Schulich School of Medicine & Dentistry

Western University

Department of Medicine Resident Research Day

Friday, May 23, 2025

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 **3.50 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.

Or go to: https://uwo.eu.qualtrics.com/jfe/form/SV_b75LMHplgtIWXs2

Learning Objectives

Overall Learning Objectives:

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

1. Describe new research findings of relevance to Internal Medicine and related subspecialties.
2. Recognize all types of research conducted by trainees in the Department of Medicine.
3. Identify and promote research successes in the Department of Medicine.

Dr. Robert Arntfield Learning Objectives:

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

1. Review the research trajectory behind the integration of point-of-care ultrasound into acute care practice, including its clinical applications and limitations in dissemination.
2. Discuss the role of translational research and innovation in developing AI-based tools to expand access to diagnostic ultrasound, including key challenges and future directions.

Dr. Pavel Roshanov Learning Objectives:

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

1. Explain how clinical trials function both as the engine of medical evidence and as an additional treatment option for patients.
2. Articulate the strategic value of a robust trials program for physician groups and hospitals.
3. Identify the physician career pathways in clinical trials and list at least two concrete steps to enter this field.

Brief Biosketches for Keynote and Faulty Speakers

Keynote Speaker:

Dr. Robert Arntfield, MD, FRCPC

Dr. Robert Arntfield, MD, FRCPC, is a critical care and trauma physician at London Health Sciences Centre and a Professor of Medicine at Western University. He is recognized for his early leadership in integrating point-of-care ultrasound (POCUS) into acute care practice in Canada, where he built one of the country's earliest and most comprehensive POCUS education programs. Over the years, he trained thousands of clinicians and contributed extensively to the literature, publishing on the clinical applications and impact of ultrasound in intensive care and emergency medicine.

Despite these contributions, Dr. Arntfield recognized the limitations of a purely education-based approach to dissemination and began exploring the use of AI and computer vision to scale diagnostic ultrasound expertise. This pivot led to a new phase of research and innovation, culminating in the founding of *Deep Breathe Inc.*, a medical technology company focused on delivering expert-level ultrasound interpretation through autonomous AI. His current work sits at the intersection of clinical medicine, machine learning, and health system accessibility.

Faculty Speaker:

Dr. Pavel Roshanov, MD, FRCPC

Dr. Pavel Roshanov is a clinical epidemiologist and medical specialist in kidney disease and kidney transplantation. Patients with kidney failure are among those with the highest risk of heart disease, stroke, infections, bleeding, and overall frailty. They are more prone to, for example, a lung infection or a hip fracture, and have more complications after such events. At the same time, they are either poorly represented or entirely excluded from most studies that guide medical practice. Expanding research to patients with advanced kidney disease and kidney failure would better inform their care. Dr. Roshanov is always looking to work with other researchers, graduate and undergraduate students, and medical trainees on projects that can inform the care of patients with kidney disease or that improve research methodology.

Dr. Roshanov's primary areas of focus currently involve:

- Preventing bleeding and transfusion during and after surgery, and especially in people with kidney failure where blood transfusion may delay access to kidney transplantation
- Reducing the risk of medical complications in the weeks to months after surgery
- Reducing chronic inflammation in patients with kidney disease to prevent cardiovascular events
- Large simple trials in hemodialysis

AGENDA

DoM Resident Research Day 2025

Friday, May 23, 2025

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 (6)** (Crystal Ballroom North) *6 min presentations, 3 min Q&A*	
9:40	10:30	**Keynote – Dr. Robert Arntfield** **"Scaling Clinical Expertise: A Research Journey from Point-of-Care Ultrasound to AI-Driven Diagnostics"** (Crystal Ballroom North) *35 min presentation, 10 min Q&A*	
10:30	11:30	**BREAK**	**Poster Presentation and Judging** (Crystal Ballroom South)
11:30	12:45	**Trainee Oral Presentations – (8)** (Crystal Ballroom North) *10 min presentations, 5 min Q&A*	
12:45	13:45	**LUNCH**	**Poster Presentation and Judging** (Crystal Ballroom South)
13:45	14:00	**GROUP PHOTO** **Everyone is invited to gather in the Crystal Ballroom North for a group photo**	
14:00	14:20	**Faculty Presentation - Dr. Pavel Roshanov** **"The why and how of the clinical trials physician."** (Crystal Ballroom North) *15 min presentation, 5 min Q&A*	
12:20	12:30	**Presentation of Awards & Final Remarks** (Crystal Ballroom North)	

Trainee Oral Presentations

Morning

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8:49	Vithuyan Sugumar	MD Student	Kristin Clemens	Hospital-based care strategies to support underserved people living with diabetes: a scoping review of the medical literature	52
8:58	Wenqi Yang	Undergraduate	Jenny Ho	Single-Cell Multiomic Analysis of Leukemic Transformation in Myeloproliferative Neoplasms	59
9:07	Mohammed Albaghdadi	PGY-2	Robert McKelvie	CC2H Reduces 30-, 60-, and 90-Day Readmissions and Emergency Department Visits in Heart Failure Patients	15
9:16	Nancy Shi	PGY-2	Pavel Antiperovitch	Rhythm Identification of Wide Complex Tachycardia on 12-lead ECG using a Convolutional Neural Network	50
9:25	Sahanah Thirukumar	MSc Student	Tianqing Peng	Targeting Cardiac Necroptotic Cell Death in Diabetic Cardiomyopathy with Murine Cytomegalovirus M45	53

Afternoon

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11:39	Matthew Laird	PGY-2	Karen Bosma & Paul Cameron	Evaluating Weaning Strategies from Mechanical Ventilation in Tracheostomized Adult Patients: A Systematic Review	37
11:48	Ali AbuHelal	PGY-2	Sanjay Mehta	Risk Factors for Diagnosis of Chronic Thromboembolic Pulmonary Hypertension Following Acute Pulmonary Embolism: A Systematic Review	14
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12:06	Gabrielle Buckley	MSc Student	Lillian Barra	Adjuvant Affects Arthritis Severity in Pre-Clinical Models of Rheumatoid Arthritis	22
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12:33	Mahmoud Riyam Jouid	PGY-2	Qasim Khan	Safety, Tolerability and Efficacy of GLP-1 Receptor Agonists (GLP1-RA) in the Management of Post-Liver Transplant Weight Gain: A Multi-Centre, Observational Study	33

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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 electronically completed by internists, medical oncologists, and hematologists across Canada within 10 minutes. Our survey aims to determine how practitioners incorporate diagnostic investigations to evaluate erythrocytosis and how they approach interventions in the management of secondary erythrocytosis. The survey was constructed in RedCap and will be distributed to 450 Canadian specialists through email. Survey data will be analyzed using descriptive analysis to identify trends, as well as, differences between specific groups of practitioners (e.g. community versus academic and hematologists versus 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 the continuum 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 was distributed in February 2025. We are currently collecting data until mid-April 2025. Conclusion: We have developed a cross-sectional survey that will provide insight on current clinical approach to the evaluation and management of secondary erythrocytosis. This will guide future studies and development of guidelines.

Salem AbuAl-Burak

Balancing Integrity and Compromise: Physicians' Navigation of Ethical Dilemmas in Teaching Hospitals

Salem Abu Al-Burak Shreya Sharma, Yaser Almoayad, Ibrahim Alsalkhadi, Jacqueline Torti

Background: Healthcare professionals in teaching centers often face ethical dilemmas that challenge their professional values, decision-making and patient care. While leadership frameworks in healthcare have been explored, there is limited understanding of how character-based leadership shapes physicians' navigation of moral conflicts. This study explores how physicians and trainees conceptualize and address ethical dilemmas through a character-based leadership lens. Methods: Field observations (110 hours across 19 sessions) and semi-structured interviews (n=8) were conducted in two hospital teaching centers, involving 8 attending physicians, 9 senior and 22 junior trainees. A Thematic analysis of the interview transcripts is ongoing, examining how participants make decisions in ethically complex situations. Results: Preliminary findings suggest that clinicians often struggle with navigating perceived legitimate vs. illegitimate compromises, balancing ethical concerns with institutional constraints. Emotional and hierarchical influences shape decision-making, at times leading to the continuation of treatment despite uncertainty. Participants described instances of selective application of ethical principles, prioritizing legal and institutional guidelines over moral considerations. Institutional pressures, communication breakdowns and resource allocation further exacerbate moral dilemmas. Many

participants emphasized the importance of focusing on the decision-making process rather than categorizing the dilemmas into rigid classifications of right and wrong. Conclusion: Ethical dilemmas may benefit from character-based leadership, helping healthcare professionals balance competing demands in complex environments. Preliminary findings highlight the need for tailored education and mentorship to enhance awareness, reflection, and decision-making around moral tensions. Further analysis will deepen the understanding how physicians navigate moral tensions in practice.

Ali AbuHelal

Risk Factors for Diagnosis of Chronic Thromboembolic Pulmonary Hypertension Following Acute Pulmonary Embolism: A Systematic Review

Ali Abu Helal Nada Taha, Arjun Pandey, Alla Iansavichene, Kyle Yakubowski, Sanjay Mehta

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a common, serious long-term complication following acute pulmonary embolism (APE). As a potentially curable form of PH, early diagnosis of CTEPH could improve clinical outcomes, but current clinical practice guidelines recommend against routine screening of patients post APE for development of CTEPH. This systematic review aims to identify risk factors predicting CTEPH following APE. Methods: We searched Medline and Embase for relevant publications until January 2023. Title, abstract and selected full-text screening, data extraction, and risk of bias assessment were performed independently in duplicate. When possible, pooled odds ratios (OR) were calculated using the random effects model. Results: In patients following APE, pooled incidence of CTEPH was 3.2% (95% CI: 2.9, 3.6). The most consistent risk factors associated with CTEPH post APE include recurrent venous thromboembolism (VTE; OR: 2.6, 95% CI 1.7, 4.0), higher initial or follow-up degree of radiographic pulmonary vascular obstruction (PVO; OR 3.1, 95% CI 1.1, 8.7, and 38.7, 95% CI 8.6, 173.6, respectively), longer symptom duration before PE diagnosis, and high initial or follow-up echo systolic pulmonary arterial pressure (sPAP), although specific sPAP thresholds varied. Age, sex, obesity, hypothyroidism, unprovoked PE, and thrombophilias were not consistent risk factors for CTEPH. Conclusion: Certain patients are at higher risk for developing CTEPH following APE, including those with a history of recurrent VTE, longer symptom duration before PE diagnosis, or greater PVO and/or elevated echo sPAP. Such patients may benefit from more intensive clinical monitoring or selective screening for CTEPH post APE.

Mohammed AlAgha

Is it necessary to repeat BMD for patients receiving denosumab? Results from a Quality Improvement initiative

Mohammad AlAgha Cindy Hoy, Regina Clara, Jenny Thain, Kristin K. Clemens, Tayyab S. Khan

Objective: The utility of repeating Bone Mineral Densitometry (BMD) in patients taking anti-osteoporosis therapy has been questioned, as a vanishingly small number of patients taking bisphosphonates or denosumab demonstrate convincing evidence of bone loss. This quality improvement project aimed to reduce BMD testing at ≤2-year intervals by up to 80%. Methods: We assessed lumbar spine (LS) and femoral neck (FN) BMD in postmenopausal women on chronic denosumab with at least two repeat BMDs. We evaluated BMD decline, fractures, and therapy changes. Based on initial results, a policy was implemented in October 2024 to forego BMD testing in patients without access to more potent therapies. Results: Among 54 patients (mean age 70.1 ± 8.3 years, mean denosumab duration 6.1 ± 2.7 years), baseline BMD T-scores were -2.4 ± 1.2 (LS) and -2.3 ± 0.6 (FN). The average interval between baseline and first follow-up BMD was 19.2 ± 8.5 months, and between first and second follow-ups was 21.4 ± 12.5 months. Only two patients (3.7%) had significant LS BMD loss, which later stabilized or improved. FN

BMD declined in two patients (3.7%) but stabilized on repeat testing. One patient who lost BMD sustained a fracture and switched to romosozumab; no other therapy changes were made. After policy implementation, 19 patients were reassessed: 10 (52%) were advised against repeat BMD, and 9 had extended intervals (mean 32.0 ± 12.0 months, range 24–60). Conclusion: Over 97% of postmenopausal women on chronic denosumab did not experience significant BMD loss, supporting reduced BMD testing which has potential to lower healthcare costs.

Dimah Alaskar

Pharmacological and dietary interventions for the management of upper gastrointestinal Crohn's disease: A systematic literature review

Alaskar, D Alaskar D, Chatto M, Yuan Y, Jairath V, Sedano R.

Background: Crohn's disease (CD) is a chronic inflammatory bowel disorder that can affect any part of the gastrointestinal (GI) tract, from the mouth to the anus. Upper GI involvement occurs in approximately 13% to 15% of cases. However, its true prevalence, potential complications, and optimal therapeutic strategies remain poorly understood. These knowledge gaps present significant clinical challenges in managing this subset of patients. Methods: We conducted a systematic review focusing on RCTs that investigated dietary or pharmacological interventions for patients with upper GI CD. Due to the absence of a standardized definition for "upper GI" CD, we included studies that reported data on CD affecting the esophagus to the jejunum, as well as those reporting data specifically on "small bowel CD." Results: Thirteen RCTs provided data for upper GI or small bowel CD, with none exclusively enrolling and randomizing patients who had upper GI CD. Three studies reported data specifically for patients with "small bowel" CD, nine reported data for ileum CD, and only two reported data for ileum along with the upper GI tract up to the jejunum. The investigated interventions included 5-ASAs, prednisone, thiopurines, biologics, and one study examined diet. Data could not be pooled due to the varied interventions and comparisons. Conclusion: Our findings highlight the limited evidence on upper GI CD and emphasize the need for larger, multi-center studies to improve therapeutic strategies. This review summarizes existing evidence and underscores the critical knowledge gaps that must be addressed to optimize management for this understudied CD subtype

Mohammed Albaghdadi

CC2H Reduces 30-, 60-, and 90-Day Readmissions and Emergency Department Visits in Heart Failure Patients

Mohammed Albaghdadi Karen Geuekers, Kiera Belletti, Elizabeth Farrell, Robert McKelvie

Background: Heart failure (HF) remains a major contributor to morbidity and mortality, with repeated hospitalizations driven by suboptimal post-discharge follow-up. To address this gap, we implemented a multidisciplinary transitional care program aimed at supporting HF patients during the critical post-discharge period. Methods: Between August 2018 and January 2024, HF patients admitted to our facility were referred for a 30-day transitional care program. Participants received personalized care plans developed by dedicated care managers in collaboration with HF specialists and primary care physicians. Core components included patient education, remote monitoring, 24-hour telephone support, and scheduled follow-up appointments. Enrolled patients were 1:1 matched with non-enrolled controls using the Health-Based Allocation Model Inpatient Group score. The primary outcome was a predefined composite of 30-day readmission or ED visit; secondary outcomes evaluated these events at 60 and 90 days. Results: Among 511 matched pairs, program enrollment was associated with a 37.6% reduction in the composite 30-day outcome (OR 0.62, 95% CI: 0.47–0.83, $p<0.001$; NNT=8). Similar benefits were observed at 60 days (36% reduction, OR 0.64, 95% CI: 0.50–0.83, $p<0.001$; NNT=10) and 90 days (34%

reduction, OR 0.66, 95% CI: 0.51–0.84, p<0.001; NNT=10). Conclusion: A structured transitional care program delivering multidisciplinary support, patient education, and prompt post-discharge follow-up significantly reduces readmissions and ED visits among HF patients, with benefits sustained through 90 days. These findings highlight the value of coordinated supportive care in improving HF outcomes and suggest this approach will potentially reduce healthcare costs for this patient population.

Alia AlDarwish

Inflammatory Phenotype as a Predictor of Treatment Response in Ulcerative Colitis

Alia AlDarwish R Kim, L Cameron, A Wilson

BACKGROUND AND AIM: The exact link between the inflammatory phenotype and UC disease outcomes and treatment responses over time is still incompletely defined. We aim to evaluate the pattern of surrogate markers of Th1 and Th2 immunity, neutrophils and eosinophils, in patients with UC and their ability to predict treatment response, particularly corticosteroids and anti-TNF-a. METHODS: In this retrospective cohort study, we included treatment naïve adult patients diagnosed with UC between 2005 and 2022 and received corticosteroids and antiTNF-a. WBC was collected at diagnosis and following exposure to corticosteroids or TNFa antagonists in addition to partial and endoscopic Mayo scores at baseline and following treatment among other outcomes. Descriptive statistics, Fisher's Exact test and ROC analysis were used for analysis. RESULTS: The baseline neutrophil and eosinophil count did not correlate with corticosteroid or anti-TNFa response. The eosinophil count on anti-TNFa following withdrawal of induction steroids correlated with disease activity and disease relapse(r=0.25, 95%CI=0.062-0.42, p=0.0081). Using a ROC analysis, an increase in eosinophil count of 0.3 following withdrawal of glucocorticoid induction most accurately identified participants who would relapse on anti-TNFa therapy (AUC=0.61, 95% CI 0.51-0.72,P=0.029). The neutrophil count on anti-TNFa therapy following withdrawal of induction glucocorticoids did not correlate with disease relapse on anti-TNFa (r=0.11, 95%CI=-0.08-0.29, p=0.27). CONCLUSION: This study showed that increase in the peripheral eosinophil count of 0.3 following the withdrawal of steroids predicted disease relapse while on TNFa antagonist.

Abrar Alharbi

Concordance between Multi-Disciplinary Discussion Diagnosis of Fibrosing Interstitial Lung Diseases and Lung Explant Pathology

Marco Mura Abrar Alharbi, Zinia Abid

Background: Interstitial lung disease (ILD) encompasses a heterogeneous group of disorders characterized by progressive fibrosis and impaired gas exchange. Accurate diagnosis is crucial for guiding treatment, particularly in lung transplant (LTx) candidates. The multidisciplinary discussion (MDD) approach integrates clinical, radiological, and histopathological data, increasing diagnostic confidence. However, its accuracy against explant pathology remains unverified. Objective: To assess the diagnostic accuracy of MDD by comparing pre-transplant diagnoses with lung explant pathology findings. Methods: We analyzed 54 patients with fibrosing ILD who underwent LTx, comparing their MDD diagnoses with explant pathology. In discordant cases, the evolution of CT scan patterns before LTx was examined. Results: Overall, 46 cases (85%) were concordant, and 9 cases (15%) were discordant. Among discordant cases, 5 UIP cases were identified on explant pathology, despite not being diagnosed with MDD. CT evolution toward a UIP pattern was observed in 3 of these 9 cases. The most prevalent MDD diagnosis was Idiopathic Pulmonary Fibrosis (IPF), observed in 32 cases. Conclusions: MDD is a reliable method for diagnosing fibrosing ILD, though its accuracy is not absolute. Discordance suggests

underutilization of lung biopsy. Some UIP cases may emerge as a superimposed pattern in progressive fibrosing ILD or present with atypical CT features.

Yazeedhezama Alotaibi

Epidemiology and Clinical Correlates of Esophageal Motility Disorders: A Retrospective analysis of 3,500 High-Resolution Esophageal Manometry studies in a Canadian Tertiary Centre

Yazeed Alotaibi Yigan Han, Arpana Wadhwani, Reyad Elzaanoun, Saleh Alobaid, Brenda Lin, Mahmoud Riyam Jouid, Nabeeha Anwar, Keith McIntosh, Rokhsana Mortuza, Rocio Sedan

Background High-resolution manometry (HRM) is the gold-standard diagnostic test for esophageal motility disorders.HRM is typically indicated for evaluation of unexplained dysphagia, pre-operative assessment prior to anti-reflux surgery, unexplained non-cardiac chest pain, and refractory gastroesophageal reflux symptoms.Interpretation of HRM findings is standardized by the Chicago Classification. Aim We aim to determine the prevalence and clinical characteristics of esophageal motility disorders by retrospectively analyzing HRM data from a large patient cohort in London, Ontario. Methods We performed a retrospective review of all esophageal HRM studies conducted at a tertiary care center in London, Ontario, encompassing approximately 3,500 adult patients. For each patient, we collected the following data : Demographics & clinical presentation Biological Sex (Female/Male), Age (Y), Height/weight, concomitant medications, comorbidities, indication Manometric parameters LES Residual and baseline pressure (IRB) (mmHg), , UES Residual and baseline pressure (mmHg),)LES proximal (cm), Hiatal hernia (Y/N), Distal contractile integral (mmHg-cm-s), Distal Latency (sec), % Failed peristalsis, % panesophageal pressurization, % premature contractions, % rapid contractions, % large breaks, %small breaks Endoscopic Findings Normal, Esophagitis, stricture etc Expected Results Analysis of the 3,500 HRM studies is in progress. We will report the distribution of HRM-based diagnoses across the cohort, including the prevalence of various major motility disorders. Conclusion This large-scale retrospective study will yield novel epidemiological data on esophageal motility disorders in Canada, addressing a significant knowledge gap in the field. The findings are expected to inform clinical practice by establishing baseline prevalence figures and typical clinical presentations for motility disorders in a Canadian setting.

Abdulrahman Aloun

The Utility of SpyGlass Cholangioscopy in Managing Biliary Complications Following Liver Transplantation

Abdulrahman Aloun Nitin Kanna, Karim Qumosani, Juan Glinka, Anton Skaro, Ken Leslie, Ephraim Tang

Abstract Biliary complications are common after liver transplantation, occurring in 10-30% of recipients. These complications often require timely intervention to prevent serious outcomes. While endoscopic retrograde cholangiopancreatography (ERCP) is standard, it has limitations in complex cases. This retrospective case series evaluates the utility of SpyGlass cholangioscopy in managing post-transplant biliary complications. Methods: Six adult liver transplant recipients with biliary complications underwent SpyGlass cholangioscopy. Indications included anastomotic strictures, intrahepatic strictures, biliary cast syndrome, and difficult bile duct stones. Procedures involved direct visualization, guidewire placement, and interventions like electrohydraulic lithotripsy. Results: Technical success was achieved in all cases, with five patients experiencing clinical success. SpyGlass facilitated guidewire placement in complex strictures and allowed for effective lithotripsy. No major complications were reported. Conclusion: SpyGlass cholangioscopy enhances diagnostic accuracy and facilitates targeted therapies, offering a valuable tool for managing post-liver transplant biliary complications. Further studies are needed to establish standardized protocols and assess long-term outcomes. References: 1.Hampe T, Dogan A, Encke J, Mehrabi A, Schemmer P, Schmidt J, et al. Biliary complications after liver transplantation. Clin

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Rasha Aqel

A Case of Difficult-to-Treat Dermatophyte Infection due to Emerging Pathogen Trichophyton mentagrophytes Subtype Indotineae

Rasha Aqel Megan Devlin, Fatimah Almutawa

Background: Chronic dermatophyte infections are challenging to diagnose and treat, particularly in immunocompromised patients. Trichophyton mentagrophytes subtype indotineae is an emerging pathogen known for its resistance to common antifungals. We present a case of a 63-year-old woman with severe rheumatoid arthritis (RA) on multiple immunosuppressive medications, who developed a persistent dermatophyte infection caused by Trichophyton indotineae. Case Presentation: The patient, had a 25-year history of severe RA managed with tocilizumab, methotrexate, and prednisone. Six years before presentation, she developed a pruritic rash that spread to her trunk and upper limbs. Despite treatments with various therapeutics, including topical clotrimazole, tacrolimus, and ciclopirox, as well as oral terbinafine, and itraconazole, the rash persisted. A skin biopsy three years prior showed chronic dermatitis with fungal spores and hyphae, and cultures isolated Trichophyton mentagrophytes. Collaborating with our microbiology colleagues, subsequent testing done 3 years into treatment identified the strain as Trichophyton indotineae, resistant to fluconazole and terbinafine but susceptible to itraconazole. Despite initial improvement with fluconazole, the patient relapsed upon dose reduction. The introduction of appropriately dosed itraconazole resulted in significant clinical improvement. Conclusions: This case underscores the challenges of treating dermatophyte infections in immunocompromised patients. The emergence of Trichophyton indotineae complicates management, requiring a multidisciplinary approach and careful adjustment of immunosuppressive therapy. Long-term follow-up and adaptability in treatment are essential. The evolving epidemiology of dermatophyte infections necessitates awareness and collaboration among healthcare providers to address these emerging pathogens effectively.

Areeba Asghar

Suboptimal management of cardiovascular risk in women with diabetes across Ontario: methodology and significance

Areeba Asghar Stephanie Dixon, Salimah Shariff, Leila Amirfakhrian, Kristin Clemens

Background: Diabetes mellitus (DM) is a known risk factor for cardiovascular disease (CV), promoting a disproportionately higher risk of stroke, heart failure, and chronic kidney disease in females. While biological factors and hormones contribute to differences in CV risk, sex and gender-related disparities in screening and management remain prevalent. In this population-based analysis, we aim to elucidate changing trends in the monitoring and management of CV risk factors in women with DM, and capture measurable patient-level, provider, and system-level factors that may be contributing. Methods: This is a population-based cohort study using linked health administrative (ICES) and survey data (Canadian Community Health Survey (CCHS) People aged 40 and older, have a diagnosis of DM, and have completed the 2017-2018 CCHS survey will be included. Over 365 days of follow-up, we will examine for CV care gaps including suboptimal HBA1c, LDL-c, and ACR screening , and for a sub-cohort of patients 65 years +, suboptimal prescription of statins, ACE/ARB, GLP-1RA, and SGLT2i ; suboptimal cutoffs are

determined using current clinical guidelines. Comparative analyses of suboptimal screening and management in males and females will be reported, and if sufficient sample, a stepwise regression analysis will be conducted to determine factors contributing to suboptimal management. Additional analyses for a subset with both DM and chronic kidney disease may be conducted. Significance: We anticipate our findings will lead to provincial clinical and policy-level interventions in addressing prevalent care gaps.

Cameron Ashe

Review and Optimization of Thrombolytic Instillation in Chest Tubes

Cameron Ashe Abdullah Almazrooa, Jana Aljohani, Mina Ishak

Introduction: The use of Alteplase and Dornase in patients with complex pleural effusions and empyema has been associated with improved outcomes when instilled through chest tubes. However, there have been concerns regarding variability in the process locally, ranging from medication formulation to patient administration. This quality improvement project aimed to quantify these variations and collaborate with stakeholders to identify potential solutions. Methods: Respirology fellows tracked the time intervals between medication orders and patient administration. Additionally, a comprehensive mapping of the medication formulation and delivery process was conducted using Quality Improvement methodologies. Results: A total of 16 patients were identified, with data from 13 patients analyzed. In total, 36 thrombolytic administrations were reviewed. The mean time from medication order to instillation was 142 minutes. Various factors were identified which prevented timely administration. Conclusions: The thrombolytic preparation and administration process involves multiple factors, contributing to delays in patient care. Streamlining this process by storing thrombolytics on the floor and having the Respirology team handle preparation has been approved by the Drug Therapeutics Committee. Implementation of these changes will commence shortly.

Bishoi Aziz

Machine Learning-Based Prognostic Tool for Autoimmune Hepatitis

Bishoi Aziz Ellina Lytvyak, Surain B. Roberts, Woo Jin Choi, Lawrence Worobetz, Catherine Vincent, Jennifer A. Flemming, Angela Cheung, Mark Swain, Dusanka Grbic, Hin Hin Ko, Kevork M. Peltekian, Lusine Abrahamyan, Monika Saini, Kattleya Tirona, Pietro Invernizzi, Cy

Background: Autoimmune hepatitis (AIH) is a chronic, immune-mediated liver disease characterized by T-cell-driven loss of tolerance to liver autoantigens. Prednisone remains the standard induction therapy; however, relapse rates after treatment withdrawal range from 50–87%, contributing to increased risks of cirrhosis and liver transplantation (LT). Currently, there are no prognostic tools to guide treatment withdrawal. Aim: To develop a machine learning (ML) model that predicts relapse, liver-related survival, and overall survival in AIH. Methodology: Data: We will utilize the Canadian Network for Autoimmune Liver Disease (CaNAL) registry, which includes longitudinal data from 15 tertiary Canadian centres. The dataset comprises extensive demographic and clinical variables. Endpoints: The primary endpoint is relapse, defined as ALT and/or AST levels >2× upper limit of normal following cessation of induction therapy. Secondary endpoints include liver-related survival (LT or hepatic death) and overall survival (LT or all-cause death). Imputation: Missing labs, assumed to be missing-not-at-random, will be imputed using multiple strategies: mixed-effects models, time-aware Gaussian processes, MissForest, and, for comparison, missing-at-random methods like mean imputation, forward/backward fill, MICE-Random Forest, and linear interpolation. Inclusion requires at least one lab value in the first six months post-induction. Model: We will use time-series ML models trained on the first-year lab data to predict outcomes. Models include decision trees, random forest, and long short-term memory (LSTM) networks.

A 10-fold cross-validation will be used, with performance assessed by AUC, sensitivity, and specificity. Results: Among 1,851 AIH patients (1965–2024), 12.3% died (145/1181), 12% received LT (129/1073), and 19.8% relapsed (56/283).

Kiera Ball

Blood transfusion to replenish plasma cholinesterase in nerve agent toxicity

Kiera Ball Marc Descoteaux, Sara Bohnert, John Mickler, Luc Vienot, Delaney Watkins, Ian Ball

Background: Chemical weapon nerve agents exert toxicity by inhibiting plasma cholinesterase, thereby prolonging acetylcholine's actions at nicotinic and muscarinic receptors. In the event of ageing, standard oxime therapy may be ineffective. Red blood cell transfusion has the potential to attenuate nerve agent toxicity by replenishing plasma cholinesterase activity. Methods: We conducted a systematic review of the literature using 3 medical databases from inception until September, 2024. We included randomized trials of nerve agent exposures in animals treated by red blood cell or plasma transfusion. Results: 906 abstracts were identified. After duplicate removal, 537 were reviewed by independent reviewers (KB, MD). Conflicts were adjudicated by a third reviewer (IB). 19 full texts were reviewed. Final interpretation of full text review is underway and will be ready for presentation at DOM Resident Research Day. Conclusions: This systematic review is the first phase of a research program designed to inform the treatment of nerve agent toxicity.

Maya Barua

Exogenous surfactant as a pulmonary drug delivery system for N-acetyl-lysyltyrosylcysteine amide (KYC)

Maya Barua Sara Yagoub, Ibrahim Farooq, Ruud Veldhuizen

Introduction: Bronchopulmonary dysplasia (BPD) is a chronic condition in preterm infants characterized by improper lung development. No effective treatments exist, indicating a need for novel therapies. N-acetyl-lysyltyrosylcysteine amide (KYC) is a novel peptide that inhibits myeloperoxidase, which is implicated in BPD development. However, the structure of the lung poses a barrier to KYC administration to the alveoli. Exogenous surfactants, which spread and reduce surface tension in the lung, are established therapeutics in preterm infants. Combining surfactant with KYC may facilitate alveolar delivery unless the peptide interferes with surfactant function. We hypothesized that the addition of KYC will not interfere with surfactant function. Methods: Four exogenous surfactants were tested. KYC to surfactant lipid ratios of 1:5 (low) and 1:1 (high) by weight, with surfactant concentrations of 2mg/mL and 1mg/mL respectively, were tested. Surfactant function was tested on a constrained drop surfactometer, which measures surface tension during initial spreading (adsorption) and alternating compression and expansion cycles which mimic breathing. Results: All surfactants tested effectively reduced surface tension during adsorption and across 20 expansion and compression cycles. This was not affected by the addition of KYC at a low ratio. At a high ratio, adsorption was also not affected but minor variations in minimum surface tensions were observed with different surfactants. Conclusion: KYC does not appear to impair the spreading or surface tension lowering capabilities of surfactant. Surfactant delivery may be an option for administering KYC, but more investigation on KYC function when combined with surfactant is required for clinical efficacy.

Garth Blackler

Metabolic Stress Disrupts Synovial Macrophage-Fibroblast Communication Enhancing Fibroblast Activation in Osteoarthritis

Garth Blackler Joseph Klapak, Dariana Ocica, C. Thomas Appleton

Introduction: Metabolic stress increases osteoarthritis (OA) risk, pain, and tissue damage by reducing the synovial joint's ability to withstand biomechanical stress. Synovial tissue function is fundamental for synovial joint function and relies on coordinated cellular communication between synovial fibroblasts and macrophages. Given that metabolic stress dysregulates tissue function and cell-cell communication in other organ systems, we hypothesize that it may also cause synovial tissue and cell dysfunction impairing the synovial joint's ability to withstand biomechanical stress. Objective: (a) Identify the effects of metabolic stress on synovial fibroblasts and macrophages and (b) synovial macrophage-to-fibroblast communication. Methods: (a) Synovial cells were isolated from male Sprague Dawley rats fed either a lean or metabolic stress-inducing diet prior to induction of biomechanical stress through surgically induced joint destabilization. A single-cell RNA sequencing (scRNA-seq) dataset was generated and analyzed to identify transcriptional differences in synovial fibroblasts and macrophages. (b) Macrophage-to-fibroblast communication was inferred using CellChat and an in vitro macrophage-fibroblast co-culture system was used to study altered communication. Results: scRNA-seq demonstrated that metabolic stress induces metabolic reprograming and cell activation in both synovial fibroblasts and macrophages. Further, metabolic stress altered synovial macrophage and fibroblast responses to biomechanical stress by inducing neurogenic pathways and enriching fibroblast activating communication. Lastly, in co-culture, metabolic stress alters macrophage-to-fibroblast communication increasing production of Htra1, a pathogenic protease in OA. Discussion: This study uncovers novel mechanisms underlying the effect of metabolic stress on synovial tissue, which may be a key effector of disease in patients suffering from OA.

Leann Blake

Association of Cerebral Hemodynamic Markers Measured by Transcranial Doppler (TCD) Ultrasound with Clinical Outcomes in Sepsis and Septic Shock: A Systematic Review

Leann Blake Jocelyn Wang, Marat Slessarev, Ahmad Bafaraj, Bram Rochwerg , Christopher Louis McChesney, Diyaa Bokhary, Henri Fero, Ian Ball, Kimia Honarmand, Kyle Fiorini, Logan Van Nynatten, Luke Dingwell, Marina Mir-Parramon, Nicolas Orozco, Ross Prager, Simon Pupul

Sepsis-associated encephalopathy (SAE) results from systemic inflammation, blood-brain barrier disruption, and impaired cerebral perfusion. It manifests as delirium, cognitive impairment, or coma and is associated with increased mortality and prolonged ICU stays. Despite targeting a mean arterial pressure (MAP) of 65 mmHg during septic shock resuscitation, cerebral perfusion may remain inadequate. Transcranial Doppler (TCD), a non-invasive tool for assessing cerebral hemodynamics, could aid resuscitation. This review examines the association between TCD-derived markers, SAE, and sepsis mortality. Following PRISMA guidelines, we searched MEDLINE, SCOPUS, and EMBASE for randomized trials or controlled observational studies. We analyzed study design, patient characteristics, TCD parameters, operator expertise, and outcomes while narratively assessing bias and synthesizing findings. Nineteen studies (n = 983) met inclusion criteria. Six studies (n = 410) linked Pulsatility Index (PI) to SAE, prolonged ICU stays, and mortality, while one (n = 98) found no association. An RCT (n = 50) showed that TCD-guided resuscitation (PI < 1.3) reduced SAE and mortality. Five studies (n = 400) associated the Resistive Index with SAE and mortality, though one (n = 51) did not. Lower Diastolic Velocity correlated with SAE in four studies (n = 270). Impaired cerebral autoregulation predicted SAE and mortality in four studies (n = 300), while one (n = 98) found no association. TCD-derived cerebral hemodynamic markers

are frequently associated with SAE and mortality in sepsis. TCD may detect cerebral perfusion deficits and guide resuscitation beyond MAP targets. Further trials are needed to validate its integration into sepsis management protocols.

Hasan Bualbanat

Assessing Post-TACE Liver Decompensation Risk in HCC: A Comparative Analysis of MELD 3.0, MELD-Na, Child-Pugh, and ALBI Scores

Hasan Bualbanat David Hudson, Karim Qumosani, Anouar Teriaky

Background & Aim: Patients with hepatocellular carcinoma (HCC) undergoing transarterial chemoembolization (TACE) are at risk of hepatic decompensation. Pre-procedural prediction of such events is crucial for patient selection. This study aims to evaluate and compare the predictive accuracy of MELD 3.0, MELD-Na, Child-Pugh, and Albumin-Bilirubin (ALBI) Methods: This retrospective cohort study included 280 patients with HCC who underwent TACE at our institution. We calculated MELD 3.0, MELD-Na, Child-Pugh, and ALBI scores for each patient immediately prior to TACE treatment. The primary endpoint was the occurrence of hepatic decompensation post-TACE, recorded as a binary outcome (yes/no). Receiver Operating Characteristic (ROC) curve analysis was performed to determine and compare the predictive accuracy of each scoring system, with the Area Under the Receiver Operating Characteristic Curve (AUROC) as the primary measure. Optimal cutoff values for MELD 3.0 and MELD-Na scores were identified using Youden's index. Results: MELD 3.0 demonstrated the highest predictive accuracy with an AUROC of 0.81. MELD-Na showed slightly lower accuracy (AUROC 0.79), followed by Child-Pugh (AUROC 0.78), and ALBI scores (AUROC 0.75). The optimal cutoff scores for predicting hepatic decompensation were ≥16 for MELD 3.0 (sensitivity 69.0%, specificity 87.2%) and ≥14 for MELD-Na (sensitivity 66.7%, specificity 85.7%). Conclusion: Our findings suggest that MELD 3.0 score provides superior predictive accuracy for hepatic decompensation in patients with HCC undergoing TACE, compared to MELD-Na, Child-Pugh, and ALBI scores. A MELD 3.0 score of 16 or higher effectively identifies patients at increased risk, aiding in decision-making and targeted patient management to minimize post-procedural complications.

Gabrielle Buckley

Adjuvant Affects Arthritis Severity in Pre-Clinical Models of Rheumatoid Arthritis

Gabrielle Buckley Jaspreet Toor, Sofya Ulanova, Ewa Cairns, Lillian Barra

Background: Development of novel Rheumatoid arthritis (RA) therapies requires effective preclinical models that mimic human disease. Currently, the collagen-induced arthritis (CIA) mouse model is widely used for RA research, but these mice lack the expression of HLA-DR4, the strongest genetic risk factor for RA development. HLA-DR4 is critical for generating antigen-specific immune responses to citrullinated and homocitrullinated proteins (CitP/HCitP). Consequently, we developed an HLA-DR4 transgenic (DR4tg) mouse model. Our model mimics human autoantibody responses when immunized with HCitP in Complete Freund's Adjuvant (CFA), an inflammatory agent that enhances and prolongs antigen exposure. Objective: To determine the optimal CFA concentration for inducing RA-like disease. Methods: DBA1J mice were immunized with collagen in 1.0 or 2.0 mg/mL CFA to induce CIA. DR4tg mice were immunized with HCitP in 1.0 or 2.0 mg/mL CFA and received HCitP into the knee to induce arthritis. Joint swelling (via caliper measurements), pain-like behavior (via Von Frey withdrawal testing), autoantibodies (via ELISA), and joint histopathology were assessed. Results: In CIA mice, 1.0 mg/mL CFA induced greater joint swelling and histopathological damage/inflammation (synovial thickening, pannus formation, intra-articular exudate, and cartilage erosion) than 2.0 mg/mL; however, there was no difference in anti-collagen and HCitP antibody titres. Similarly, DR4tg mice immunized with 1.0 mg/mL CFA had significantly

greater swelling, but no differences in pain-like behavior or HCitP autoantibody production. Significance: Optimizing CFA concentration in our humanized DR4tg preclinical model will be crucial for future testing of a novel immunotherapy we developed to suppress the antigen-specific RA immune responses.

Madison Burella

The impact of covid-19 pandemic on trainees' diagnostic performance in ecg and core cardiology topics

Madison Burella Sarah Blissett, Ashlay Huitema, Neville Suskin, Pavel Antiperovitch

Western University's Cardio Guide modules serve as a fundamental tool for trainees to refine their diagnostic testing abilities in ECG interpretation. Although ECG interpretation is a core component of medical training, accuracy remains disconcertingly low. The COVID-19 pandemic has brought significant changes in medical education including a shift towards virtual learning. The aim of the study is to compare diagnostic accuracy on ECG modules during and post-pandemic. We conducted a retrospective cohort study to assess the interactions with Cardio Guide and diagnostic performance in the learning modules during the COVID-19 pandemic and post-pandemic period. All trainees in PGY1 to PGY3 who complete a cardiology rotation at Western University were included in the study. The primary outcome is the diagnostic accuracy of trainees' ECG interpretation during and after the pandemic. The module was predominantly completed by PGY1 (72%). The overall pandemic cohort (mean grade 48%, P 0.02*) scored higher than the post-pandemic cohort (mean grade 44%). Based on the first attempt score, PGY1 trainees started with a similar skill level in ECG interpretation during (mean grade 42%) and post-pandemic (mean grade 43%). Although scores increased upon multiple attempts, PGY1 had a lower mean score on their last attempt during the pandemic (P <0.0001****) and their performance reduction persisted in PGY2 post-pandemic cohort. The findings suggest that the pandemic affected postgraduate trainees' diagnostic performance in ECG interpretation. To address areas of diagnostic difficulty, learning modules for the post-pandemic cohort could be adapted to provide additional supportive instruction to maximize online learning effectiveness.

Cory Byrne

Sustainability of Medical Assistance in Dying (MAiD) Provision in Ontario: Provider Perspectives

Cory Byrne Ian Ball, John Basmaji, Marat Slessarev, Dawn Papanayotou, Robert Sibbald

Background: Medical Assistance in Dying (MAiD) remains novel in Canada, having been legalized in 2016. It is both a rapidly growing and evolving field. The increasing number of MAiD provisions each year has outpaced the number of new MAiD providers. This escalating workload combined with frequently changing regulations, limited training, and inadequate compensation poses significant challenges for MAiD providers. Consequently, Canadians' access to and autonomy over end-of-life decisions may be at risk. This study aims to explore MAiD providers' perceptions of their work and its sustainability. Methods: An online questionnaire was distributed to MAiD providers across Ontario via a network of MAiD navigators. Snowball sampling was employed, allowing participants to share the survey with colleagues. Questions were answered with a Likert scale and analyzed using descriptive analysis. Mann-Whitney U and Kruskal-Wallis tests were used to assess for significant differences between groups. Results: Respondents (n=38) were well-experienced MAiD providers from a variety of specialties. They reported high satisfaction relating to their work with MAiD and felt their current workload was sustainable for their long-term well-being. While some providers felt the compensation and training were sufficient, others felt it could be improved. Providers were well connected with MAiD resources and coped well with the stress of their work. Conclusions: Despite the inherent challenges and complexities of providing MAiD, clinicians report positive experiences and view the work as sustainable. While existing literature and media often

emphasize the challenges or controversial aspects of MAiD, the experiences of providers highlight a positive and manageable workload.

Sarah Catania

Practical Strategies for Addressing Weight Bias in Healthcare

Sarah Catania Vanesa Berati, Bal Ruprai

Background: Weight bias, characterized by negative attitudes, beliefs and assumptions about individuals due to their weight, negatively impacts patient outcomes and well-being. Despite growing awareness of the complex etiology of obesity, weight bias by healthcare professionals (HCPs) remains a significant factor deterring individuals from seeking care. Methodology: A systematic literature review using PubMed, PsycINFO, and SCOPUS was conducted to assess patient perspectives and interventions aimed at reducing weight bias among HCPs and trainees. The search was limited to English-language studies published in 2020 or later, due to renewed interest in weight bias following COVID-19 and to build on pre-COVID published reviews. Results: From 1,820 initially identified records, 25 studies met the inclusion criteria. Most interventions focused on education and showed effectiveness in reducing explicit bias, but inconsistent changes in implicit bias. Strategies incorporating patient narratives, genetic explanations of obesity, and patient-centred communication techniques yielded more sustained improvements in HCP attitudes and behaviours. Additionally, interventions that included motivational interviewing and shared decision-making were well-received by patients. Through this research, we developed educational infographics as a means for knowledge translation to promote awareness. Discussion: Recent findings highlight the effectiveness of patient-centred approaches in reducing weight bias among HCPs. While educational interventions are beneficial, short-term programs alone may not be sufficient to address implicit biases. Our group's development of educational infographics aims to complement existing strategies by providing accessible resources to promote awareness and encourage behavioural change. Future research should refine these interventions, explore sustainable programs, and implement systemic equity reforms.

Katherine Chan

Evaluation of absolute eosinophil count as a biomarker of disease activity in eosinophilic esophagitis

Katherine Chan Aze Wilson

Background and Aim: Eosinophilic esophagitis (EoE) is a chronic Th2 immune-mediated disease. The esophagus reacts to food and/or environmental allergens leading to esophageal eosinophilic infiltrates and symptoms of dysphagia, vomiting, food impaction and deleterious health outcomes. The gold standard for EoE diagnosis and monitoring is upper gastrointestinal endoscopy (EGD) and biopsy of the esophageal mucosa. Unfortunately, the need for multiple and/or sequential treatments in this population can lead to patients needing recurrent, invasive EGDs for evaluation of disease activity and treatment response over time. We aim to evaluate if peripheral absolute eosinophil count (pAEC) is effective for monitoring EoE disease activity without the need for EGD. Methods: A retrospective cohort study in adult EoE patients will assess if pAEC is a biomarker of esophageal eosinophil count and treatment response (disease remission) in an EoE population. Participants will be followed from the time of diagnosis for up to 4 endoscopic follow-up visits with available bloodwork. pAEC, histological disease activity, endoscopic findings, and symptoms will be collected pre- and post-treatment. The relationship between pAEC and clinical outcomes will be assessed using correlation and regression analyses. A receiver operator characteristic analysis will be used to identify a threshold pAEC associated with the clinical outcomes. Results and conclusions: Data collection remains ongoing. We aim to include 194 participants in our final

analyses. With completion of this study, we hope to identify a simple and clinically-actionable biomarker of EoE disease activity. This may reduce the need for repeated, invasive endoscopies in an otherwise healthy population.

Christopher Chiang

Demystifying post-pandemic decline in cardiac rehabilitation referrals

Christopher Chiang Tim Hartley, Neville Suskin, Robert McKelvie, Ashlay Huitema

Background: Cardiac rehabilitation (CR) improves patients' morbidity and mortality. Following the COVID-19 pandemic, St. Joseph's Cardiac Rehabilitation and Secondary Prevention program (CRSP) experienced a significant decline in referral rates. This decline was despite preserved numbers of cardiology and cardiac surgery procedures completed. An electronic medical record (EMR)-based discharge order set including automatic CR referral was implemented, but referral rates have yet to recover. The objective of this study was to identify eligible patients that were not referred and their characteristics. Methods: This retrospective chart review compared CRSP-referred and non-referred patients discharged from cardiology and cardiovascular surgery at London Health Sciences Centre (LHSC) between September 1, 2022 and February 28, 2023. Patient demographics, hospitalization characteristics, and CR referral status were collected. Statistical analysis was performed with significance value of $p<0.05$ and logistic regression modelling was done for significant variables. Results: A total of 410 patients were referred and 648 patients were not referred to CRSP. Twenty-one percent of eligible patients had a missed referral and were hospitalized for either congestive heart failure (CHF) (45%), cardiac surgeries (27%), and acute coronary syndrome (19%). Patients were more likely not to be referred if they were older, female, used a walker, discharged by an internal medicine resident, or admitted with CHF. Conclusion: Over 20% of cardiac patients discharged from LHSC are missing the opportunity for CR referral. To improve CR referral rates, educating internal medicine residents on overall CR benefits for ACS and CHF patients may help remedy the referral gap

Jodi Chiu

Development of a Combined Risk Assessment Model for Venous Thromboembolism and Bleed in Hematopoietic Stem Cell Transplantation Patients

Jodi Chiu Brianna Ananthan, Matthew Lawrence, Mohamed Aly, Dhuvaraha Srikrishnaraj, Madeleine Weichel, Uday Deotare, Anargyros Xenocostas, Alejandro Lazo-Langner

Background: Venous thromboembolism (VTE) and bleeding are common complications in hematopoietic stem cell transplant (HSCT) patients. Balancing bleeding and thrombosis risks is challenging due to pancytopenia and coagulopathy. We aimed to create a combined risk assessment tool for VTE and bleeding in the first 90 days post-transplant. Methods: We conducted a retrospective cohort study of adult HSCT patients at London Health Sciences Centre from 2011-2021. Patients were followed until VTE, bleeding, or death occurred. VTE was defined as confirmed thrombosis (deep vein thrombosis, pulmonary embolism, cerebral, or splanchnic thrombosis). Bleeding was defined as major or clinically significant non-major bleeding unrelated to anticoagulation. Risk factors were evaluated with logistic regression, and final scores were derived and validated using bootstrapping. Results: 476 patients were included (317 autologous, 159 allogeneic). 47 (9.8%) had VTE, and 32 (6.7%) experienced bleeding. The VTE risk tool included second central venous catheter insertion (2 points) and prior steroid use (1 point). High-risk VTE patients had 31.8% cumulative incidence versus 7.6% in the low-risk group. The high-risk group was associated with higher mortality at 90 days (15.9% versus 3.2%, $p <0.001$). The bleeding risk tool included baseline platelet count <90 (1 point) and hemoglobin <96 (1 point). High-risk bleeding patients had 17.2% cumulative incidence versus 4.3% in the low-risk group. Conclusion: We developed

and internally validated a combined VTE and bleeding risk score for use in the first 90 days post-HSCT. These models can guide prophylaxis and surveillance strategies to improve patient outcomes.

Melissa Côté

Prospective Evaluation of AI-Driven Lung Ultrasound Interpretation for Pneumothorax Detection Post Chest Tube Removal

Melissa Côté Khoa Tran, Ross Prager, Robert Arntfield

Pneumothorax is a common concern following chest tube removal, and chest x-ray remains the standard method for detecting this complication. While widely used, chest x-rays can delay clinical decisions and exposes patients to radiation. Lung ultrasound offers a rapid and accurate bedside alternative, with reported sensitivity exceeding 98% for ruling out pneumothorax. Despite this, broader adoption is limited by the need for trained operators. To address this barrier, we developed an artificial intelligence model designed to detect pleural contact based on ultrasound artifacts. This study evaluates the diagnostic accuracy of the AI model when interpreting clips acquired by novice point-of-care ultrasound (POCUS) users, including nurses and medical students. It also examines the temporal and anatomical distribution of lung sliding following chest tube removal. In this prospective observational study, 80 patients from cardiac and trauma units were scanned at three time points: before chest tube removal, five minutes after removal, and at the time of routine follow-up chest x-ray. Novice users, following a focused 30-minute training session, acquired 3-second lung ultrasound clips from five standardized anterior and lateral chest wall locations using a handheld device. Ground truth was established by expert sonographers blinded to clinical data. The AI model was retrospectively applied and compared with expert consensus interpretation. Preliminary findings suggest the model can accurately detect pleural contact shortly after tube removal. If validated, this approach could support timely and reliable pneumothorax detection across a range of clinical settings.

Jane Ding

Polymorphisms of P-glycoprotein (ABCB1) and asthma control: a longitudinal study

Ding J Cameron L, Serajeddini H, Kim RB, Mackenzie CA

Inhaled corticosteroids (ICS) are a cornerstone of asthma management. However, there persists significant interindividual variability in response to these therapies, with underlying mechanisms poorly understood. Identifying genetic predictors of drug response, particularly regarding drug metabolism and transport, may offer crucial insight. P-glycoprotein (P-gp), encoded by the ABCB1/MDR1 gene, is a drug efflux transporter involved in glucocorticoid transport expressed by pulmonary epithelium and endothelium. Single nucleotide polymorphisms (SNPs) in ABCB1 have been associated with corticosteroid response in Crohn's disease. This study examined the association of ABCB1 genetics with asthma progression over ten years. Forty patients with confirmed asthma followed by a respirologist at London Health Sciences Centre were enrolled between 2012-2016. Patients were genotyped for the common SNP ABCB1 c.3435C>T(rs1045642;C___7586657_20). Markers of asthma control, including PFTs, serum eosinophil counts, Asthma Control Questionnaire, fraction of exhaled nitric oxide, ICS requirements, and biologic therapies were collected at enrollment and retrospectively in 2024. Of 40 patients, 23 were female, and average follow-up was 9.93 ± 1.36 years. Patients with the ABCB1 C/C genotype had significantly lower initial percent predicted FEV1 (n=8, mean=59±8.7) compared to those with C/T, T/T polymorphisms (n=22, mean=78±17; n=10, mean=79±17; p=0.01). This study suggests ABCB1 polymorphisms influence asthma outcomes. The C/C genotype is associated with comparatively higher expression and function and may lead to increased transport of ICS away from the site of action,

reducing therapeutic effect. The role of ABCB1 in ICS transport and efficacy in the lung remains unclear and requires further study.

Maria Luz Garagiola

Assessing Curricular Priorities to Address the Evolving Role of Generalists: Lessons from the Canadian Adult Congenital Heart Disease Landscape

Maria Luz Garagiola Sarah Blissett

The growing population of adults with congenital heart disease (ACHD) has expanded the role of general cardiologists in their care. In response, the Canadian Adult Congenital Heart Network has proposed several strategies, including targeted education for generalists. Our aim was to identify educational priorities for a targeted ACHD curriculum for generalists. An electronic survey was distributed to all Canadian generalist and ACHD cardiologists. They self-identified as ACHD specialists or not. The survey explored: 1) self-identified knowledge gaps of generalists, 2) current scope of practice of generalists; and 3) ACHD specialists' perspectives on recommended scope of practice of generalists. Educational priorities were defined as diagnoses or topics frequently identified in the three categories. There were 133 respondents (32 ACHD specialists and 101 generalists). One third (33%) of generalists did not have an ACHD specialist on-site, and 24% reported no ACHD specialist within 100 kilometers. Generalists encountered ACHD patients in the inpatient (42%) and outpatient settings (42%) while ACHD specialists predominantly encountered outpatients (81%). Frequent self-identified knowledge gaps included great complexity diagnoses, and management of pregnancy, arrhythmias and heart failure. Recommended and current scope of practice involved simple and moderate diagnoses. Both generalists and specialists contributed to identifying the crucial role of generalists in the care of ACHD patients. Their input highlighted key educational priorities. These findings can inform the development of a tailored curriculum aimed at better preparing general cardiologists to care for ACHD patients. Furthermore, our methodology and insights may be applicable to other healthcare contexts as well.

Sarah Ghnaim

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

Sarah Ghnaim Bonnie Liu, Rahman Ladak, Albert Huynh, Radha Joseph

Background: The transition from pre-clerkship to clinical clerkship marks a pivotal step in medical training. While immersive, it can provoke stress and anxiety that hinder learning. At Western University, third-year students begin their Internal Medicine training with a 6-week rotation on the Clinical Teaching Unit (CTU). This design thinking project aims to improve the CTU experience for novice clerks—students starting clerkship on the CTUs. Methods: Students who began CTU rotations in September 2023 (2023–2024 clerkship cohort) participated in two virtual focus groups as part of a co-design process. This approach actively engages end-users to shape solutions iteratively. We followed the five-stage Stanford d.school design thinking model: Empathize, Define, Ideate, Prototype, and Test. Results: Insights from the 2023–2024 cohort during the ‘Empathize’ stage were reframed as opportunity areas. The primary challenge was defined as: How might we impart the skills needed to complete effective daily assessments on the CTU using an Internal Medicine approach? ‘Pain points’ identified include how to: efficiently review a patient record; conduct focused but accurate histories and physical exams; and write good notes. The same participants then brainstormed creative solutions to this challenge. These insights and solution ideas are now being shared with the 2024–2025 clerkship cohort to assess relevance, and to determine which solutions are considered most feasible and desirable. Discussion: Novice clerks often feel unprepared for CTU responsibilities. This human-centered co-design process identified key learning gaps. Top student-prioritized ideas will now be prototyped and tested.

Virginia Guisandes Bueno

HLA Decision Study – the use of HLADQA1*05G>A-genetic screening for the selection of non-tumor necrosis factor-a antagonist (TNFA) advanced therapies in inflammatory bowel disease

Virginia Guisandes Bueno Aze Wilson

HLADQA1*05G>A genetic screening can identify tumor necrosis factor-α antagonist (TNFA) anti-drug antibody (ADA) risk as well as TNFA loss of response and discontinuation. We hypothesize that an additional use for HLADQA1*05G>A screening is guiding the selection of TNFA versus non-TNFA-based advanced inflammatory bowel disease (IBD) treatments. A prospective cohort study was conducted in IBD patients. Participants were divided into 2 cohorts: 1) those where therapy selection was based on physician preference (controls); 2) those where genetic screening was used to select the use of TNFA (wild type genotypes) versus non-TNFA therapy (variant genotypes) (screened cohort). Participants were assessed for clinical remission at 1-year, as well as other important clinical outcomes. To date, 48/400 participants are included (screened, n=26; controls, n=22). Genotype distribution in the screened cohort was 22 GG, 4 GA, 0 AA. TNFA therapy was most used in both groups (screened, N=22/26, 84.6%; controls, N=22/24, 91.7%). A similar frequency of clinical remission at 1-year was seen between screened participants versus controls (N=20/26, 77% versus 16/22, 72.7%, p=0.75). Screened participants reported fewer adverse events (N=7/26, 26% versus N=11/22, 58%, p=0.14), ADAs (N=0/26, 0% versus N=3/22, 13.6%, p=0.09) and drug discontinuation (N=4/26, 19% versus N=8/22, 36%, p=0.11). Similar frequencies of hospitalization, surgery and rescue glucocorticoid use were seen. HLADQA1*05 screening was associated with disease remission, treatment persistence and fewer adverse events when used to select TNFA versus non-TNFA therapy. With completion, we hope to confirm if an additional role for screening is guiding IBD drug selection.

Shyann Hang

Case series: PPARG mutations in individuals with hypertriglyceridemia and no clinical diagnosis of Familial Partial Lipodystrophy Type 3

Shyann Hang Zahra Taboun, Julieta Lazarte, Adam McIntyre, Amanda Berberich, Robert Hegele

Severe hypertriglyceridemia (HTG), defined biochemically as fasting plasma triglyceride (TG) concentration >10 mmol/L (> 885 mg/dL), affects ~1 in 400 adults in Ontario. Genetic predisposition to severe HTG or multifactorial chylomicronemia syndrome (MCS) in adulthood is complex and includes heterozygous pathogenic variants and polygenic predisposition from multiple common single nucleotide polymorphisms (SNPs). We recently identified a heterozygous peroxisome proliferator-activated receptor gamma (PPARG) pathogenic variant in a patient with severe pregnancy-associated HTG and pancreatitis. This led us to hypothesize that additional patients with severe HTG have undiagnosed familial partial lipodystrophy type 3 (FPLD3) due to PPARG loss-of-function variants. We tested this hypothesis in our MCS cohort. This single-centre, retrospective chart review included patients from the Lipid Genetics Clinic at London Health Sciences Centre, University Hospital (London, ON, Canada). Inclusion criteria comprised patients aged ≥18 with severe HTG defined as TG >10 mmol/L (>885 mg/dL). We excluded patients with clinically relevant mutations in other genes causing hypertriglyceridemia. Among 182 patients with MCS, 6 (1 woman and 5 men, mean age 50.3 ± 13.4 years) had heterozygous PPARG variants: p.Lys184fs, p.Glu217Lys, p.His453fs, p.Met284Ile, p.Ser383Arg, and p.Arg181Trp. None had been clinically recognized as having lipodystrophy. Metreleptin was recently approved by Health Canada for treatment of lipodystrophy patients, and without genetic testing this new therapeutic option would not be available for these patients. Clinicians should consider PPARG variants to diagnose FPLD3 when

genetically screening patients with severe HTG, alongside routine screening of the LPL gene and its four co-factors.

Fahad Hannan

Evaluating the Neuroprotective Effects of Caplacizumab in Immune-mediated Thrombotic Thrombocytopenic Purpura

Fahad Hannan Daniel Mendes, Lee Ting-Yim, Christopher J. Patriquin, Katerina Pavenski, Jonathan D. Thiessen, Susan HS. Huang

Despite modern treatments for immune-mediated thrombotic thrombocytopenic purpura (iTTP), patients often face increased risks of cerebrovascular disease, cognitive decline, and depression. Caplacizumab, which prevents platelet aggregation, has shown promise in iTTP treatment. This study examines whether Caplacizumab reduces brain tissue damage compared to standard of care (SOC) treatment. Thirteen iTTP patients, including six refractory to SOC, underwent MRI, contrast-enhanced CT perfusion scans, and cognitive/neuropsychiatric assessments at baseline, 30-days post-remission, and within one year. Blood-brain barrier (BBB) permeability, cerebral blood flow, and cognitive function were evaluated. BBB disruption was present in all patients. At baseline, the whole brain permeability surface (PS) product was 0.35 ± 0.09 mL/min/100g in the Caplacizumab group, higher than SOC (0.27 ± 0.10 mL/min/100g). Follow-up showed a significant reduction in the Caplacizumab group (0.24 ± 0.08 mL/min/100g, $p = 0.047$). Cognitive scores remained low, with white matter hyperintensities persisting across all patients. No significant changes were found in follow-up cognitive scores, but an inverse correlation with PS was observed across cognitive domains. Depression and concentration difficulties persisted. Caplacizumab may offer neuroprotective effects by reducing BBB permeability, but it does not appear to improve existing cognitive impairments. Further longitudinal studies are needed to confirm its long-term benefits, though these findings suggest Caplacizumab could be integrated into iTTP treatment to mitigate neurocognitive complications.

Fahad Hannan

Mapping Cognitive Decline in iTTP Survivors: A Diffusion Tensor Imaging Study

Fahad Hannan Stefan E. Poirier, Christopher J. Patriquin, Katerina Pavenski, Jonathan D. Thiessen, Susan HS. Huang

This study explores whether white matter damage in immune-mediated thrombotic thrombocytopenic purpura (iTTP) survivors contributes to cognitive decline. Despite advances in treatment, over 50% of iTTP survivors are at risk for cognitive impairments, with the underlying mechanisms poorly understood. We hypothesize that damage to key white matter tracts may be a significant factor in this decline. Using diffusion tensor imaging (DTI), we assessed 23 iTTP patients 30 days post-remission and 22 healthy controls. DTI metrics such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were measured across 25 regions of interest (ROIs). Cognitive performance was assessed using Cambridge Brain Sciences, focusing on reasoning, short-term memory, verbal ability, and concentration. iTTP survivors showed significant white matter abnormalities, with decreased FA in 15 of 25 ROIs, reflecting axonal degeneration or demyelination. Increased MD and RD were observed in 2 and 11 ROIs, respectively, suggesting possible inflammation or myelin damage. These alterations were particularly pronounced in tracts related to memory, such as the superior longitudinal fasciculus. Cognitive assessments revealed reduced scores in short-term memory and concentration, corresponding with observed DTI changes. These findings indicate that white matter damage in iTTP survivors, particularly axonal degeneration and demyelination, contributes to cognitive impairment. This study emphasizes the

need for long-term neurological follow-up, including routine neuroimaging and cognitive assessments, and highlights the potential for future research into neuroprotective interventions for iTTP survivors.

Shaun Hanycz

Patent Foramen Ovale leading to Platypnea Orthodeoxia Syndrome in a Patient with Normal Right Atrial Pressure

Shaun Hanycz Stuart Smith, Marilyn Phung

A Patent Foramen Ovale (PFO) is present in approximately 25% of the general population. It is usually of minimal consequence. However, occasionally during an acute illness, right-to-left shunting can occur through a PFO leading to platypnea orthodeoxia syndrome (POS). We present a case of an 86-year-old female with a past medical history significant for paroxysmal atrial fibrillation, hypertension, osteoporosis, thoracic kyphosis, and asthma. She presented to a tertiary care hospital with acute on chronic dyspnea initially attributed to atelectasis, with a negative CT pulmonary angiogram. Throughout her hospitalization her dyspnea progressed, with disproportionately increasing supplemental oxygen requirements including requiring high flow nasal cannula. When her supplemental oxygen fell off, she did not desaturate. Additionally, she was found to have orthodeoxia and platypnea, prompting a transthoracic echocardiogram bubble study to investigate for an intra-cardiac shunt. Her bubble study confirmed a large intra-cardiac shunt via a PFO and the anatomy was further delineated with a TEE. The PFO was closed percutaneously with complete resolution of her symptoms. This case highlights a systematic approach to a patient presenting with hypoxia. Shunts should be considered in the diagnostic approach to a patient with hypoxia, when they do not respond to initial management strategies with disproportionately increasing oxygen requirements. PFOs are usually of minimal consequence, but occasionally during an acute illness, horizontal displacement of the heart can result in preferential right-to-left shunting of blood leading to hypoxia. Following percutaneous closure of the PFO, the patient's hypoxia completely resolved.

Geneva Herold

Synovial myeloid subtypes in knee joint health, injury and osteoarthritis

Geneva Herold Garth Blackler, Holly Philpott, Frank Beier, Tom Appleton

Background: Chronic inflammation following knee injury can drive osteoarthritis (OA) and pain. Pathogenesis of knee OA is complex, with synovial myeloid cells playing a key but poorly understood role in sustaining inflammation (synovitis). Single-cell RNA sequencing (scRNA-seq) has been applied to OA but not healthy or injured knees, despite injury being a strong OA risk factor. This study integrates scRNA-seq datasets across these joint states to identify synovial myeloid subtypes and biological process (BP) enrichment in knee pathophysiology. Methods: Publicly available scRNA-seq datasets from healthy controls (n = 15), ACL reconstruction (ACLR) patients without synovitis (n = 4), and OA patients with synovitis (n = 8) were analyzed. Synovial cells underwent quality control and integration. Myeloid clusters (macrophages, dendritic cells, mast cells) were computationally subset and annotated. Differentially expressed genes (DEGs) were identified across conditions and analyzed for gene ontology (GO) enrichment. Results: Among 48,513 cells, nine myeloid subtypes were identified. S100A8+ macrophages dominated OA (42.2%) but were rare in healthy (0.4%) and ACLR (0.2%). CD163+ macrophages were most abundant in healthy (48.4%), lower in ACLR (17.5%), and absent in OA. Dendritic cells were proportionally higher in healthy (26.6%) and ACLR (31.9%) than OA (8.2%). DEG analysis identified 397 overlapping genes across joint states. GO analysis revealed immune remodeling, inflammation, neurovascular remodeling, apoptosis, and autophagy enrichment, with TGF-beta signaling and wound

healing unique to OA. Conclusion: Synovial myeloid subtypes and processes differ across joint states and may serve as therapeutic targets for preventing post-injury OA, addressing an unmet clinical need.

Abdurahman Ibrahim

Patient Oriented Wellbeing Program Implementation In Survivors Of Allogeneic Stem Cell Transplant

Syed I. Mir Xavier S. Borsato, Abdurahman Ibrahim, Sulaf Elkhalifa, Jennifer He, Christina Lim, Jennifer Elliot, Adrienne Fulford, Uday Deotare

Background: Long term survivors of Allogeneic Hematopoietic Cell Transplant (Allo-HCT) are at elevated risk for decreased physical well-being (PWB). This reduced PWB decreases quality of life and increases healthcare burden. One validated scale, Functional Assessment of Cancer Therapy – Bone Marrow Transplant (FACT-BMT) (v.4, 2013), evaluates the long-term well-being of Allo-HCT patients with different subscales namely, physical, social/ family, emotional and functional wellbeing. Aim/Objective: Our quality improvement project aimed to improve the PWB of patients by an average of 3.5 points as measured by the FACT-BMT scale by implementing a physical therapy program by May 1, 2025. Methods: Baseline data and subsequent Ishikawa Fishbone Diagram of 71 patients revealed four main factors of reduced PWB including fatigue, pain, body image and sexual dissatisfaction. For the First PDSA from Mar 2024, we distributed a walking-based physical activity pamphlet to improve PWB. Three-months post implementation, FACT-BMT scores and a statement of subjective adherence were obtained. Results: Analysis of FACT-BMT scores post PDSA cycle 1, revealed a worsening of PWB scores by 8-points. We hypothesize there may be substantial skew due to sample size constraints and patient non-adherence. Conclusions and Lessons Learned: Although PDSA 1 cycle had limitations, it suggests passive interventions do not sustainably impact patient PWB. Accordingly, our second PDSA (started in Jan 2025) utilizes a one-on-one Physiotherapy session to improve PWB scores more actively.

Faramarz Jabbari-Zadeh

Evaluating the role of Thrombopoietin Receptor Agonists in the Treatment of Acquired Amegakaryocytic Thrombocytopenia: A Case Report and Review of the Literature

Faramarz Jabbari-Zadeh Mujtaba M. Basharat, Benjamin Chin-Yee, Chai W. Phua, Selay Lam, Anargyros Xenocostas, Eric To, Cyrus C. Hsia

Background Acquired 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 fifteen 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. Methods We conducted a case report along with a review of the literature. The case report examined a patient who was diagnosed with AAMT at London Health Sciences Centre and treated with eltrombopag, which is a TPO-RA. Our review of the literature focused on analyzing the fifteen other aforementioned cases. Results Our patient ultimately had an increase in platelets to 115 x109/L fifteen months after treatment with eltrombopag 150mg once daily (later tapered to 50mg)compared to a nadir of 18 x109/L prior. He did not have any adverse drug effects, including no bleeding, thrombosis, or cytopenias. He did not require any platelet transfusions. Our literature review demonstrated several findings, including the efficacy of eltrombopag, the efficacy of other TPO-RAs (such as avatrombopag), the synergistic effects that TPO-RAs can have when combined with other medications (such as cyclosporine), and the link between AAMT and aplastic anemia. Discussion Including our case, there are sixteen cases of AAMT treated with TPO-RAs, which highlight the variability in the management of AAMT.

Our case demonstrates that TPO-RAs can be effective novel therapeutic agents and improve patient outcomes for this rare condition.

Vinay Jayachandiran

Defining Essential and Extraneous: Consensus-Based Marking Schemes to Assess Competency Using Free-Text Echocardiogram Reports

Vinay Jayachandiran Aws Almufleh, Nicolas Thibodeau-Jarry, Parvathy Nair, Sarah Blissett

Free text summary statements of transthoracic echocardiography (TTE) reports are the most accurate tool to assess competency of TTE interpretation. The inherent variability in how free-text summaries are composed by trainees and experts creates challenges for developing marking schemes. This study aims to develop robust, consensus-based marking schemes for TTE summary statements. Methods A Modified Delphi approach with two rounds of surveys and a consensus finalizing meeting was used to establish items that should be included in the summary statement and items critical to fulfill competency. Items related to cardiac structures in general, and in specific indications (e.g. hypertrophic cardiomyopathy). We used >80% agreement to define consensus. Results Twenty-seven Canadian echocardiography experts provided ratings on the surveys. Eleven experts participated in the consensus finalizing meeting. Through this process, we established 79 items that should be included in the summary statement. Five general items (left ventricular (LV) size, LV systolic function, right ventricular (RV) size and RV function, and a statement about valves) should be included in all summary statements. The remaining 74 items should be included in specific indications or if there is abnormality related to the item. Eighteen items were critical for competency. Only LV systolic function was critical to fulfill competency in all summary statements, with the remaining 17 items critical in specific indications. Conclusion Our findings inform robust, consensus-based marking schemes for free-text TTE summary statements. When integrated into novel assessment platforms, our findings will improve competency assessments of TTE for Canadian Cardiology trainees.

Will Jeong

Transposable Element-Driven Viral Mimicry as a Potential Defense Against Colitis-Associated Colon Cancer

Will Jeong Frederikke Larsen, Parisa Shooshtari, Samuel Asfaha

Colon cancer remains one of the leading causes of cancer-related morbidity worldwide. However, its gradual progression provides opportunities for prevention, particularly in high-risk populations such as those with inflammatory bowel disease (IBD). Recent evidence suggests that transposable elements (TEs) can re-express under inflammatory conditions like IBD, triggering a protective antiviral or “viral mimicry” response that may mitigate malignant transformation in these otherwise tumorigenic environments. We analyzed two publicly available human IBD RNA biopsy datasets: one comparing active IBD to healthy controls and another comparing non-dysplastic IBD to IBD-associated dysplasia. Using a standard HISAT2 pipeline, we aligned reads to a standard reference genome without discarding repetitive elements. We then performed differential expression and GO enrichment analyses to evaluate TE transcripts and viral mimicry-related interferon responses across disease states. Elevated TE expression and antiviral gene signatures were detected in active IBD relative to healthy controls, mirroring murine colitis findings. In contrast, IBD-associated dysplasia samples exhibited markedly reduced TE levels and diminished interferon-related pathways. Pathway enrichment confirmed that antiviral signaling was specifically suppressed in dysplastic lesions, suggesting that loss of viral mimicry could facilitate malignant progression in chronically inflamed colonic epithelium. These findings support the concept that viral mimicry via TE re-expression may serve as an endogenous defense against neoplastic transformation in inflamed colonic environments. The observed suppression of this mechanism in

dysplastic lesions highlights a potential driver in IBD-related oncogenesis. Further elucidation of TE-driven antiviral responses in human IBD could yield novel prophylactic or therapeutic strategies for colitis-associated colorectal cancer.

Hanyu Jiang

Lysophosphatidylcholine and microvascular dysfunction in knee osteoarthritis

Hanyu Jiang Tom Appleton

Background: Nutrient delivery via the synovial microvasculature is crucial for joint health. Histological features of synovial microvascular dysfunction (MVD) are linked to knee osteoarthritis (OA) pain, but underlying mechanisms remain unclear. Lysophosphatidylcholine (LPC) and its metabolite lysophosphatidic acid (LPA) regulate angiogenesis and vascular maturity, yet chronic activation may contribute to MVD. Elevated synovial fluid (SF) LPC and LPA levels in OA suggest their role in synovial microvascular changes. However, the association of MVD with pain and the role of LPC-LPA-LPA receptor (LPAR) signaling in synovial MVD remain poorly understood. Methods: (A1) Histological analysis of synovial biopsies from knee OA patients (n=146) quantified MVD features—microvessel perfusion distance, vessel diameter, and wall thickness—correlating them with pain via multivariate regression. (A2) Single-cell RNA sequencing (scRNAseq) identified autotaxin (ATX) and LPAR expression in OA synovium, validated via immunofluorescence. Human microvascular endothelial cells (HMEC-1) were exposed to OA SF with or without an LPAR6 inhibitor, assessing activation and angiogenesis in vitro. Results: Increased microvessel perfusion distance, vessel size, and wall thickness correlated with pain. scRNAseq and immunofluorescence showed high ATX and LPAR6 expression in perivascular fibroblasts and endothelial cells. OA SF expedited scratch closure and tubule formation, but tubules disintegrated rapidly. LPAR6 inhibition slowed scratch closure but improved tubule formation and stability. Conclusion: LPA-LPAR6 signaling may be critical for angiogenesis, but chronic activation likely promotes MVD, strongly associated with OA pain.

Mahmoud Riyam Jouid

Safety, Tolerability and Efficacy of GLP-1 Receptor Agonists (GLP1-RA) in the Management of Post-Liver Transplant Weight Gain: A Multi-Centre, Observational Study

Mahmoud Riyam Jouid Gopika Punchhi, Amani Bajunayd , Arpana Kumari Wadhwani, Rokhsana Mortuza, Mohammad Qasim Khan

Background: Post-liver transplant weight gain increases the risk of diabetes, kidney dysfunction, malignancy, and major adverse cardiovascular events. GLP-1 receptor agonists (GLP-1 RAs) can mitigate weight gain and improve liver transplant recipients (LTRs) outcomes. Purpose: This study evaluated the safety, tolerability, and efficacy of GLP-1 RAs in managing weight gain in LTRs. Methods: This retrospective cohort study analyzed adult patients who underwent successful primary liver transplants between January 1, 2010, and December 31, 2021. Exclusion criteria included severe allograft dysfunction, previous bariatric procedures, or concurrent weight loss pharmacotherapies. Regular GLP-1 RA use (≥ two refills with no gaps in supply > 30 days) post-transplant was the exposure of interest. The primary outcome was body weight and weight change at 1-year post-exposure to GLP-1 RA or equivalent time points for controls matched by age, sex, BMI, diabetes status, and transplant year. Secondary outcomes included glycemic and lipid profile changes, major adverse cardiovascular events (MACE), and allograft function. Results: A total of 104 patients were analyzed. Thirty-seven used GLP-1 RAs post-liver transplant. Mean weight loss was similar (-2.77 kg vs. -2.01 kg) between users and non-users, but GLP-1 RA users showed a trend towards greater weight loss. GLP-1 RA users improved HbA1c levels and kidney function more than non-users. Both groups improved lipid profiles. GLP-1 RA

use was safe and didn't worsen liver enzymes or allograft function in LTRs. Conclusion: GLP-1 RAs appear safe in liver transplant recipients. They improve glycemic profiles, preserve kidney function, and may lead to weight loss.

Jaspreet Kaur

Novel Peptide Immunotherapy Reduces Joint Swelling and Pain in an Animal Model of Rheumatoid Arthritis

Jaspreet Kaur Ewa Cairns, Lillian Barra

Introduction: Rheumatoid arthritis (RA) is an autoimmune disease caused by a breakdown of immune tolerance against citrullinated and homocitrullinated peptides (CitP and HomoCitP), resulting in joint pain, swelling, and damage. Our lab has developed a novel peptide immunotherapy that aims to restore tolerance to CitP and HomoCitP. We hypothesize our peptide treatment will prevent disease progression in the collagen-induced arthritis (CIA) mouse model of RA. Methodology: CIA mice received either CitP + HomoCitP peptide cream or mock cream treatment (N=7 for each) on days 4, 5, 6 and 18 post swelling onset. Joint pathology was assessed by calipers, von Frey pain testing, microCT, histopathology, and immunofluorescence microscopy. T cell proliferation was measured using flow cytometry and serum antibodies via ELISAs. Results: Peptide-treated mice had significantly lower arthritic swelling scores compared to mock-treated mice ($p = 0.0123$). Swelling decreased by day 14 post swelling onset in the peptide treatment group and was significantly lower than the mock treatment group by day 24 post swelling onset ($p = 0.0050$). Peptide vs. mock treatment significantly reduced pain responses in hind limbs ($p = 0.0217$). Average pain responses in peptide-treated mice were lower at days 7 and 24 post swelling onset compared to mock-treated mice. Treatment did not affect splenic T cell proliferation, nor serum anti-collagen IgG and anti-CitP IgG at day 24 post swelling onset. Conclusions: Our peptide immunotherapy may reduce pain and swelling in a pre-clinical animal model, providing support for testing this treatment in future RA clinical trials.

Simranjit Kaur

Using Quality Improvement Methodology to Enhance Enrolment in the Obesity Management for Kidney TRANSPLANTation trial: (OK-TRANSPLANT2)

Simranjit Kaur & Charlotte Adams Kristin Clemens, Duncan Birkinshaw, Tsan-Hua Tung, Heather Lapier, Leila Amirfakhrian, Louise Moist

Background: Randomized controlled trials (RCTs) focused upon weight loss interventions in participants with chronic kidney disease (CKD) face challenges with low recruitment. OK-TRANSPLANT2 (OKT-2) is the vanguard phase of a pragmatic, parallel armed RCT embedded in routine care. The RCT will study the effectiveness of individualized weight loss programs vs. standard of care in individuals with high-risk CKD including dialysis. Methods: We conducted an environmental scan of the literature on RCT recruitment barriers in chronic disease. Then, alongside stakeholders, we identified potential root causes of suboptimal recruitment in the OKT-2 RCT and quantified most frequent causes using Pareto charts. Since September 2024, we have executed iterative tests of change (i.e. recruitment strategies), refined through a Plan-Do-Study-Act (PDSA) cycle. An SPC chart has been used to monitor the impact of tests of change on trial recruitment. The adaptive process has ensured data-driven improvement in participant enrolment. Results: In our literature review, we learned the importance of using patient-centred methods to design our trial and recruit participants. Of the root causes for suboptimal recruitment identified by our stakeholders, narrow inclusion criteria and limited recruitment processes emerged as the most critical and frequent recruitment challenges. Our team has since implemented a broad, inclusive recruitment strategy (online, in-person recruitment from multi-care kidney clinics through to hemodialysis centres). We have

also identified and addressed newly identified barriers (e.g. paper consent forms). Conclusions: Early identification of recruitment barriers and the implementation of PDSA cycles have provided valuable insights to inform broader recruitment for OKT-2.

Seung Kim

A spatial transcriptomic atlas of fibrosing interstitial lung diseases

Seung Kim Elissa Woo, Leah McDonald, Matthew J. Cecchini, Marco Mura

Rationale: Fibrosing interstitial lung diseases (ILDs), including idiopathic pulmonary fibrosis (IPF), non-specific interstitial pneumonia (NSIP), and chronic hypersensitivity pneumonitis (CHP), are characterized by progressive lung scarring. While single-cell RNA-seq (scRNA-seq) has advanced our understanding of the cellular landscape in lung diseases, a comprehensive spatial map of these conditions is lacking. This study aims to create a spatial transcriptomic atlas for fibrosing ILDs. Methods: We used formalin-fixed, paraffin-embedded lung biopsies from treatment-naïve patients with IPF (n=10), NSIP (n=8), CHP (n=10), and unclassified ILDs (n=17). Spatial transcriptomics was performed using the Visium platform (10X Genomics) to capture a 6.5mm x 6.5mm area. Quality control was followed by integrating scRNA-seq data from the Integrated Human Lung Atlas and mapping cell type proportions using “cell2location.” Non-negative matrix factorization (NMF) and ‘scanpy’ were used to identify co-localizing cell types and differentially expressed genes. Results: Cell type mapping was consistent with histological findings, identifying marker genes for each cell type. Specific genes (DDIT4, TSC22D3, SFTPC, TIMP1, TAGLN) were strongly associated with fibroblasts in IPF, CHP, and NSIP. While no specific cell types were enriched in a particular ILD subtype, NMF revealed distinct co-localization patterns, notably in CHP, where AT1 and AT2 cells formed separate clusters—unlike in IPF and NSIP. Conclusion: This study provides the first large-scale spatial transcriptomic atlas of fibrosing ILDs, integrating scRNA-seq to predict cell type proportions in spatial contexts. Further analysis will focus on algorithm development and correlation with clinical outcomes.

Merit Kirolos

Green Inhaler Use in CTU

Merit Kirolos Constance Mackenzie Acknowledgement: Special thanks to Yassmin Behzadian, Mike Apostol, and Victoria Forbes who provided materials used in this project.

Background: Inhalers, including metered-dose inhalers (MDIs), dry powder inhalers (DPIs), and soft-mist inhalers (SMIs), vary in their environmental impact. MDIs, in particular, have been shown to contribute significantly to greenhouse gas emissions without providing additional health benefits over alternatives. Despite this, MDIs remain the most commonly prescribed inhaler type at LHSC, highlighting the need for educational initiatives to promote environmentally friendly alternatives. Goal: This project aimed to educate residents rotating through the CTU about the environmental impact of different inhalers, with the goal of reducing the proportion of MDIs prescribed by at least 5%. Activities: Baseline data was collected from October to December 2023. Key interventions included monthly educational presentations during CTU morning reports, collaboration with CTU pharmacists, and the display of inhaler education posters in team rooms. The project ran from October 2024 to February 2025, with current data reflecting the period from October to December 2024. Impact: Baseline data indicated that MDIs comprised 53% of prescriptions within LHSC CTU teams in 2023. After implementing the interventions, MDI prescriptions decreased to 50%. Lessons Learned: Although a 3% reduction in MDI prescribing was achieved, the 5% target was not met. Factors contributing to this shortfall included suboptimal resident attendance at educational sessions. Additionally, the most frequently prescribed MDI, salbutamol, lacks a suitable alternative at LHSC, with the nebulized version being the only option. Future efforts could involve

collaboration with formulary stakeholders to introduce alternatives, such as the ventolin diskus or Bricanyl, which are more environmentally friendly.

Merit Kirolos

Cracking the code: Aligning Physician Assessment with Hospital Coding in Pneumonia

Merit Kirolos Cavizsh Skanthan, Erin Spicer,Radha Joseph, Kelly MacIsaac, Stephanie Handsor, Danny Kim, Kathryn Myers

BACKGROUND: Diagnostic coding accuracy is essential for data integrity, benchmarking outcomes, quality assurance and reimbursement. Assignment of the most responsible diagnosis (MRDx) by hospital coders relies on documentation by physicians, coder expertise, and coding algorithms. Data from fiscal year 2024-2025 thus far shows that 471 of 606 discharges (78%) with an MRDx of pneumonia were coded as pneumonia unspecified, with only a minority assigned bacterial, viral or aspiration pneumonia codes. OBJECTIVE: This study aims to identify discrepancies in the coding of “pneumonia unspecified” as the discharge MRDx, as assessed by three groups of reviewers: hospital coders, resident physicians, and Decision Support (DS). METHODS: Patients discharged with a MRDx of “pneumonia unspecified” were identified by DS. Independent chart reviews for accuracy of the MRDx were performed by two senior coders (following established coding algorithms) and by two resident physicians (using clinical definitions developed by content experts). DS used NLP algorithms to assess MRDx. Agreement between the original MRDx and the chart reviews were analyzed using descriptive statistics. RESULTS: Of 471 charts reviewed, hospital coders agreed with the original MRDx “pneumonia unspecified” in 80% of cases. Conversely, physician reviewers assigned a diagnosis of either bacterial or viral pneumonia in 100% of the initial 101 cases reviewed. Analysis of NLP data will be available at the time of the presentation. CONCLUSIONS: We found substantial discrepancy in application of pneumonia codes, with physician reviewers assigning more specific causes of pneumonia. Future efforts will identify root causes and develop change ideas to improve coding accuracy.

Victoria Labuda

Whole Blood Immune Profiling Uncovers Differential Immune Responses to Endotoxins in Non-septic and Septic Critically Ill Patients

Victoria Labuda Michelle Si, Ayana De Silva, Josephine Liu, Gemma Barber, Kerry-Ann Nakrieko, Mark Chandy, Aleksandra Leligdowicz

Sepsis is a “dysregulated” immune response to infection, but what constitutes a “regulated” immune response remains unclear. One feature of the dysregulated immune response is a reduced ex vivo response to Gram-negative endotoxin (LPS). However, ex vivo immune responses to endotoxins are poorly characterized. It is unknown which immune cells contribute to the response and whether this is conserved across Gram-positive endotoxin (LTA). Whole blood was collected from non-septic (n=21;NS) and septic (n=17;S) critically ill patients and healthy controls (n=10;HC). Blood was incubated for 4 hours at 37°C alone, with LPS, or LTA. High-dimensional flow cytometry assessed leukocyte composition and phenotype. Clusters representing the 5 major leukocyte populations (granulocytes, monocytes, T cells, B cells, NK cells) were identified by lineage marker expression and interrogated for activation marker expression of HLA-DR and CD69. Intracellular cytokine staining for TNF-α assessed ex vivo responses to LPS and LTA. Clustering revealed an increased proportion of granulocytes in NS and S patients, and a decreased proportion of all 4 other leukocyte populations. Critically ill patients exhibited reduced HLA-DR expression on monocytes, suggesting an immunosuppressed state. TNF-α production was preserved and dominated by monocytes in HC, but impaired and dominated by granulocytes in NS and S patients. NS and S patients display an immunosuppressive phenotype and defective ex vivo responses to endotoxins.

Immune responses are monocyte-skewed in health and granulocyte-skewed in critical illness. These findings further our understanding of immune dysregulation and could improve our approach to immunomodulatory therapies in critical illness.

Matthew Laird

Evaluating Weaning Strategies from Mechanical Ventilation in Tracheostomized Adult Patients: A Systematic Review

Matthew Laird James Stevenson, Neciula de Paula Carneiro Porto Gomes, Ron Butler, Alla Iansavitchene, Paul Cameron, Karen J. Bosma

Purpose: This study aims to systematically review and evaluate weaning strategies for tracheostomized adults experiencing prolonged mechanical ventilation, with the goal of identifying effective approaches. Background/Objectives: A significant knowledge gap exists regarding effective weaning strategies for tracheostomized adults on invasive mechanical ventilation. Variations in practice across patient populations, healthcare settings, and multidisciplinary teams create an opportunity to identify optimal strategies Methods: We conducted a systematic review of studies involving adults (≥18 years) with tracheostomy requiring prolonged mechanical ventilation (> 21 days). Following PRISMA guidelines, we performed a systematic literature search in MEDLINE, EMBASE, CENTRAL, CINAHL, Scopus, and PEDro without language exclusions up to December 2023. Abstracts and full texts were screened in duplicate and data extraction was completed in duplicate. The primary outcome was weaning success, defined by proportion of successfully weaned patients, the duration of weaning, and/or ventilator-free days. Secondary outcomes encompass mechanical ventilation duration, tracheostomy decannulation, ICU and hospital length of stay, hospital mortality, post-hospital survival rates, and physiologic and psychologic endpoints. Results: Of 2118 identified studies, 55 studies were included. Preliminary findings suggest successful weaning is associated with a multi-disciplinary team approach, trach collar trials of increasing duration, and inspiratory muscle training. Additionally, the use of in-line speaking valves resulted in improved lung recruitment. Other key insights include that Neurally Adjusted Ventilatory Assist (NAVA) may lead to shorter weaning durations compared to Pressure Support Ventilation (PSV). Conclusions: Ultimately, this review will contribute to the development of optimal weaning strategies for patients with prolonged mechanical ventilation.

Frederikke Larsen

p53 suppresses transposable elements in colitis-associated cancer

Frederikke Larsen Alice Shin, Mathieu Derouet, Liyue Zhang, Samuel Asfaha

Introduction: Colorectal cancer is the second leading cause of cancer death with a major risk factor being chronic inflammation. Interestingly, colitis-associated cancer (CAC) is often associated with TP53 mutations. However, acute p53 loss has been shown to induce expression of transposable elements (TEs), endogenous viral elements in our genome. Expression of TEs activates a type-I interferon response through the cGAS/STING and MDA5/MAVS pathways, a response known as viral mimicry. Thus, we hypothesize that p53 loss induces viral mimicry to inhibit CAC initiation. We previously described a CAC model in which tumors arise from Dclk1+ cells following APC loss and colitis. In this study, we used this model to examine the role of p53 in CAC. Methods: Dclk1/Apcf/f and Dclk1/Apcf/f/Trp53f/f mice were administered tamoxifen followed by dextran sodium sulfate to induce CAC. Fourteen weeks later, we assessed tumor number. RNA expression of TEs and type-I interferon genes was measured as a readout of viral mimicry. Lastly, we inhibited the viral mimicry response by crossing Dclk1/Apcf/f/Trp53f/f mice to mitochondrial antiviral sensing protein (MAVS) knockout mice or by inhibiting cGAS. We examined the effects of viral mimicry inhibition on tumor number and Dclk1+ cell

stemness. Results: p53 loss inhibited colonic tumorigenesis and stemness of Dclk1+ cells. Furthermore, p53 loss increased the expression of TEs and type-I interferon response genes. Knockout of MAVS or cGAS inhibition reversed the effects of p53 loss on tumorigenesis and Dclk1+ cell stemness. Discussion: Our findings demonstrate that p53 loss inhibits CAC initiation through activation of viral mimicry.

Benson Law

The Use of Recombinant Factor VIIa in the Management of Adult Traumatic Hemorrhage: A Systematic Review

Benson Law Melissa Cote, Shane Smith, Richard Hilsden, Kelly Vogt, Fran Priestap, Alla Iansacitchene, Ian Ball

Used initially to manage hemophiliac patients with Factor FIII or Factor IX deficiency, Recombinant Factor VIIa's (rFVIIa) off-label use as a salvage therapy has proliferated in recent decades to include massive hemorrhage control in surgery and trauma. More than 75% of US Level 1 trauma centers have recommended the use of Recombinant Factor VIIa in their massive transfusion protocol. Some theorized benefits of using rFVIIa include reduced mortality and blood product use. However, given rFVIIa's potent coagulation properties, there have been concerns regarding thromboembolic complications. This systematic review aimed to evaluate the existing evidence to determine rFVIIa's role in the management of acute traumatic hemorrhage. In total, 1512 titles/abstracts and 133 full-text articles were screened, of which 18 were subject to data extraction. The results suggest that rFVIIa yields no mortality benefit at the 24-hour, 48-hour, or 30-day time point. rFVIIa reduces the need for packed red blood cell (RBCs) transfusions, although it does not reduce the use of other types of blood products. Regarding adverse events, there appears to be no increased risk for thromboembolic complications when using rFVIIa. Given its high cost, rFVIIa should likely not be routinely administered in settings where PRBCs are routinely available. There may be a role for rFVIIa in military settings and rural hospitals where blood availability is limited, and surgery may be delayed.

Sangmin Lee

Update on Employment Status Post-Liver Transplant: United Network for Organ Sharing Database

Sangmin Lee Qasim Khan

Background: Liver transplantation significantly improves survival in individuals with acute liver failure or end-stage liver disease. However, post-transplantation employment remains critical to quality of life and rehabilitation. Previous studies have shown that low post-transplant employment rates significantly decline compared to pre-transplant employment levels. The shift in liver transplant indications, such as metabolic-associated steatohepatitis (MASH) and alcohol liver disease (ALD), may introduce additional psychosocial factors impacting employment. Understanding employment patterns post-transplant is crucial to improving the overall quality of life post-liver transplant. Objectives: 1) To determine the prevalence of employment within 12 months and 24 months after liver transplantation between 2009 and 2019; 2) To evaluate the factors associated with post-transplant employment status, including age, race, sex, BMI, comorbidities, pre-transplant employment, education, and indication for liver transplant. Methods: Data will be extracted from the United Network for Organ Sharing (UNOS) database for individuals aged 18-60 who underwent first-time liver transplantation from 2002 to 2019. Post-transplant employment status at 12 and 24 months will be determined, with factors influencing employment assessed through univariate analyses with the Mann-Whitney U test for continuous variables and chi-square analysis for categorical variables. A significance level of 0.05 will be set a priori. Results: To be determined. Conclusion: The findings from this study will provide an updated prevalence of unemployment rates post-liver transplant and significant factors associated with unemployment. These

findings will highlight the need for targeted rehabilitation strategies to improve post-transplant employment outcomes, subsequently improving the quality of life in liver transplant recipients.

Jessica Liu

Diagnosis, management, and outcomes of hypoxia-induced erythrocytosis: A systematic review

Jessica Liu Sara Sadeghi, Benjamin Chin-Yee, Jenny Ho, Sanjay Mehta, Alla Iansavitchene, Cyrus C. Hsia

Background: Secondary erythrocytosis 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. Chronic hypoxia is one of the most common causes of secondary erythrocytosis. Frequently implicated conditions include chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), and smoking. Current guidelines on the diagnosis and management of hypoxia-induced erythrocytosis are limited, and the risks of thromboembolism, bleeding, and mortality in this condition are not well described. We therefore conducted a systematic review to inform the clinical management of hypoxia-induced erythrocytosis. Methods: Following PRISMA guidelines, we performed a systematic literature search in MEDLINE, EMBASE, CENTRAL (all via Ovid), and Google Scholar. We included patients aged 18 years and older and studies published from 2005, the year of JAK2 discovery, to February 2025. We excluded case reports and case series with fewer than 5 patients. Two reviewers independently screened the studies, with disagreements resolved by a third party. Data was extracted on variables pertaining to hypoxia-induced erythrocytosis and will be synthesized using descriptive analysis. (PROSPERO CRD42024508643) Results: Our systematic search identified 2,233 studies for screening. Sixty-two studies were included, with 21 studies on COPD, 18 studies on OSA, 10 studies on smoking, and 13 studies on other causes of hypoxia. Results are currently pending. Conclusion: Hypoxia-induced erythrocytosis is a heterogeneous condition for which there is no clear consensus about the diagnosis and management. Pending the results of this systematic review, full conclusions will be drawn.

Qi Liu

Tumor cell-derived SerpinA3 protects cardiomyocytes against doxorubicin-induced injury

Qi Liu Meggie Vo, Xiaoyun Ji, Morgan Black, Dongmei Sun, Elena Tsvetkova, Tianqing Peng

Doxorubicin is a widely used chemotherapeutic agent for many solid malignant tumors, but its clinical application is limited due to its dose-dependent cardiotoxicity. However, the pathogenesis of doxorubicin-induced cardiotoxicity remains incompletely understood; specific therapeutic approaches are limited; and there is a lack of reliable biomarkers to predict doxorubicin-induced cardiotoxicity. Recent studies have indicated a bidirectional crosstalk between the heart and tumors, where tumors can influence cardiac disease, and conversely, cardiac disease can promote tumor progression. Since SerpinA3 has been implicated in tumor progression and cardiac disease, this study investigated the role of tumor cell-derived SerpinA3 in doxorubicin-induced cardiotoxicity. We report that doxorubicin treatment induced a robust SerpinA3 expression in breast cancer cells whereas moderately increased SerpinA3 in human endothelial cells and cardiomyocytes. Ectopic expression of SerpinA3 reduced doxorubicin-induced injury in cardiomyocytes. Incubation with culture medium from doxorubicin-treated breast cancer cells attenuated cell injury in doxorubicin-stimulated cardiomyocytes; however, the protective effect of culture medium was abrogated when SerpinA3 was knocked down in breast cancer cells. In patients with breast cancer, chemotherapy containing doxorubicin increased serum SerpinA3 levels. Incubation with patient's serum post chemotherapy reduced doxorubicin-induced injury in cardiomyocytes as compared to patient's serum before chemotherapy. Lastly, over-expression of SerpinA3 mitigated myocardial injury and improved myocardial function in a mouse model of doxorubicin-induced cardiotoxicity. In conclusion, tumor cell-

derived SerpinA3 provides cardioprotective effects in doxorubicin-induced cardiotoxicity. This study also suggests that SerpinA3 may serve as a potential biomarker to predict doxorubicin containing chemotherapy-induced cardiac injury, which merits further investigation.

Paramveer Love

Genistein in transthyretin receptor amyloid cardiomyopathy (GASPAR)

Paramveer Love Grace Adetunde, Kerry-Ann Nakrieko, Michelle Si, Ryan Davey, Sabe De, Mark Chandy

Background: Transthyretin amyloid cardiomyopathy (ATTR-CM) and heart failure with reduced ejection fraction (HFrEF) are associated with inflammation, oxidative stress, and impaired cardiac function. Current treatments focus on symptom management but do not fully address the underlying inflammatory and metabolic derangements. Genistein, a soy-derived isoflavone, has demonstrated anti-inflammatory, antioxidant, and transthyretin-stabilizing properties. This study evaluates the safety and therapeutic potential of genistein in patients with ATTR-CM and HFrEF. Methods: This Phase 1b/2a open-label study will enroll 40 patients aged 40-80 with ATTR-CM or HFrEF. Participants receive escalating oral doses of genistein (250 mg twice daily for 4 weeks, 500 mg twice daily for 4 weeks, and 750 mg for 4 weeks), followed by a 6-week washout period. The primary endpoint is the change in inflammatory markers (IL-6, TNF-α, hsCRP, NT-proBNP) from baseline to 3 months, along with an assessment of safety and tolerability. Secondary endpoints include changes in cardiac function (as assessed by echocardiography) and exercise capacity (as measured by the 6-minute walk test). Exploratory outcomes assess alterations in the microbiome and changes in proteomic biomarkers. Results and Conclusion: This study will provide critical insights into the safety of genistein in heart failure, as well as its potential role in reducing inflammation, stabilizing transthyretin, and improving cardiac function. If successful, these findings may support future larger-scale trials investigating genistein as an adjunct therapy for heart failure and ATTR-CM.

Haitao LU

ADAR1 and RIPK1 orchestrate the ZBP1-RIPK3 complex-mediated PANoptosis and heart transplant rejection

Haitao lu Jifu Jiang, Xuyan Huang, Aaron Haig, Anthony M. Jevnikar, Lakshman Gunaratman, Zhu-Xu Zhang

Background: PANoptosis is a unique form of programmed cell death regulated by a cytoplasmic PANoptosome. The roles of ADAR1 and RIPK1 in orchestrating the ZBP1-RIPK3 complex to mediate PANoptosis are not fully understood, particularly in the context of heart transplantation.This study investigated the mechanism mediating PANoptosis and its implications in mouse heart transplantation. Methods: We employed co-immunoprecipitation, western blotting, and siRNA to elucidate the dynamics of the interactions between ADAR1, RIPK1, ZBP1, and RIPK3. Additionally, we assessed the impact of ZBP1 on mouse heart transplantation. Results: Our studies revealed that ADAR1 and RIPK1 collaboratively regulate the ZBP1-RIPK3 complex for PANoptosis in a time-dependent manner. The interaction of ADAR1 with ZBP1 protected against Z-DNA-induced cell death by limiting the activation of ZBP1 and RIPK3 at an early stage of cell death. As well, RIPK1 regulated ZBP1-RIPK3 interaction. The sustained interaction of ZBP1-RIPK3 mediated PANoptosis at a late-time stage. Our in vivo studies showed that the expression of ZBP1 and its ligand Z-DNA/Z-RNA were significantly increased in mouse heart grafts post-transplantation. Importantly, ZBP1 deficiency in the heart graft inhibited cardiac PANoptosis, attenuated acute graft injury, and induced long-term graft survival. Conclusions: This study elucidates the roles of ADAR1 and RIPK1 in orchestrating the ZBP1-RIPK3 complex and PANoptosis. Inhibition of ZBP1 can prevent heart graft injury and rejection. Understanding these mechanisms provides

valuable insights into the regulation of cell death in transplanted organs and may inform the development of novel therapeutic strategies targeting programmed cell death pathways to improve outcomes.

Christine Luu

Posterior reversible encephalopathy syndrome as a complication of cytarabine in acute myeloid leukemia

Christine Luu Jane Lin, Anargyros Xenocostas, Maria Macdonald, Andrew Leung

A 54-year-old male with a history of well controlled juvenile myoclonus epilepsy was diagnosed with acute myeloid leukemia (AML). He underwent induction therapy with cytarabine, daunorubicin, and gemtuzumab ozogamicin (GO). This was complicated by neutropenia and fungal pneumonia. Two days after consolidation chemotherapy, the patient developed an episode of tonic-clonic seizures, but MRI was negative for acute structural changes. The event was attributed to his generalized tonic-clonic seizure disorder triggered by sleep deprivation and stress. One month later, the patient was admitted to the hospital for headaches, hypertension, confusion, and multiple episodes of tonic-clonic seizures. MRI showed T2 FLAIR white matter hyperintensities in the parieto-occipital lobes, bilateral frontal lobes, and bilateral cerebellar hemispheres. With prompt supportive medical treatment, the patient returned to his neurological baseline within five days and repeat MRI three weeks later showed significant interval improvement. This case demonstrated delayed onset posterior reversible encephalopathy syndrome (PRES) post-cytarabine therapy. The rapid development and resolution of clinicoradiological features were characteristic of PRES. Risk factors such as underlying seizure disorders may predispose patients to PRES and there is increased evidence of PRES as a potential complication of cytarabine. This rare side-effect should be considered in the assessment of AML patients undergoing consolidation therapy with cytarabine.

Michael MacNeill

Post-Renal Transplant Erythrocytosis Risk Factors, Management, and Outcomes: A Regional Transplant Centre Retrospective Review

Michael MacNeill Jessie Sanghe, Dervla Connaughton, Corinne Weernink, Jenny Ho, Ben Chin-Yee, Cyrus Hsia

Introduction: Post-transplant erythrocytosis (PTE) is a condition of elevated hematocrit/hemoglobin typically presenting within 8-24 months after renal 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 PTE development as well as the efficacy on the various PTE management strategies on clinical outcomes. Methods: We conducted a retrospective observational 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, 2015 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. Treatment choices, risk factors, and relevant adverse events were assessed, including thromboembolisms, hyperviscosity syndrome, and renal graft function. Results: pending Conclusion: pending

Brandon Mitchell

Comparison of clinical prediction tools for diagnosing pulmonary embolism: a pragmatic retrospective cohort study

Brandon Mitchell Kathleen Winger, Taylor Bechamp, Angela Wang, Matthew Leeder, Lauren Chan, Christine MacDonald, Alejandro Lazo-Langner

Background: Multiple clinical prediction scores combine clinical pre-test probability and D-dimer thresholds to diagnose pulmonary embolism (PE). Some algorithms result in reduced imaging while maintaining diagnostic safety. However, comparisons of various scores remain limited. Aims: To compare the diagnostic performance of the original Wells score, Modified Wells score, YEARS, PEGeD, Focused D-Dimer, and Age-Adjusted D-Dimer algorithms. Methods: We conducted a retrospective cohort study of 2,365 patients presenting with PE symptoms at LHSC from November 2018 to December 2020. Demographics, Wells score components, D-dimer, and imaging results at initial presentation and 90-day follow-up were collected on all patients. We calculated diagnostic performance statistics, missed cases rate and imaging reduction for each score. Results: 2365 patients were included, of which 1394 had complete follow-up at 90 days. 85 (3.6%) patients were diagnosed with PE at initial presentation. The sensitivity of the YEARS and PEGeD algorithms was 83.5% and 81.2% respectively, while for all other scores it was over 95%. Negative predictive value (NPV) was over 98% for every score. At 90 days, the YEARS and PEGeD missed 15 (1.0%) and 17 (1.22%) events while the other algorithms missed 4 (0.29%). The YEARS and PEGeD would have reduced imaging in 38.3% and 33.4% of patients respectively. Conclusion: All scores demonstrated similar diagnostic accuracy and safety, with high NPV. The PEGeD and YEARS scores had lower sensitivities resulting in more missed events at baseline, though the upper limit of confidence remained less than 2% with a greater than 30% possible reduction in imaging.

Mihir Modi

Improving Inpatient On-Call Communication Between Nurses and Internal Medicine Residents - A Touchy Subject

Mihir Modi Nikesh Adunuri

Background: Effective communication between nurses and residents is essential for patient safety, workflow efficiency, and resident wellness. At Windsor Regional Hospital's Clinical Teaching Unit (CTU), frequent non-urgent calls outside designated communication intervals negatively impact productivity and patient care. Objective: To implement a structured touchpoint call protocol to reduce non-urgent calls to residents during non-touchpoint hours by 30%. Methods: This prospective quality improvement project follows the Plan-Do-Study-Act (PDSA) framework. Structured touchpoint intervals were established four times daily (6:30–7:00 AM, 10:00–10:30 AM, 4:00–4:30 PM, and 9:30–10:00 PM) to address routine, non-urgent patient care issues. Nurses took part in monthly education sessions and received quick reference guides to reinforce protocol adherence. An escalation policy ensured timely responses to urgent and emergent issues outside these intervals. Calls were logged, recording reason, time, and duration during pre- and post-intervention phases. Each PDSA cycle will expand from the initial unit (7th floor) to an additional unit (4th floor). Results: Data collection and analysis are ongoing. The primary outcome is the daily average of non-urgent calls per patient during non-touchpoint hours. Secondary outcomes include resident wellness, satisfaction among nurses and residents, and discharge time. Balancing measures track the total daily call volume per patient, ensuring urgent and emergent issues are promptly addressed. Conclusion: Structured touchpoint scheduling aims to reduce non-urgent calls during non-touchpoint

hours, maintaining timely management of urgent patient care issues, thereby enhancing productivity, patient safety, and resident wellness.

Ahmed Mohammad

Effects of renal denervation on kidney function in patients with chronic kidney disease: a systematic review and meta-analysis

Ahmed Mohammad Ahmed A Mohammad, Khaled Nawar, Olivia Binks, Mohammed H Abdulla

This study evaluates clinical outcomes following renal denervation (RDN) in hypertensive patients with chronic kidney disease (CKD). Prospective studies (January 1, 2010 – November 15, 2022) were systematically reviewed for RDN effects on blood pressure, estimated glomerular filtration rate (eGFR), creatinine, and procedural characteristics from Medline, PubMed, and EMBASE. A random effects model was used to combine risk ratios and mean differences. Outcomes were analyzed at 6, 12, and 24 months, with significance set at $p \leq 0.05$. Eleven prospective trials with 226 treatment-resistant hypertensive patients met inclusion criteria (age 42.5 ± 13.8 to 66 ± 9). RDN significantly reduced systolic/diastolic office blood pressure at 6 [−19.8 ($p < 0.00001$)/−15.2 mmHg ($p < 0.00001$)] and 12 months [−21.2 ($p < 0.00001$)/−9.86 mmHg ($p < 0.0005$)]. Similar reductions were observed in 24-hour ambulatory blood pressure at 6 [−9.77 ($p = 0.05$)/−3.64 mmHg ($p = 0.09$)], 12 [−13.42 ($p = 0.0007$)/−6.30 mmHg ($p = 0.001$)], and 24 months [−16.30 ($p = 0.0002$)/−6.84 mmHg ($p = 0.0010$)]. eGFR changes were +1.60 ($p = 0.55$), +5.27 ($p = 0.17$), and +7.19 mL/min/1.73m² ($p = 0.36$) at 6, 12, and 24 months, respectively. Creatinine changes were +0.120 ($p = 0.41$), +0.100 ($p = 0.70$), and +0.07 mg/dL ($p = 0.88$), suggesting stabilization of CKD. Procedural complications were minimal (4.86%). These findings support RDN as a promising intervention for resistant hypertension and CKD, reinforcing its potential for broader clinical application.

William Myers

Investigating the Biology of Impaired Neurocognition in Critical Illness: Feasibility of Longitudinal Creyos Assessment with Biological Sampling

William Myers Aleksandra Leligdowicz

Critically ill patients are characterized by a life-threatening physical state associated with decreased functioning in major neurocognitive domains: memory, reasoning, and verbal ability. However, the physiological mechanisms underlying these impairments and their long-term impacts remain unclear. Creyos is a validated online neurocognitive assessment. This study conducted biological sample collection and longitudinal Creyos testing in critically ill patients. Biological samples (blood, bronchoalveolar lavage fluid, tracheal aspirate, rectal swab) were collected at up to six time points during hospitalization and analyzed for protein biomarkers, RNA sequencing, microbiome sequencing, and flow cytometry. Patients were assessed using Creyos at discharge and remotely at three, six, and twelve months post-discharge. Over nine months of the planned ten-year duration, 122 patients were identified as eligible. 54 were excluded due to death or staffing limitations. Of the remaining 68 patients, 24 were discharged before staff contact. Creyos testing was attempted for 44 patients at discharge, but 18 attempts failed due to fatigue, delirium, or lack of consent. Samples and Creyos assessments were successfully collected from 26 patients, with 5 completing the three-month and 2 completing the six-month follow-up. One patient was unable to finish Creyos due to fatigue. Creyos score validity analysis found that 80% of collected scores are valid. This study establishes Creyos as feasible for assessing neurocognition in large cohorts of critical illness survivors. Procedures for sample collection and Creyos testing have been optimized, setting the stage for future research to better understand biological and clinical characteristics linked to neurocognitive impairments in this population

Karina Nabieva

Circulating Proteins Implicated in Venous Congestion: A Scoping Review

Karina Nabieva Logan R. Van Nynatten, Aleksandra Leligdowicz

Venous congestion (VC) is a pathologic state that promotes tissue edema. VC can be due to decompensated cardiac disease, renal failure, or intravenous fluid administration. However, the pathobiology of VC is poorly investigated, particularly in critical illness. We conducted a scoping review to identify proteins potentially implicated in the mechanisms of VC. Studies published between January 2013-October 2023 were retrieved from MEDLINE and EMBASE and included if they investigated human adult subjects, measured plasma or serum proteins in disease states related to VC, and reported measures of assessing VC. 145 texts met inclusion criteria. The median number of proteins measured was 2. Most studies (80%) reported measures of VC in the context of cardiac disease. Five studies (3%) were performed in critical care settings. Variability was noted in the reported measures of VC, with physical examination (45% of studies) being used most often. There were few studies (<30%) specifically dedicated to investigating biomarkers, and <15% characterized the biology of congestion. The candidate proteins measured included proteins related to myocardial function, endothelial signaling, and inflammation. This scoping review identifies proteins with a possible role in mediating VC at a molecular level. There is a paucity of robust studies investigating the biology of VC with unbiased protein quantification methods and robust methods of VC measurement, especially in critical illness. Understanding these mechanisms may assist in measuring response to volume resuscitation, stratification in trials focusing on appropriate volume administration and removal, and the identification of novel therapies that target pathways implicated in VC.

Meera Patel

A Matter of the Heart: Women’s Perceptions on Gaps in Cardiovascular Care in Diabetes

Meera Patel Louise Moist, Kristin Clemens

Although cardiovascular (CV) care has advanced significantly, substantial gaps persist in women with diabetes (DM), despite cardiovascular diseases (CVD) being a leading cause of their mortality. We conducted a scoping review of the medical literature to investigate patient-identified causes of CV care gaps in women with DM. Our aim was to gain insight into the underlying disparities from a female perspective, and how to address them. Guided by a librarian, our search focused on qualitative studies exploring women’s experiences with CV care. While there were no devoted studies of women with DM, there were 12 relevant studies on women’s general perceptions of CV care. Key themes included a lack of awareness about CVD, unique psychosocial and cultural barriers to treatment, and systemic healthcare and research gaps. Despite growing knowledge about heart disease, women also commented upon misconceptions and gender stereotypes leading to delays in diagnosis and treatment. Competing responsibilities, stress, and societal norms also hinder women from seeking timely care. This review has established important groundwork for developing women-centered interventions and systemic changes to improve the quality and accessibility of CV care and patient outcomes for women, ultimately reducing morbidity and mortality. Our next steps will be to interview women with a lived experience of DM and study and create gender-sensitive care programs to close the gap in women's heart health.

Cameron Proceviat

Awareness, Interest and Use of a Hospital-Based Overdose Prevention Site in Vancouver, Canada

Cameron Proceviat Seonaid Nolan, Lianping Ti, Jeffrey Morgan, Jingxin Lei, Samantha Young, Piper Dickhout

Aims: An overdose prevention site (OPS) was implemented as a harm-reduction strategy to mitigate the consequences associated with the injection of substances at one Canadian hospital. This study sought to examine awareness, interest, and use of a hospital-based OPS among individuals who inject drugs and accessed addiction care in a hospital setting. Design: Data were collected from the Outcomes for Patients Accessing Addiction Care (OPAC) study, a single-site hospital-based cohort study that enrolled individuals with a substance use disorder who accessed addiction care. Setting: St. Paul's Hospital (SPH) in Vancouver, Canada. Participants: Participants from the OPAC study between May 2018 and March 2020 who reported injection drug use. Measurements: Participants were asked about sociodemographic characteristics, substance use patterns, and awareness and use of a hospital-based OPS. Factors associated with hospital-based OPS use were identified using a Multivariable Logistics model. Findings: Overall, 142 study participants met criteria for inclusion, with 119 (84%) reporting awareness of the hospital-based OPS and 82 (58%) reported having accessed the OPS. In multivariable analyses, craving in the previous 24 hours ever having experienced an overdose, and having a previous patient-initiated discharge (PID) event were positively associated with use of the hospital's OPS. Conclusions: Having previously experienced an overdose, having cravings in the preceding 24-hour period, and having a patient-initiated discharge event were strong predictors of hospital-based OPS use, demonstrating that this harm reduction approach may be useful in preventing adverse health outcomes in this high risk population of substance users

Matthew Renaud

A reciprocal machine learning approach to defining physiologic compensation of the synovial joint in adult knee osteoarthritis

Matthew Raphael Renaud Hayden Atkinson, Robert Dima, Garth Blackler, Trevor Birmingham, Tom Appleton

Osteoarthritis (OA) is a disease of the synovial organ underscored by an inability of the organ to respond to physiologic stresses. An organ-based model of joint (de)compensation does not exist. We propose that a compensated synovial organ maintains homeostasis in response to load, thereby preserving function. Conversely, a decompensated synovial organ cannot maintain homeostasis which results in OA and loss of function. Our objective was to produce a candidate clinical definition of joint (de)compensation using a reciprocal machine learning (ML) methodology. The ML pipeline applied data-driven and ground-truth classifiers to the Western Ontario Registry for Early Osteoarthritis cohort (n=774 knees). Variables were derived from a clinical assessment battery (n=34). The data driven classifier used a principal component analysis (PCA) and k-means clustering to identify 3 patient groups. The ground-truth classifier utilized patient-reported functional pain to define 3 (de)compensation clusters. A random forest algorithm then identified clinical features predicting (de)compensation. Four principal components explained 58.0% of the variance ($p < 0.001$). K-means clustering showed features with the most variance were knee injury and osteoarthritis outcome score (KOOS; 66.2 ± 15.6), mechanical axis angle (MAA; -3.5 ± 13.2), BMI (32.1 ± 2.12), age (62.5 ± 4.3), and uric acid (321.3 ± 57.4). The random forest revealed that KOOS pain, MAA, BMI, age, and peak knee flexion were predictive of (de)compensation (vector similarity = 0.80; Θ = 36.87). Our findings support the proposed model of (de)compensation and offer candidate clinical features to determine the compensatory status of the synovial organ of the knee.

Eryn Rooney

OSM, IL13RA2 and TREM-1 as predictive biomarkers for anti-TNF response in inflammatory bowel disease

Eryn Rooney Gio Dela Cruz, Terry Ponich, Jamie Gregor, Nilesh Chande, Melanie Beaton, Reena Khanna, Michael Sey, Richard B. Kim, Aze Wilson

Response to tumor necrosis factor alpha antagonists (anti-TNFs) in patients with inflammatory bowel disease (IBD) may be linked to three biomarkers: interleukin-13 receptor alpha 2 (IL13RA2), triggering receptor expressed on myeloid cells-1 (TREM-1), and oncostatin M (OSM). Elevated gene expression of these biomarkers was identified in anti-TNF non-responders but inconsistencies in whole blood expression and small cohort limitations make further investigation necessary. We aim to evaluate this association and assess the value of combining biomarkers for identifying non-responders. Plasma samples from a retrospective IBD cohort were collected prior to initiating anti-TNF therapy. Clinical remission at 1-year was determined using the Harvey Bradshaw Index (HBI<5) for patients with Crohn's disease (CD) and the partial Mayo score (<2) for patients with ulcerative colitis (UC). IL13RA2 and TREM-1 levels were quantified using enzyme-linked immunosorbent assays. OSM data came from prior studies in our lab (Guo et al. 2022). 100 patients (68 CD, 32 UC) were eligible. Among CD patients, remitters (n=46) had a median IL13RA2 concentration of 1.21ng/ml, whereas non-remitters (n=22) had 58.11ng/ml (p<0.0001). For UC patients, remitters (n=19) had a median IL13RA2 concentration of 1.66ng/ml, whereas non-remitters (n=13) had 42.35ng/ml (p<0.001). TREM-1 concentrations showed no association. Combining IL13RA2 and OSM data enhanced prediction accuracy compared to either biomarker alone (CD, sensitivity=72.7%, specificity=93.5%; UC, sensitivity=84.6%, specificity=78.9%). In conclusion, plasma IL13RA2 is associated with anti-TNF response and its prediction accuracy improves when combined with OSM.

Yashasavi Sachar

Assessing the role of the "weekend effect" on patient outcomes following transjugular intrahepatic portosystemic shunt procedure in a North American tertiary care centre

Yashasavi Sachar Nisha Howarth, Ropo Ebenezer Ogunsakin, Amol Mujoomdar, Anouar Teriaky1, Karim Qumosani, David Hudson, Mayur Brahmania, Juan Pablo Arab, Mohammad Qasim Khan

Background: The "weekend effect" is an unexpected determinant of adverse outcomes observed in multiple medical disciplines. This study assessed if transjugular intrahepatic portosystemic shunt (TIPS) procedures conducted over a weekend led to worse outcomes. Methods: This retrospective, single-centre study evaluated adults ≥18 with cirrhosis who underwent a TIPS procedure between January 1, 2014, and December 31, 2023. Patients were stratified based on whether TIPS occurred on a weekend vs. weekday. The primary outcome was 1-year mortality. Cox proportional hazards regression was carried out on 4 binary outcomes (1-year mortality; 6-week mortality, post-TIPS hepatic encephalopathy (HE), and need for TIPS revision). Results: Of 165 cases, 152 TIPS procedures occurred on weekdays, and 13 on weekends. Baseline characteristics were similar between groups. Compared to weekday TIPS, weekend TIPS was not associated with 1-year mortality (p >0.9), 6-week mortality (p =0.7), HE (p=0.9), or need for revision (p=0.6). However, weekend TIPS had greater median LOS (10 days (IQR 6-15) vs. 3 days (IQR 2-10), p=0.035). On multivariable analysis, day of procedure was not a significant predictor of mortality or post-TIPS adverse events. However, pre-TIPS MELD 3.0 significantly influenced 1-year mortality (HR 1.20, CI 1.05-1.59), 6-week mortality (HR 1.27, CI 1.01-1.60), p<0.05, while MELD-Na was not significant. No other variables were significant determinants of either primary or secondary outcomes. Conclusions: A weekend effect of TIPS procedures increasing the risk of mortality or post-procedure complications was

not noted. Weekend TIPS was associated with longer LOS, likely representing increased acuity of undertaken procedures.

Yashasavi Sachar

Reclassification of Liver Disease and its Impact on TIPS Outcomes

Yashasavi Sachar Nisha Howarth, Derek H. W. Little, Ropo Ebenezer Ogunsakin, David Peck, Amol Mujoomdar, Derek W. Cool, David Hocking, Anouar Teriaky, Karim Qumosani, Ephraim Tang, Anton Skaro, Mayur Brahmania, Juan Pablo Arab, Mohammad Qasim Khan

Background In 2023, the classification of steatotic liver disease shifted from NAFLD and ALD to a spectrum including MASLD, MetALD, and ALD. As research suggests MetALD exhibits distinct trends from MASLD and ALD, this study evaluates post-TIPS outcomes in tertiary care following reclassification. Method This retrospective, single-center study included adults initially diagnosed with NAFLD or ALD who underwent TIPS from 2014 to 2023. Patients were reclassified as MASLD, MetALD, or ALD. Cox proportional hazards analysis assessed four outcomes: Primary: 1-year mortality; Secondary: 6-week mortality, revision, and post-TIPS hepatic encephalopathy (HE). Explanatory variables included age, gender, MELDNa, and liver disease etiology. Results Of 98 patients, 45 had NAFLD and 53 had ALD. Under reclassification, 25 were MetALD, 35 MASLD, and 38 ALD. MetALD patients were 60% from ALD (n=15) and 40% from NAFLD (n=10). ALD patients were younger than MetALD and MASLD (56 IQR 11 vs. 64 IQR 13 vs. 65 IQR 10.5 years; p<0.01). The MetALD group was predominantly female (88%) versus MASLD (36%) and ALD (56%) (p<0.01). No significant differences in MELDNa, TIPS indications, were observed between MASLD, MetALD, and ALD. Etiology of the disease did not significantly impact 1-year mortality, nor 6-week mortality, post-TIPS HE, or revision. Conclusions MetALD accounted for 26% of reclassified patients, with a disproportionate female representation. Outcomes remained similar across MASLD, MetALD, and ALD, suggesting prior TIPS evidence for NAFLD may be applicable to MASLD in future studies.

Yashasavi Sachar

Examining the Impact of Inflammatory Bowel Disease in Post-LT Outcomes in Primary Sclerosing Cholangitis

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

Background Primary sclerosing cholangitis (PSC) is an immune-mediated disease characterized by biliary inflammation and fibrosis, frequently associated with inflammatory bowel disease (IBD) in 80% of cases. The impact of IBD on post-liver transplant (LT) outcomes remains unclear. This study evaluated the role of IBD in post-LT survival, infections, and incidental intrahepatic cholangiocarcinoma. Methods A retrospective cohort study identified PSC patients from 1999–2021. Statistical analyses included Kaplan-Meier survival curves, binary logistic regression for infection risk, and competing-risk analysis for post-LT mortality, with re-transplantation as a competing risk. Results Among 251 PSC patients, 122 underwent LT (mean age 44.9±12.6 years; 74.6% male; 81.2% with IBD). PSC phenotypes included classic (85.3%), PSC-AIH overlap syndrome (13.9%), and small duct (0.8%). Median MELD-Na at LT was 22 [17–28]. During follow-up (median: 1,248 days), 29 patients (23.8%) died, and 5 (4.1%) required re-LT (median: 1,460 days). Estimated graft survival was 93.2% at 1 year and 81.3% at 5 years. Competing-risk analysis identified older age (sHR 1.05, p=0.018), higher MELD-Na (sHR 1.07, p=0.005), and prior ERCP (sHR 6.33, p=0.008) as predictors of increased post-LT mortality. IBD was not associated with mortality (sHR 1.02, p=0.962) or infections at 30 days (OR 1.01, p=0.615). Conclusions Older age, higher MELD-Na,

and prior ERCP were independent risk factors for post-LT mortality in PSC patients. However, IBD was not linked to increased mortality or infection risk post-LT.

Manpreet Saini

Improving patient knowledge to reduce readmissions of CTU Patients- A QI study

Manpreet Saini Saira Zafar

Background: Hospital discharge processes can be convoluted and unclear for patients with complex care needs. This project aims to improve patient education during hospitalization by identifying key information that the patient often is unaware of regarding their hospital stay. In turn, the hope is that this will reduce readmissions to CTU medicine. Methods: This study employes a transitional coach(TC) that educates patients by creating a patient-centred booklet designed to organize information pertaining to a patient diagnosis, medications , blood tests, any imaging done, warning signs and follow up plans with physicians. The goal is to identify which information pertaining to their hospitalization is often missed and can be improved for both better patient care and reduction in CTU re admission. Through multiple PDSA cycles, the booklets were re-edited to ensure information is informative for patients. Patients are then followed up with using the LACE screening tool to ensure they have the resources to avoid hospital re admission. TC went over with the patient information provided in the booklet for knowledge consolidation Results: A cohort of approximately 20 patients were interviewed regarding their hospital stay and it was found that a majority of patient were unaware of the investigations done in hospital (ex. CT scans, ultrasound, blood cultures etc). Hence, an emphasis was placed on investigations in the booklet and this information was prioritized during patient discharge. The study is currently ongoing. During follow up calls, all patients had booklets with them. Readmission data is still pending

Stefan Sampy

Nicotinamide mononucleotide can restore bactericidal activity in neutrophils by enhancing autophagic flux during sepsis

Stefan Sampy Tianqing Peng

Introduction Sepsis is a life-threatening condition caused by a dysregulated immune response to infection, causing multi-organ failure. To date, no pharmacological cure has been found. Recent studies suggest that nicotinamide mononucleotide (NMN), a precursor of NAD+, may enhance neutrophil bactericidal function during sepsis by promoting autophagic flux. However, the role of autophagic flux in neutrophils during sepsis remains poorly understood. Objective This study aims to examine whether NMN can restore bactericidal activity in neutrophils by enhancing autophagic flux and bacterial killing during sepsis. Methods Murine bone marrow-derived neutrophils were incubated under four conditions: Saline, Lipopolysaccharide (LPS, 100 ng/mL), NMN (500 μM), and NMN + LPS. Western blotting assessed LC3-II and p62 levels as key autophagic flux markers. LC3-II levels were also assessed in the presence of LPS + Bafilomycin-A1 (0.1 uM) to verify the effect of LPS on autophagy. Phagocytic and bactericidal activity was evaluated by colony-forming unit assays and uptake of fluorescence-conjugated Escherichia coli BioParticles in the presence of NMN. Current Results LPS caused significant accumulation of LC3-II and p62, indicating abnormal autophagic flux in neutrophils ($p<0.001$). Co-treatment with bafilomycin-A1 and LPS did not significantly alter LC3-II levels compared to LPS alone, clarifying that LPS blocks autophagic flux. Remarkably, NMN restored LC3-II turnover in LPS-treated neutrophils ($p<0.01$), demonstrating that NMN could reverse LPS-induced inhibition of autophagic flux. Conclusion Our results demonstrate that NMN may be a promising therapeutic for sepsis by restoring autophagic flux in neutrophils. Future in vivo studies will expand on NMN's therapeutic action in neutrophils.

Jessie Sanghe and Regan Toltesi

Enhancing Patient Experience on a 'Watch & Wait' Protocol: Insights from patients with Chronic Lymphocytic Leukemia and Indolent Non-Hodgkin Lymphoma

Jessie Sanghe and Regan Toltesi Adrienne Fulford, Joy Mangel

Background: Newly diagnosed patients with indolent Non-Hodgkin Lymphoma (iNHL) or Chronic Lymphocytic Leukemia (CLL) who do not require immediate treatment are often followed on a Watch & Wait protocol (W&W). While this approach delays treatment-related side effects, it can contribute to emotional distress and uncertainty for patients. Methods: Patients with iNHL or CLL were invited to participate in private interviews to discuss their experiences with W&W. Interviews featured ten open-ended questions exploring the understanding of their diagnosis, its impact on different aspects of their lives, coping mechanisms, and suggestions for improving this experience for future patients. Interviews were recorded, transcribed, and analyzed thematically. Results: A total of 25 patients (10 male, 15 female), with a median age of 70 years (range: 52–82), diagnosed with indolent non-Hodgkin lymphoma (iNHL) (n=19) or chronic lymphocytic leukemia (CLL) (n=6) were interviewed. Most patients were unaware of Watch and Wait (W&W) as a management option and were initially surprised by the approach. Once explained, many felt relieved not to require active treatment, while others struggled with anxiety and uncertainty. Patients expressed a desire for educational resources about their diagnosis and W&W, as well as a peer support group and more frequent follow-ups, particularly in the early months. Despite emotional challenges, most felt well-supported by their healthcare providers. Conclusions: These insights will inform the development of resources and supports aimed at improving the overall experience for patients during the W&W phase.

Dilraj Sanghera

Comparative Analysis of Peritoneal Dialysis Catheter Insertion Techniques: Focus on Paramedian vs Midline Approach

Dilraj Sanghera Arsh Jain

Peritoneal dialysis (PD) catheter insertion technique is critical for optimizing outcomes in patients with end-stage renal disease (ESRD). This study compares midline and paramedian percutaneous PD catheter insertion techniques using data from the ISPD North American PD Catheter Registry, encompassing 1,861 patients. The midline approach involves an incision below the umbilicus, thought to offer easier access to the peritoneum but potentially higher hernia/leak risk. Conversely, the paramedian approach, through the rectus muscle, may enhance catheter stability while increasing bleeding risk. Existing literature presents conflicting evidence regarding the superiority of these techniques. More recent studies suggest fewer mechanical complications and better catheter survival with the paramedian approach, resulting in recommendations of this approach in multiple guidelines. Primary outcomes include flow dysfunction, leak rates, and catheter-related complications. Secondary outcomes assess bleeding, catheter survival, and time to PD initiation. Large study size allowed adjustment for confounders such as age, BMI, prior abdominal surgery, and comorbidities. Cox proportional hazards models were used to evaluate outcomes. Results demonstrated no significant differences between approaches in flow dysfunction (13% midline vs. 12% paramedian, p=0.54), leak rates (2% both groups, p=0.79), or overall catheter-related complications (31% both groups, p=0.74). However, midline insertion was associated with a shorter median time to PD initiation (21 vs. 25 days, p<0.0001), potentially benefiting urgent-start patients. This study provides the largest comparative analysis of these techniques to date and highlights that both approaches are viable options. Findings emphasize patient-specific factors and institutional expertise in guiding technique selection to optimize PD outcomes.

Yinxiang Shao

Retrospective Cohort Comparing Patients with Erythrocytosis: A Focus on the SH2B3 mutation

Yinxiang Shao Aidan McKee, Iman M'Hiri, Cyrus Hsia, Benjamin Chin-Yee

Introduction Primary erythrocytosis often refers to polycythemia vera, caused by a mutation in the JAK2 gene. Other mutations may be implicated, such as SH2B3 - an encoder LNK protein acting as a negative feedback regulator of hematopoiesis through downregulation of JAK2 activity. Mutations in SH2B3 therefore attenuate LNK production, causing unregulated hematopoiesis and thereby possibly associated with myeloproliferative neoplasms. It is unclear how erythrocytic patients with SH2B3 mutations compare clinically with respect to thrombotic and overall outcomes. Methods We compared the largest cohort of secondary erythrocytosis patients with SH2B3 mutations and patients: i) with JAK2 mutations and ii) with secondary causes. A retrospective chart review was conducted encompassing over five years of patients who underwent routine next generation screen at London Health Sciences Centre. Patients meeting WHO 2016 thresholds for erythrocytosis were included, and excluded if they had another concurrent hematologic diagnosis. Patient demographics, causes of secondary erythrocytosis, relevant hematological treatments, venous, arterial thrombosis and death outcomes were collected. Data was reported descriptively. Results 16 patients were included in the SH2B3 cohort, 568 patients in the JAK2 negative cohort, and 112 patients in the JAK2 positive cohort. All groups had similar baseline characteristics, including hemoglobin and hematocrit at diagnosis. Patients with erythrocytosis and SH2B3 mutations were not associated with any more incidence of venous or arterial thromboembolism events than treated JAK2 positive patients or secondary erythrocytosis patients, nor a difference in overall mortality. Conclusion Erythrocytic patients with SH2B3 mutations do not seem to have increased incidence of thrombotic events or death.

Nancy Shi

Rhythm Identification of Wide Complex Tachycardia on 12-lead ECG using a Convolutional Neural Network

Nancy Shi Meichen Liu, Iris Liu, Pavel Antiperovitch

Wide complex tachycardia (WCT) remains one of the most challenging dilemmas in cardiac rhythm interpretation. Sustained ventricular tachycardia (VT) is a life-threatening rhythm that requires cardioversion and potentially an implantable cardioverter-defibrillator which carries cumulative lifetime device-related complications. Supraventricular tachycardia (SVT) which can often mimic VT is not life-threatening and, in most cases, do not require cardioversion or device implant. Recent advances in artificial intelligence (AI) show significant promise in the realm of ECG interpretation. Using XML data of 14573 WCT 12-lead ECGs (defined as QRS > 120ms, heart rate > 120 bpm; 12624 SVT, 1349 V-paced, 600 VT), we developed a convolutional neural network with a training/validation (10883) and test set (3690). The test set consisted of 3147 SVT, 176 VT, and 367 V-paced rhythms, all adjudicated by a Cardiologist and reported officially on MUSE. The average age was 76.9 years, 35% female, with comorbidity history as follows: hypertension 62.9%, diabetes mellitus 32.5%, heart failure (systolic or diastolic) 48.2%, cerebrovascular accident 12.8%, severe coronary artery disease (acute coronary event or history of coronary bypass/percutaneous coronary intervention) 30.6%. 27.8% of patients had a documented left ventricular ejection fraction of 40% or lower. The model predicts probability (0-1) for the following three classes: SVT, VT, V-paced rhythm. The weighted sensitivity of AI was 92.3%, weighted specificity was 92.1%, PPV 93.0%, NPV 85.9%. The AI’s ROC AUC for the three classes were: 0.96 (SVT), 0.93 (VT), 0.96 (V-paced). Conclusion: AI is a valuable tool in assisting clinicians with interpretations of WCT.

Igor Sljivic

Effect of Incentive Spirometry on Length of Hospital Stay in Non-Critically Ill Patients Admitted to a General Medicine Unit

Igor Sljivic Keren Moyorov, Gabrielle Nguyen, Arani Sivakumar, Nikesh Adunuri

Introduction: Incentive spirometry (InSp) utilizes a device to encourage maximum sustained lung inspiration. This enables recruitment of atelectatic lung to improve ventilation. Few studies evaluating the efficacy of InSp in non-critically ill, dyspneic patients. Our ongoing randomized controlled trial aims to assess the efficacy of InSp in hypoxemic inpatients. Methods: Patients admitted to CTU with hypoxemia secondary to COPD, CHF or pneumonia are are randomized into the intervention or control group. In the study group, patients are instructed to maintain a sustained maximal inspiration for 5 seconds on an Incentive Spirometer, eight times a day. Outcomes include length of hospital stay, time on supplemental oxygen, and pulmonary complications. Results: 24 patients have been enrolled thus far, with 13 receiving InSp. The most common diagnoses were pneumonia (8 patients), COPD-related disease (7), and congestive heart failure (7). The average length of stay was 9.7 days in the control group and 6.3 days in the treatment group. Oxygen supplementation was required for a total of 176 hours in the control group, compared to 102 hours in the treatment group. Conclusions: Despite the early course of our study, Incentive Spirometry appears to demonstrate a trend towards shorter hospital length of stay and less time spent on supplemental oxygen for hypoxemic patients with COPD, CHF or pneumonia. Ongoing patient enrollment will further characterize these findings, which may have widespread clinical and administrative impacts.

Shreyas Sreeraman

Venous Excess Ultrasound (VExUS) and Acute Kidney Injuries in Admitted Medicine Inpatients

Shreyas Sreeraman Prince Taylor, Michael Sattin, Jeff Yu, Marko Mrkobrada

Background: Venous Excess Ultrasound (VExUS) is an innovative tool in point-of-care ultrasound to assess organ congestion via doppler ultrasound. VExUS interrogates velocity profiles in the inferior vena cava, portal, hepatic, and intrarenal veins and assigns a grade (0-3) based on these profiles. Initially derived from post-cardiac surgery patients with cardiorenal syndrome, we sought to validate the utility of VExUS in predicting acute kidney injury (AKI) in internal medicine inpatients. Methods: We conducted a retrospective case-control study of adult medicine inpatients with VExUS between January 2020 and December 2023 at London Health Sciences Centre (LHSC). Primary outcome: odds of AKI amongst inpatients with moderate/severe congestion on VExUS (Grade 2 or 3). Secondary outcomes: improvement of renal function; requirement of renal replacement therapy, and all-cause mortality within 28 days. Results: Amongst 204 patients included, 124 (60.8%) patients had none or mild congestion (Grade 0 or 1) while 80 (39.2%) had moderate or severe congestion (Grade 2 or 3). 102 patients (50%) had an AKI. For patients with moderate or severe congestion, the odds ratio of AKI was 2.51 (1.36-4.69 95% CI, p = 0.002). Multiple logistic regression analysis is underway with results pending. Conclusions: In medicine inpatients at LHSC, moderate to severe congestion on VExUS is associated with increased odds of AKI. This retrospective, proof-of-principle study demonstrates that VExUS can be utilized in this population to evaluate venous congestion and risk of subsequent renal dysfunction. Prospective studies are required to evaluate its impact on clinical decision making.

Julia Steriopoulos

The Molecular Mechanism of TLR3 Initiated Cell Death

Julia Steriopoulos Zhu-Xu Zhang

Allograft rejection continues to be the greatest challenge to the longevity of cardiac transplants. Our lab found that the abrogation of TLR3, a receptor which senses double stranded RNA (dsRNA), improved cardiac graft outcomes in mice. TLR3 mediates cell death through its adaptor molecule TRIF, which is capable of binding key cell death pathway molecules RIPK1 and RIPK3 through their shared RHIM domains. We aim to identify the constituents in the molecular cascade during the initiation of cell death in bone marrow derived macrophages (BMDMs) and endothelial cells (ECs). To investigate this, we induced apoptotic and non-apoptotic cell death using synthetic dsRNA. Cell death was measured using propidium iodide staining and imaging by the Cytation plate reader. The activation and expression of key cell death cascade molecules was examined via western blotting. Co-immunoprecipitation is being used to determine binding partners of these key molecules during the initiation of cell death. Our results show that TLR3 stimulation of ECs and BMDMs can result in cell death. Western blotting has revealed the activation of key executors of necroptosis in these cell types when undergoing TLR3 initiated cell death. The ability of necrostatin, a RIPK1 kinase activity inhibitor, to reduce death in these cell types suggests that RIPK1 is involved in cell death cascades in both BMDMs and ECs. We will continue to investigate the involvement of our molecules of interest.

Vithuyan Sugumar

Hospital-based care strategies to support underserved people living with diabetes: a scoping review of the medical literature

Vithuyan Sugumar, Yunxu Zhu Tanya Doshi, Kristin Clemens

Background Diabetes (DM) has a disproportionate impact on underserved populations, including people who are marginalized, racialized, and from gender minority groups. These groups face disparities that can reduce access to quality DM care and lead to suboptimal outcomes. We aimed to identify hospital-based interventions to support DM care in patients from underserved populations. Methods We searched five databases and the grey literature for relevant hospital-based interventional studies executed in high-income countries. Included papers had to be focused on underserved populations, including gender minority groups, racialized and Indigenous populations, migrants, and patients with disabilities, experiencing homelessness, or coming from a low socioeconomic background. Outcomes of interest included glycemic control, lifestyle changes, medication usage, and hospital readmission rates. Results There were 1825 citations identified. 178 proceeded to full-text screening, and 29 papers met inclusion. 6 major types of interventions were studied within the literature: hub and spoke models, where multidisciplinary teams connect virtually with community primary care providers; telehealth clinics; restructuring of existing clinics to provide more efficient care; interdisciplinary care clinics; patient education; and reducing socioeconomic barriers to care. Interventions had positive impacts on glycemic control, as well as weight loss, medication usage, and lifestyle adjustments. Conclusion Overall, the literature demonstrates many models of hospital-based care to improve DM outcomes in underserved groups. This work will be used to inform new care pathways for underserved patients in our community. It is critical that innovative approaches are appropriately funded to ensure that all patients with DM, irrespective of background, are treated effectively.

Sahanah Thirukumar

Targeting Cardiac Necroptotic Cell Death in Diabetic Cardiomyopathy with Murine Cytomegalovirus M45

Thirukumar, S Ni R, Zhang J, Peng T

Diabetic cardiomyopathy (DCM) is defined by diabetes-induced structural and functional myocardial abnormalities, possibly leading to heart failure. We and others have reported that cardiac cell necroptosis contributes to DCM. Murine cytomegalovirus encodes M45, a protein that disrupts necroptotic protein activity via its N-terminal RIP homotypic interaction motif (RHIM). We hypothesize that delivery of the RHIM-encoding, N-terminal 1-90 residue (N90) of M45 can inhibit necroptosis and reduce diabetes-related cardiac damage. Mouse cardiac endothelial cells (MCECs) and cardiomyocytes were exposed to high glucose and BSA-conjugated palmitate (HG-Pal) to create diabetic conditions in vitro. This was found to reduce cell viability and increase necroptotic protein expression, thereby rationalizing the model. MCECs were then transfected with a plasmid expressing DDK-tagged N90 and concomitant EGFP and treated with HG-Pal to measure changes to cytotoxicity and necroptotic biomarkers. N90 delivery reduced the injury and death of MCECs exposed to HG-Pal, with analogous outcomes expected in cardiomyocytes, for which specialized magnetic nanostructures will replace transfection measures. An in vivo approach explored the cardioprotective effect of N90 on Akita mice, a well-established type 1 diabetes model, via serum analysis, echocardiography, and tissue collection. N90-treated Akita mice show decreased pRIPK3 expression, RIPK1-to-RIPK3 interactions, and cardiac troponin I levels, indicating reduced myocardial injury. Echocardiographic analyses reveal preserved cardiac function in N90-expressing mice four weeks post-treatment of an additional N90 dose. Our preliminary findings display the protective potential of N90 against myocardial damage, which can serve as a novel therapeutic approach to DCM and allow mechanistic insight for alternative applications.

Alexandra Troitskaya

Impact of age on sepsis: Overwhelming inflammation in the lung

Alexandra Troitskaya Amin Manji, Onon Batnyam, Eric Patterson, Ruud Veldhuizen, Sean Gill

Background: The body’s immune response to infection, called inflammation, can become dysregulated, leading to life-threatening organ dysfunction known as sepsis, particularly affecting the lungs. Sepsis has a 20% global mortality rate, with higher rates in elderly hospitalized patients. Most pre-clinical research has relied on young animal models to study sepsis. To address this gap, we investigated the response to sepsis in aged versus young mice, hypothesizing that aged mice would exhibit more severe pulmonary inflammation. Methods: Young (2-3 months) and aged (22-23 months) mice were randomized to an intraperitoneal injection of fecal slurry (septic) or a dextrose solution (sham control). Mice were monitored using the mouse sepsis score (MSS). At four hours, lung inflammation was measured via RT-qPCR for inflammatory markers and bulk RNA sequencing for the global lung transcriptome. Results: All septic mice showed a higher MSS than sham controls, with aged septic mice exhibiting significantly higher scores than young septic mice. Several inflammatory markers were significantly elevated in aged septic mice compared to young septic mice. RNA sequencing revealed activation of more pathways in aged mice compared to young mice, especially with sepsis, with most upregulated pathways responsible for inflammation. Discussion: We conclude that aging contributes to greater lung inflammation, and that this dysregulated response contributes to detrimental outcomes. Our findings highlight the necessity of using age-appropriate models in pre-clinical research. Future studies can leverage this model to explore mechanisms underlying differences in lung responses and worse outcomes in the aging population.

Sofya Ulanova

A New Player in Rheumatoid Arthritis: Homocitrulline-Specific T Cells

Sofya Ulanova Gabrielle Buckley, Ewa Cairns, Lillian Barra

Introduction: Rheumatoid Arthritis (RA) is an autoimmune disease affecting 1 in 100 Canadians. Both B and T cells contribute to RA pathogenesis, with immune responses targeting peptides containing post-translational modifications such as homocitrulline (a modified lysine). While B-cell responses to homocitrullinated peptides (HomoCitP) are well-documented, the role of T-cell responses remains unclear. This study investigates HomoCitP-specific T cells in RA patients to elucidate their role in disease pathology. Methods: RA patients and age- and sex-matched healthy controls (HCs) were recruited from the rheumatology clinic at St. Joseph's Health Care. CD4+ T cells were isolated from peripheral blood and stained with HomoCitP-loaded MHC-II tetramers. Peripheral blood mononuclear cells (PBMCs) were analyzed for proliferation and cytokine production, while sera were used for antibody detection. Results: Tetramer assays revealed a threefold increase in HomoCitP-specific T cells in RA patients compared to HCs. These cells predominantly exhibited a pro-inflammatory phenotype, with 51% classified as Th1 and 39% as Th17 cells. Restimulation with HomoCitP in vitro induced robust proliferation of Th1 and Th17 cells. Additionally, HomoCitP-stimulated PBMCs from RA patients produced elevated levels of pro-inflammatory cytokines, including TNF-α, IFN-γ, IL-22, IL-6, and IL-2. HomoCitP-specific antibodies were detected in 13/16 RA patients but only in 1/12 HCs. Conclusions: This study identifies HomoCitP-specific T-cell responses as key contributors to RA pathogenesis, highlighting their pro-inflammatory nature, preferential differentiation into Th1 and Th17 subsets, and heightened cytokine production. These findings offer novel insights into RA immunopathology and position HomoCitP-specific T cells as potential therapeutic targets for disease intervention.

Venkat Vaibhav

Evolving therapies for cardiac sarcoidosis – the choice of cardiac devices for pacing and prevention of sudden cardiac death

Salem Abu Al-Burak, Venkat Vaibhav Paramveer Love, Nikolaos Tzemos, Habib R. Khan

Cardiac sarcoidosis (CS) is an inflammatory disease characterized by non-caseating granulomas that can lead to conduction abnormalities, arrythmias, myocardial fibrosis and sudden cardiac death (SCD). While corticosteroids and immunosuppressive agents reduce inflammation, they do not fully mitigate the risk of arrythmias. Implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) have become critical interventions for high-risk patients; however, challenges remain in determining optimal patient selection and timing for such device implantation. Recent advancements in imaging modalities, such as cardiovascular magnetic resonance (CMR) and fluorodeoxyglucose positron emission topography (FDG PET), have improved risk stratification and guided treatment options. Despite such improvements, there remains a gap in predicting long-term outcomes and determining which patients most from device therapy. Emerging conduction system pacing (CSP) techniques, such as His-bundle pacing (HBP) and left bundle branch area pacing (LBBAP), offer a more physiological alternative to traditional right ventricular pacing and CRT by preserving natural conduction pathways. Preliminary data suggests that CSP may improve ventricular synchrony, hemodynamics and patient outcomes; however, future research is needed to establish its long-term efficacy. This review highlights key gaps in existing guidelines, including patient selection criteria and the comparative effectiveness of CSP against traditional CRT. Given the heterogeneity of CS, a multidisciplinary approach incorporating both pharmacological and device-based strategies is essential. Future research should be directed towards large-scale, randomized

clinical trials to refine therapeutic approaches and clinical decision making. Advancing the understanding of device therapy will be critical for improving survival and quality of life in the diverse patient population.

Akshay Varghese

A Case Series of Heterozygous Familial Hypercholesteremia with PCSK9 Inhibitor Failure

Akshay Varghese Robert Hegele, Amanda Berberich

Monoclonal antibodies (MABs) to proprotein convertase subtilisin/kexin 9 (PCSK9) are commonly used to treat heterozygous familial hypercholesterolemia (HeFH). Both evolocumab and alirocumab have demonstrated efficacy in reducing low-density-lipoprotein cholesterol (LDL-C) in patients with HeFH. While a few reports describing patients with initial non-response to PCSK9 MAbs, with proposed mechanisms including the development of anti-drug antibodies, medication injection technique and LDLR variant classification, we describe here the rare scenario of initial robust response followed by subsequent loss of response to PCSK9 MAbs in two individuals with HeFH. We describe two patients with HeFH with a history of autoimmunity with initial LDL-C >5mmol/L. Despite maximally tolerated statin therapy, LDL-C did not improve and both were started on PCSK9 inhibitors. Both patients did see significant improvement of serum LDL-C to target, but after one year, LDL-C subsequently worsened despite remaining on PCSK9 inhibitors. Both were trialed on alirocumab and evolocumab and LDL-C continued to worsen. One patient is awaiting approval for Inclisiran and the other has been started on Ezetimibe. These two cases demonstrate an unusual loss of response to PCSK9 MAbs after initial successful reduction in LDL-C. We have identified only one other report describing this clinical phenomenon in a patient taking alirocumab. The mechanism underlying these observations is unclear but could include the development of neutralizing antibodies. Both patients described here have a history of autoimmunity, which may suggest a common causal link. Further research is needed to understand the underlying mechanisms and the likelihood of this occurring in other patients.

Ivy Verriet

An Enigmatic Tale Of Macrophages In Bone Marrow Causing Inflammation Of The Brain

Ivy E. Verriet Jessica Liu, Adrienne Fulford, and Uday Deotare

Background: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening immune disorder characterized by excessive inflammation and multiorgan involvement. Rarely, HLH can manifest with signs and symptoms isolated to the central nervous system (CNS). Treatment historically involved systemic steroids and immunosuppressive therapies, however allogeneic hematopoietic stem cell transplant (HSCT) has become a promising cure. Few cases have successfully cured CNS-isolated HLH after prolonged disease course years after initial presentation, with the longest documented period being seven years. This case report highlights the unique clinical course of CNS-isolated HLH in a 19-year-old female who, despite a nine-year delay in diagnosis, achieved disease remission following a HSCT. Methods: The patient initially presented at 9 years old with seizures, ataxia, and progressive cognitive decline. MRI showed new leptomeningeal enhancement and nodular brain parenchyma. A brain biopsy diagnosed small vessel vasculitis with T-cell lymphocytosis. She was refractory to treatment for nine years until March 2018, when genetic testing confirmed familial HLH with PRF1 gene mutations confirmed in both parents. Results: The patient underwent HSCT from an 10/10 HLA-matched unrelated donor. Despite significant complications, including multiple infections and renal failure, she achieved remission. Six years post-transplant, the patient exhibited stabilization of neurological function, cessation of seizures, and absence of active HLH. Conclusion: This case underscores the importance of considering genetic testing in patients with unexplained CNS symptoms and atypical radiological findings. Timely HSCT, even

in cases with delayed diagnosis, can lead to remission and improved quality of life despite prolonged disease progression.

Sudheer Kumar Vuyyuru

High inflammatory burden is a more important determinant of long-term outcomes than disease duration: A Post-hoc Analysis of the REACT-2 Trial

Sudheer Kumar Vuyyuru Shane W Goodwin, Rocio Sedano, Guangyong Zou, Parambir Dulai, Siddarth Singh, Neeraj Narula, Christopher Ma, Vipul Jairath

Background: Earlier treatment initiation in Crohn's disease (CD) is associated with a lower risk of complications, though disease duration alone may not predict severity or long-term complication risk. Methods: We performed a post-hoc analysis of the Randomized Evaluation of an Algorithm for Crohn's Treatment-Study 2 (REACT-2) cluster randomized trial to evaluate the impact of baseline disease duration (<2 and ≥2yrs) and C-reactive protein (CRP) on CD-related complications at 24 months in patients treated with enhanced care (EC) algorithm targeting absence of mucosal ulcers (>5mm) compared to step-care (SC) targeting only clinical improvement (HBI≤4) using Cox proportional hazard and modified Poisson regressions. Results: Of 1094 patients, 205 had a disease duration of <2yrs (18.7%; EC=111 and SC=94). On analysis by disease duration, there was no significant difference in CD related complications between patients with short- and long disease duration. On analyzing effect modification by CRP, patients with shorter disease duration and high CRP (>5mg/L) experienced statistically higher CD-related surgeries (RR 9.79, 95%CI [2.44-39.33]), and patients with low CRP and shorter disease duration had significantly lower CD-related non-surgical complications (RR 0.50, 95%CI [0.26-0.95]) treated with enhance care. A similar pattern was observed when analyzed using disease duration cut-off of 5 years. Conclusions: In this post-hoc analysis, there was no difference in outcomes between short and long disease duration but a high CRP at baseline was associated with worse disease outcomes despite early combined treatment. Therefore, inflammatory burden seems to be a more significant predictor of long-term outcomes than disease duration.

Arpana Wadhwani

Crohn's Disease of the Pouch: A Retrospective Case Series from a Canadian Tertiary Centre

Arpana Wadhwani Rokhsana Mortuza, Vipul Jairath, Rocio Sedano.

Background: Crohn's disease of the pouch (CDP) is an important complication impacting 5-15% of patients undergoing restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC). Although CDP is associated with significant morbidity, its pathogenesis and predictive markers remain poorly understood, leading to life-threatening delays in diagnosis. This study will evaluate patients with CDP to identify potential predictive factors that may guide early diagnosis and interventions. Methods: A Retrospective case series will be conducted, with patients treated at LHSC and SJHC, London, Ontario, Canada. Eligible participants must be diagnosed with CDP after an initial IPAA for UC. Patients with IPAA secondary to familial adenomatous polyposis, or primary pouch failure unrelated to inflammatory processes will be excluded. Results: Descriptive statistics will summarize patient demographics, UC disease characteristics, and preoperative management. Categorical variables will be analyzed through percentages and frequencies, while means with standard deviations will be calculated for continuous variables. Comparative analysis of predictors will be conducted via multivariable regression to examine the correlation of CDP absence/presence with independent variables. Cox proportional regression will be used to understand temporal characteristics, including time to CDP development. Discussion/Conclusions: Our retrospective analysis will examine clinical, endoscopic/imaging and histologic factors associated with CDP development, with a focus on

preoperative risk factors, including treatment failure or biologic nonresponse. We will highlight the urgency of early diagnosis for high-risk patients and potentially effective treatment/prevention methods. Future directions include validation of predictive markers through multicenter studies for risk stratification and treatment optimization.

Jocelyn Wang

Dynamic Measures of Fluid Responsiveness to Guide Resuscitation in Patients with Septic Shock: A Systematic Review and Meta-Analysis

Jocelyn Wang Leann Marie Blake, Nicolas Orozco, Kyle Fiorini, Chris McChesney, Marat Slessarev, Ross Prager, Aleksandra Leligdowicz, Sameer Sharif, Kimberley Lewis, Bram Rochwerg, Kimia Honarmand, Ian M Ball, Robert Arntfield, Michelle Wong, Diyaa Bokhary, Ahmad Bafar

Objective: To determine the impact of using dynamic measures of fluid responsiveness in guiding the resuscitation of adults with sepsis and septic shock. Methods: We searched MEDLINE, EMBASE, and unpublished sources from inception to July 26, 2024. We included randomized controlled trials (RCTs) that evaluated dynamic measures of fluid responsiveness to guide resuscitation compared to any other method in patients with sepsis and septic shock. We performed random effects meta-analysis, a risk of bias assessment, and rated the quality of evidence. Data Synthesis: We included 10 eligible RCTs (n=756 patients). Use of dynamic measures of fluid responsiveness (passive leg raise and global end-diastolic volume) probably reduces 28-day mortality (relative risk [RR] 0.61, 95% confidence interval [CI] 0.42 to 0.90, moderate certainty), may reduce the risk of acute kidney injury (AKI) (RR 0.66, 95% CI 0.44 to 0.98, low certainty) and cumulative fluid balance on day 3 (mean difference [MD] -1.57L, 95% CI -2.44L to -0.69L, low certainty). Dynamic measures have an uncertain impact on intensive care unit (ICU) mortality, ICU and hospital length of stay, need for and duration of mechanical ventilation, need for renal replacement therapy, vasoactive medication administration, duration of vasopressor use, and intravenous fluid administration on day 1. Conclusion: In adult patients with sepsis and septic shock, dynamic measures of fluid responsiveness may improve survival and reduce the risk of AKI. Future studies should evaluate the impact of this intervention on other important clinical outcomes and determine the comparative efficacy of specific modalities for assessing fluid responsiveness.

Chao Wang

Delivery of the gene encoding the N-terminus of murine cytomegalovirus M45 prevents PANoptosis and alleviates organ injury in septic mice

Chao Wang Rui Ni, Hu Xu, Guo-Chang Fan, Zhaoliang Su, Tianqing Peng

Introduction: Sepsis is the leading cause of death in critically ill patients with no specifically effective therapy. PANoptosis has been implicated in septic multi-organ injury, representing a therapeutic target for organ protection. The M45 protein from cytomegalovirus and its N-terminal regions containing the RIP homotypic interaction motif prevents activation of key components of PANoptosome triggering PANoptosis. This study defined the effects of the N-terminus of M45 on organ injury in sepsis. Methods: Microvascular endothelial cells (MCECs) were transfected with a plasmid expressing the gene encoding the N-terminal 1-90 residues of M45 (N90) and then stimulated with septic conditions. PANoptosis, endothelial cell barrier integrity and inflammation were analyzed. Sepsis was induced in mice by feces-injection-in-peritoneum (FIP). The gene encoding N90 was delivered to mice via tail veins. Organ injury and PANoptosis were analyzed. Results: In MCECs, septic conditions induced the formation of PANoptosome and PANoptosis. Septic conditions disrupted endothelial cell barrier integrity and promoted inflammation in MCECs. These changes of septic conditions were attenuated by expression of N90. In a mouse model of FIP-induced sepsis, expression of N90 prevented PANoptosis in heart, lung, liver and

kidney tissues of septic mice. Delivery of N90 attenuated multi-organ injury (heart, lung, liver and kidney). Expression of N90 lowered lactate and inflammation in septic mice. Lastly, the 24-hour survival was increased by N90 expression in septic mice. Conclusions: N90 reduces PANoptosis, attenuates multi-organ injury, and improves survival in septic mice. Thus, N90 may have therapeutic potential for organ protection in sepsis

Rebecca Wong

Impact of genetic testing in clinical endocrinology practice

Rebecca Bic Kay Wong Adam McIntyre, Jian Wang, Robert Hegele, Amanda J. Berberich

Advances in genetic testing have allowed for increasingly personalized health care; while many endocrinological conditions are sporadic and impacted by environmental factors, there are several conditions which have strong genetic determinants. This single-centre, retrospective descriptive study aimed to characterize the use and impacts of genetic testing in clinical endocrinology practice. 216 adults and children underwent genetic testing using next generation sequencing (n=183) or Sanger sequencing (n=33). After excluding individuals not seen clinically, family members of included probands, and those with incomplete results, 187 individuals were included in the analysis. Tested conditions were most commonly familial hypercholesterolemia (48.1%), severe hypertriglyceridemia (35.3%), and monogenic diabetes (21.9%). Other tested conditions included lipodystrophy, low high-density lipoprotein, familial hypocalciuric hypercalcemia, thyroid hormone resistance, and familial pheochromocytoma and paraganglioma syndromes. 57.2% of included individuals were female, and 77.0% of individuals had a positive family history of relevant health conditions. 70.1% of individuals had positive genetic findings, including pathogenic rare variants, high polygenic risk for hypercholesterolemia and/or hypertriglyceridemia, or variants of uncertain significance. 92.5% of genetic test results were considered clinically useful, and specific clinical action was taken in 17.6% of cases as a result of genetic findings. Actions taken included intensifying or de-intensifying treatment regimens and qualifying for drug coverage. These findings indicate that more widespread testing would inform clinical practice in many cases, help with selecting and accessing the most appropriate treatment options, and provide patients and families guidance on potential health risks.

Chuce (Bella) Xing

Prevalence and Significance of Elevated Lipoprotein(a) in Patients Participating in a Virtual Digital Cardiovascular Health Program

Chuce Xing Anthony Tang

Background – Cardiovascular disease (CVD) is a leading cause of morbidity and mortality globally. Lipoprotein(a) [Lp(a)] is a low-density lipoprotein (LDL) variant that is a significant but often overlooked independent, heritable CVD risk factor. Although the Canadian practice guidelines recommend measuring Lp(a) levels once in a person's lifetime as part of lipid screening to assess CV risk, it is rarely done. We aim to establish the prevalence of elevated Lp(a) in patients participating in a virtual digital CV health program (VIRTUES) in London, Ontario, and to explore the significance of elevated Lp(a) in this population. The hypotheses are (1) there is a higher prevalence of elevated Lp(a) (>100nmol/dL) in this population than in the general population reported in the literature; (2) Among patients with a history of Atherosclerotic (ASCVD), those with elevated Lp(a) have less traditional risk factors that those with normal Lp(a). Methods – Patients known or at risk of CVD who participate in the VIRTUES program in London, Ontario, are included. A complete medical profile was captured, which includes a complete lipid profile with measurement of Lp(a). The proportion of individuals with elevated levels of Lp(a) (> 100nmol/dl) will be identified. A correlation between the proportion of patients with ASCVD, the presence

of traditional risk factors (Diabetes Mellitus, high LDL-C, hypertension, smoking, obesity, inactivity) and Lp(a) levels will be performed. Results – to be presented

Wenqi Yang

Single-Cell Multiomic Analysis of Leukemic Transformation in Myeloproliferative Neoplasms

Wenqi Yang Jenny Ho,Tallulah Andrews

Myeloproliferative neoplasms (MPNs) are chronic blood cancers with a significant risk of progression to acute myeloid leukemia (AML), resulting in poor clinical outcomes. Transcriptomic profiling of CD34+ blasts in myelofibrosis, an MPN subtype, has revealed altered transcriptional pathways during leukemic transformation. However, the heterogeneity of CD34+ blasts, which include both early and mature hematopoietic stem and progenitor cells (HSPCs), complicates identifying the precise populations driving disease progression. This study employs a single-cell multiomic approach to address these limitations. We hypothesize that specific hematopoietic stem and progenitor cell populations undergo genetic and biological alterations that contribute to leukemic transformation in MPNs. Sample cells were isolated from 12 MPN patients (6 transformed to AML, 6 untransformed), and single-cell multiomics was used to simultaneously capture gene expression and chromatin accessibility. Data integration and quality control were performed with Seurat, while the Milo framework assessed differential abundance. DESeq2 was used for differential expression analysis on pseudo-bulked data, and FGSEA identified enriched biological pathways. Our analyses disclosed distinct cell subpopulations with significant shifts in abundance between transformed and untransformed patients. Differential expression analysis identified key genes significantly up- or down-regulated in the transformed state, while FGSEA highlighted critical regulatory pathways and gene networks involved in leukemic transformation. These results underscore the utility of single-cell approaches in resolving cellular heterogeneity and elucidating transformation mechanisms in MPNs. Integrating differential expression and pathway analyses provides a comprehensive framework that may inform the development of prognostic biomarkers and targeted therapies.

Zina Zein Abdin

Human-Induced Pluripotent Stem Cells to study cardiovascular effects of Δ^8-THC

Zina Zein Abdin Kerry-Ann Nakrieko, Hao, Yin, Michelle Si, Md Abrar Kashfi Jahin, Aleksandra Leligdowicz, Grace Parraga, Geoffrey Pickering, Mark Chandy

Cannabis use has increased worldwide following legalization, and epidemiological studies have linked it to cardiovascular disease (CVD). Cannabis contains over 100 cannabinoids, the most abundant being the psychoactive Δ^9-tetrahydrocannabinol (Δ^9-THC), which impacts endothelial function. Δ^8-tetrahydrocannabinol (Δ^8-THC), a psychoactive Δ^9-THC isomer, is gaining popularity due to its reportedly milder psychoactive effects; however, its cardiovascular effects have not been studied. To investigate the effects of Δ^8-THC, human-induced pluripotent stem cells (hiPSCs; n=3–4) were differentiated into cardiomyocytes (CMs), endothelial cells (ECs), and vascular smooth muscle cells (VSMCs), providing an unlimited source of autologous cells free from environmental confounders. Cells were treated with increasing concentrations of Δ^8-THC and Δ^9-THC, followed by viability assessments. In ECs, inflammatory marker expression was quantified via qPCR, and angiogenesis was assessed using a tube formation assay. Neither Δ^8-THC nor Δ^9-THC exhibited cytotoxicity in hiPSC-CMs, even at high concentrations (20 µM). However, in hiPSC-ECs, Δ^8-THC demonstrated greater cytotoxicity in certain donors, with a half-maximal inhibitory concentration (IC_{50}) of 5.4 µM compared to 7.4 µM for Δ^9-THC. At 2.5 µM, both cannabinoids upregulated interleukin-1 expression, with donor-dependent variability consistent with the cytotoxicity data. Preliminary findings indicate that both cannabinoids impair angiogenesis, as evidenced

by reduced tube formation. In hiPSC-VSMCs, both cannabinoids demonstrated similar cytotoxicity. Δ^8-THC contributes to endothelial dysfunction, a hallmark of CVD, similar to Δ^9-THC. Future research will explore the transcriptomic effects of cannabinoids on hiPSC-VSMCs. The long-term impact of Δ^8-THC use remains unknown and this study highlights its potential cardiovascular side effects, underscoring the need for further investigation.

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

Or go to: https://uwo.eu.qualtrics.com/jfe/form/SV_b75LMHplgtIWXs2

Thank you!