HC, and β2-microglobulin (PPV 0.96, NPV 0.78) best distinguished CKD/ESKD from HC. A variety of correlations were noted between patient variables and either plasma or urine biomarkers. Our study identifies unique biomarker profiles in the plasma and urine of patients with AKI and CKD/ESKD. Our exploratory study provides biomarker data for future hypothesis driven research on kidney disease and critical illness.

Logan VanNynatten

Evaluation of Novel Plasma Liver Biomarkers in Critically Ill Sepsis Patients

Logan R. Van Nynatten, James A. Russell, Marat Slessarev, Douglas D. Fraser

Background: Sepsis is defined as life-threatening organ dysfunction occurring secondary to dysregulated host responses to infection. Liver injury occurs in approximately 40% of septic patients, and doubles mortality in critical illness. This profoundly outweighs the impact of any other organ failure on patient death. The aim of this study was to identify novel plasma biomarkers of liver dysfunction. Methods: We prospectively enrolled 37 sepsis patients with liver injury (elevated INR, bilirubin, and transaminases), 37 sepsis patients without liver injury (normal INR, bilirubin, and transaminases), and 18 healthy control subjects. Patients were age-and sex-matched, with demographic and clinical data collected. Multiplex immunoassays were used to measure plasma levels of ARG1, MDH1, GST-α, 5-NT,and SDH, on Day 1,3,5 and 7 of hospitalization. Conventional statistics were used to compare circulating protein expression between groups. Results: Sepsis patients were clinically similar. Those patients with liver dysfunction had greater INR, bilirubin and creatinine, and lower platelet titre compared to those without liver dysfunction ($P<0.05$). Both ARG1 and SDH were significantly elevated in sepsis patients with liver dysfunction on admission to hospital ($P<0.05$). Median (IQR) expression of ARG1 and SDH in those with liver dysfunction was 7358.9pg/ml(3893.94-11329.44) and 138636.1pg/ml(77946.1-180666.8), respectively. Conclusions: Our exploratory study identified several novel plasma biomarkers of liver dysfunction in critically-ill sepsis patients. Our data suggests that further studies should be implemented to investigate the role of ARG1 and SDH as biomarkers of liver injury in sepsis.

Meggie Vo

Mitochondrial ROS-induced SerpinA3 expression protects cardiomyocytes against doxorubicin-induced injury

Meggie Vo, Xiaoyun Ji, Tianqing Peng

Drug-induced cardiotoxicity is a life-threatening side effect of anti-cancer treatment. Doxorubicin (DOX) is a widely used chemotherapeutic that induces cancer cell death through reactive oxygen species (ROS)

production. However, its usage has been demonstrated to worsen cardiac outcomes in cancer patients. Thus, there is a need for biomarkers to predict cardiotoxicity and create preventative interventions for DOX-induced cardiac injury. SerpinA3 is a target of clinical interest due to its overexpression in various cancers. However, it remains unknown if serpinA3 plays a role in DOX-induced cardiotoxicity.To address this, the AC16 human cardiomyocyte cell line was pretreated with mito-TEMPO, followed by DOX, to assess the role of mitochondrial ROS in serpinA3 expression. SerpinA3 gene and protein expression were measured via RT-qPCR and western blot analysis, respectively. Neonatal cardiomyocytes were pretreated with recombinant serpinA3 protein, then incubated with DOX or saline. A lactate dehydrogenase (LDH) assay was performed to assess cytotoxicity.Cardiomyocytes treated with DOX showed increased gene and protein expression in serpinA3. Pretreatment with mito-TEMPO prevented mitochondrial ROS production and reduced serpinA3 gene expression in DOX-induced cardiomyocytes, suggesting that mitochondrial ROS mediates DOX-induced serpinA3 expression. Pretreatment with recombinant serpinA3 protein decreased LDH levels produced by cardiomyocytes after DOX treatment, suggesting that serpinA3 plays a protective role in DOX-induced cardiotoxicity. These findings identify serpinA3 as a potential biomarker to predict cardiac injury development in patients receiving chemotherapy and may be a useful approach in determining cardiac preventative measures for those undergoing chemotherapy in clinical settings. Keywords: doxorubicin, cardiotoxicity, serpinA3, reactive oxygen species

Danielle Vucenovic

Diagnostic Kidney Genetics Referral at London Health Sciences Centre (LHSC): A Quality Improvement (QI) Study

Danielle Vucenovic, Erica Jeong, Andrea Wang

Introduction: Currently, non-invasive genomic sequencing is an effective tool to diagnose monogenic chronic kidney disease (CKD). In 2020, a diagnostic clinic for patients with suspected genetic kidney disease (GKD) was established at LHSC. Despite increasing availability of this service, genetic assessment is not routinely part of the diagnostic pathway for patients with CKD. Our aim is to perform a quality improvement study to increase accessibility and implementation of this service. Methods: We performed a chart review of all patients referred to our service from March 2020 to December 2023. Our primary outcome measure is the time of CKD diagnosis to referral to our service and temporal changes in sources over time. Results: We found a mean time from CKD diagnosis to genetic clinic referral to be 10.5 years (range 0-61.28) in 335 patients. The number of referrals have increased over time: 75 referrals in 2020, 79 in 2021, 133 in 2022 to 191 in 2023. Our cause-and-effect analysis identified one major bottleneck in the system was referring physician's knowledge regarding patients eligibility criteria for testing. Based on these findings, we developed and implemented a standardized referral document with eligibility criteria embedded. Following distribution, we plan to survey relevant stakeholders and collect process measure data including consistency of use & completeness of the form and number of referrals per year. Conclusion: To shorten the referral time to diagnostic kidney genetics and improve patient outcomes, we developed a standardized referral pathway. This study is the in post-intervention data collection phase.

Brent Wakefield

Ultrasound-measured synovitis is associated with movement-evoked pain in knee osteoarthritis: A cross-sectional and within-participant design

Brent Wakefield, Trevor B. Birmingham, Hayden Atkinson, Holly Philpott, Robert Dima, Tamara Tompkins, Songlin Zhu, C. Thomas Appleton

Objective: To examine the association between ultrasound-measured synovitis and movement-evoked pain (MEP) in patients with knee osteoarthritis (OA). Methods: 342 participants with radiographically early to late-stage OA (Kellgren-Lawrence [KL] arthritis grading scale) and frequent symptoms underwent ultrasound measures of inflammation using the Outcome Measures in Rheumatology (OMERACT) knee ultrasound scoring system. Measures of MEP, age, sex, and BMI were collected. MEP was assessed using the 6-minute walk test and a numerical rating scale for knee-specific pain before and after walking. A series of logistical regression analyses adjusted for age, sex, and BMI were used to determine the association between the presence of MEP and synovitis across KL grades. A secondary analysis using a conditional logistic regression in a subset of participants with knees discordant for MEP was performed. Results: Moderate-to-severe synovitis was associated with increased odds of MEP [OR = 1.47 95%CI 0.92 – 2.35] in the entire cohort. Synovitis was associated with an increased odds of experiencing MEP in patients with KL grade ≤ 3 [OR = 2.32 95%CI 1.40 – 3.84], and a decreased odds of MEP in knees with KL grade 4 radiographic damage [OR = 0.19 95%CI 0.03 – 1.0]. Our conditional logistical regression model strengthened the association between synovitis and MEP in patients with KL grade ≤ 3 [OR = 4.75 95%CI 1.62 – 13.97]. Conclusions: In knee OA with KL grade ≤ 3, moderate-to-severe synovitis is associated with MEP. Targeting synovial inflammation may be beneficial in early OA. In late-stage OA, additional sources, such as bone deformity, may contribute to MEP.

Derek Wu

Automated real-time detection of lung sliding using artificial intelligence: a prospective diagnostic accuracy study

Hans Claudorff, Ross Prager, Delaney Smith, Derek Wu, Chintan Dave, Jared Tschichart, Benjamin Wu, Blake Van Berlo, Richard Malthaner, Robert Arntfield

Background: Rapid evaluation for pneumothorax (PTX) is a common clinical priority. Although lung ultrasound (LUS) is often used to assess for PTX, its diagnostic accuracy varies based on patient and provider factors. To enhance the performance of LUS for pulmonary pathology, artificial intelligence (AI) assisted imaging has been adopted, however, the diagnostic accuracy of AI-Assisted LUS (AI-LUS) deployed in real-time to diagnose PTX remains unknown. Research Question: In patients with suspected PTX, what is the real-time diagnostic accuracy of AI-LUS to recognize the absence of lung sliding? Methods: We performed a prospective AI-assisted diagnostic accuracy study of AI-LUS to recognize the absence of lung sliding in a convenience sample of patients with suspected pneumothorax. After calibrating the model parameters and imaging settings for bedside deployment, we prospectively evaluated its diagnostic accuracy for lung sliding compared to a reference standard of expert consensus. Results: 241 lung sliding evaluations were derived from 62 patients. AI-LUS had a sensitivity of 0.921 (95% CI 0.792, 0.973), specificity of 0.802 (95% CI 0.735 - 0.856), area under the curve of the receiver

operating characteristic (AUC) of 0.885 (95% CI 0.828, 0.956), and accuracy of 0.824 (95% CI 0.766 - 0.870) for the diagnosis of absent lung sliding. Interpretation: Real-time AI-LUS has high sensitivity and moderate specificity to identify the absence of lung sliding. Further research to improve model performance and optimize the integration of AI-LUS into existing diagnostic pathways is warranted.

Samuel-Caleb Yeung

Effect of age on recovery of pulmonary microvascular endothelial cell barrier function under septic conditions

Samuel-Caleb Yeung, Aminmohamed Manji, Cynthia Pape, Onon Batnyam, Lefeng Wang, Sanjay Mehta, Sean E. Gill

Elderly individuals have higher morbidity and mortality rates during lung injury. Pulmonary sepsis is associated with damage to pulmonary microvascular endothelial cells (PMVEC) leading to a compromised vascular barrier, protein-rich edema leakage into the tissue, and subsequent respiratory dysfunction. Cell-cell junctions, particularly adherens junctions, play a vital role in maintaining the endothelial barrier. Our lab has demonstrated that aged PMVEC had increased junctional dysfunctions, cell death and leak compared to younger counterpart. However, the underlying mechanisms governing such age-related impairments are unknown. The objective of this project is understand the recovery response after a septic insult and unravel such mechanisms, focusing on whether the impaired barrier function in aged PMVEC is attributable to cellular proliferation. We hypothesize that aged PMVEC will have persistent leak and impaired ability to form barrier under septic conditions. To test this, PMVEC from young and aged mice were cultured and stimulated with cytomix, a mix of sepsis-relevant cytokines (tumor necrosis factor-α, interleukin-1β, and interferon-γ). Barrier integrity was assessed using the ECIS Z-Theta system, and cellular proliferation was measured by the Ki-67 assay. Leakage localization in relation to junctional proteins was examined using NeutrAvidin. Our study found that aged PMVEC had significant lower proliferation and reduced barrier integrity, while also having persistent leakage post-recovery from sepsis insult compared to younger counterpart. These outcomes are consistent with clinical observations indicating protracted intensive care unit durations for elderly patients relative to younger cohorts, who exhibit earlier discharge rates. Ultimately, this study highlights the necessity for age-specific therapeutic interventions.

Sammie Yu

Examining Canadian Trauma Centres' Analgesic Protocols for Rib Fractures

Sammie Yu, Petrease Patton, Kelly Vogt, Fran Priestep, Richard Hilsden, Shane Smith, Ian Ball

Rib fractures (RFs) commonly occur with blunt thoracic trauma patients, and their associated pain causes significant morbidity and mortality. Adequate analgesia is crucial to prevent RF-associated pulmonary complications. However, current analgesic modalities have drawbacks, and the optimal analgesia protocol remains elusive. Intravenous (IV) lidocaine infusions have a well-established safety profile and efficacy in other patient populations and may benefit patients with traumatic RFs.To better understand current practice and to inform the design of a multi-centre trial, a study determining

Canadian Trauma Centres' current analgesic practices is warranted. This study describes the current familiarity and utilization of IV lidocaine infusions for RF pain management. Secondary outcomes include the identification of common Canadian analgesic protocols for RFs and willingness to participate in a future multi-centre trial of lidocaine for traumatic RF. An online survey conducted on REDCap was distributed to 14 Canadian trauma centres. Study questions were designed to address four themes: trauma centre characteristics; pain management strategies; current use of IV lidocaine infusions; interest in future study participation. The analysis included an analysis of frequencies and a thematic analysis of descriptions. Twelve trauma centres responded. Six responding centres experience > 450, ISS > 12 trauma admissions annually. Six sites have an analgesic protocol for RFs. Four centres frequently use IV lidocaine for RFs, and ten believe further research with IV lidocaine is needed. Canadian trauma centres' current practices for RF pain management are variable. Prospective work is needed to evaluate the use of IV lidocaine as an analgesic for traumatic RFs.

Scan the QR code to complete the **Participant Evaluation** form online.

Or go to: https://uwo.eu.qualtrics.com/jfe/form/SV_9n3FC3CxXz7HqVU

Thank you!