



Schulich School of Medicine & Dentistry
Western University

Department of Medicine
RESEARCH DAY

Friday, May 28, 2021
Virtual Event

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 5.25 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.

Resident Research Day Learning Objectives:

- To describe new research findings of relevance to Internal Medicine and related subspecialties.
- To recognize clinical research conducted by the trainees in the Department of Medicine.
- To identify basic research conducted by trainees in the Department of Medicine.

Dr. Khanna Learning Objectives:

1. To describe the evolution of outcome measures in IBD and how this applies to clinical practice.
2. To describe the importance of developing a research plan.

Dr. Hegele Learning Objectives:

1. To describe what research tells us about the influence of genes on lipid levels.
2. To identify if DNA testing for lipids is ready for prime time.

Dr. Clemens Learning Objectives:

1. To describe research findings on the care and outcomes of vulnerable patients with endocrine disease.
2. To describe how real-world research can help close health and health care gaps.

AGENDA**DoM Resident Research Day 2021
Friday, May 28, 2021**

Moderators Drs. Richard Kim and Reena Khanna

Start	End	Schedule of Events
8:30	8:40	Welcome & Opening Remarks Dr. Richard Kim
8:40	9:30	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
9:30	9:55	Faculty Presentation - Dr. Reena Khanna "Outcome measure in IBD" 20 min presentation, 5 min Q&A
9:55	10:10	BREAK (15 min)
10:10	11:10	Trainee Oral Presentations 6 presenters 7 min presentations, 3 min Q&A
11:10	12:00	Keynote – Dr. Rob Hegele "Genetics in internal medicine: beyond the family history" 40 min presentation, 10 min Q&A
12:00	12:50	LUNCH BREAK (50 minutes)
12:50	1:15	Faculty Presentation - Dr. Kristin Clemens "Closing gaps in health and health care: how real-world studies can help" 20 min presentation, 5 min Q&A
1:15	2:05	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
2:05	2:20	BREAK (15 min)
2:20	3:10	Trainee Oral Presentations 5 presenters 7 min presentations, 3 min Q&A
3:10	3:30	Awards & Closing Remarks Dr. Richard Kim

Trainee Oral Presentations

Time	Presenter	Status	Abstract Title	Pg #
8:40 - 8:50 am	Shin, Alice	PhD Student	F4/80+Ly6Chi macrophages contribute to colon cancer initiation in colitis	54
8:50 - 9:00 am	Chaudhary, Rushil	PGY-2	Development of a convolutional neural network to differentiate among the etiology of similar appearing pathological B lines on lung ultrasound: a deep learning study	13
9:00 - 9:10 am	Madrazo, Lorenzo	PGY-2	"I'm not gaining anything out of this so why don't I just take a nap?": Insights on residency education during the COVID-19 pandemic	41
9:10 - 9:20 am	Abufarhaneh, Mohammed	PGY-2	Association between Genetic Mutations and Risk of Venous Thromboembolism in Patients with Solid Tumor Malignancies: A Systematic Review and Meta-Analysis	7
9:20 - 9:30 am	Sattin, Michael	PGY-5	Incident atrial fibrillation and cardiovascular risk increases in patients with increased burden of atrial ectopy	53
10:10 - 10:20 am	Xu, Laura	MSc Student	Mechanism of AIF-Regulated Nuclei Damage	61
10:20 - 10:30 am	Perrault-Sequeira, Laurent	MD Student	Discharging the Complex Patient - Changing our Focus to Patients' Networks of Care Providers	49
10:30 - 10:40 am	Chow, Lindsey	PGY-4	Diabetes and Pregnancy in a Pandemic: Clinical Resource impacts of shifting to virtual diabetes care during the Covid-19 Pandemic.	15
10:40 - 10:50 am	Kassirian, Shayan	PGY-2	Effect of Needle Size on Diagnostic Sensitivity of Endobronchial Ultrasound-Transbronchial Needle Aspiration (EBUS-TBNA) in Sarcoidosis: A Systematic Review and Meta-analysis	34
10:50 - 11:00 am	Karsenti, Nessika	MD Student	Diagnostic Accuracy of Laboratory Assays for SARS-CoV-2: A Systematic Review and Narrative Synthesis	33
11:00 - 11:10 am	Chambers, Jason	MD Student	The Impact of COVID-19 on Inflammatory Bowel Disease Patients Receiving Endoscopy: Preliminary Analyses	12

DoM Resident Research Day 2021

1:15 - 1:25 pm	Baer, Brandon	PhD Student	Exogenous Surfactant as a Drug Delivery Vehicle for Budesonide in the Treatment of ARDS	8
1:25 - 1:35 pm	Jacob, Gabriella	PGY-2	The association between orthostatic hypotension and gait in cognitively impaired elderly adults	29
1:35 - 1:45 pm	Mansory, Eman	Clinical Fellow	Venous Thromboembolism in Hospitalized critical and non-critical COVID-19 Patients: a systematic review and meta-analysis	45
1:45 - 1:55 pm	Sparrow, Robbie	PGY-2	Racial, Ethnic and Socioeconomic Disparities in Patients Undergoing Transcatheter Mitral Edge-to-Edge Repair	57
1:55 - 2:05 pm	Larsen, Frederikke	MSc Student	Hypomethylation of Dclk1+ tuft cells inhibits colitis-associated colorectal cancer	37
2:20 - 2:30 pm	Guo, Angela	MSc Student	High oncostatin-M predicts non-response to tumor necrosis factor- α antagonists in inflammatory bowel disease	24
2:30 -2:40 pm	Hindi, Zaid	PGY-4	NO EVIDENCE OF A FRIDAY EFFECT ON COLONOSCOPY QUALITY OUTCOMES	27
2:40 - 2:50 pm	Martin Calderon, Leonardo	PGY-1	Healthcare Utilization and Economic Burden in Scleroderma	46
2:50 - 3:00 pm	Alotaibi, Ammar	Clinical Fellow	INCIDENCE OF SPONTANEOUS BACTERIAL PERITONITIS AMONG ASYMPTOMATIC CIRRHOSIS PATIENTS UNDERGOING OUTPATIENT PARACENTESIS: A SYSTEMATIC REVIEW AND META-ANALYSIS	7
3:00 - 3:10 pm	Good, Hayley	PhD Student	Inhibition of NF- κ B Signaling in Dclk1+ Cells Promotes Colonic Inflammation and Colitis-Associated Cancer	24

Mohammed Abufarhaneh

Association between Genetic Mutations and Risk of Venous Thromboembolism in Patients with Solid Tumor Malignancies: A Systematic Review and Meta-Analysis

Mohammed Abufarhaneh, Rudra Kashyap Pandya , Ahmed Alkhaja , Alla lansavitchene , Stephen Welch , Alejandro Lazo-Langner, MDMSc

Background: Venous thromboembolism (VTE) is a frequent complication in cancer patients with an overall incidence of approximately 20% and is associated with significant morbidity, mortality, and burden on the health care system. We have studied the association between genetic mutations and risk of VTE in adult patients with melanoma, small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC), colon, gastric and ovarian cancers. Methods: MEDLINE and EMBASE databases were searched from inception to June 2020. We included studies presenting data on genetic mutations with > 5% frequency. Three reviewers assessed the retrieved articles independently. Results: Of 616 eligible articles, we included 31 articles. In lung cancer patients with EGFR, KRAS and ALK mutations the relative risk (RR) of VTE was 1.006 (0.768-1.318, P=0.965), 1.034 (0.514-2.081, P=0.925) and 1.571 (1.314-1.878, P<0.001) respectively using the fixed-effects model. Using the random-effects model, the RR of VTE in patients with lung cancer and EGFR, KRAS and ALK was 1.058 (0.632-1.768, P=0.831), 1.086 (0.504-2.343, P=0.833) and 1.667 (1.303-2.131, P<0.001), respectively. In colon cancer patients and KRAS mutation the RR of VTE was 1.38 (1.058-1.799, P=0.017) using a fixed-effects model and 1.319 (0.794-2.191, P=0.285) using a random-effects model. Conclusions: In patients with lung cancer, those bearing ALK rearrangements carried a significantly higher relative risk of VTE than those with wild-type ALK. In patients with colon cancer, relative risk of VTE increased significantly in patients who had KRAS mutations than KRAS wild type.

Ammar Alotaibi

INCIDENCE OF SPONTANEOUS BACTERIAL PERITONITIS AMONG ASYMPTOMATIC CIRRHOSIS PATIENTS UNDERGOING OUTPATIENT PARACENTESIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Ammar Alotaibi, Majed Almaghrabi, Osman Ahmed, David Rodrigues, Alla lansavichene, Klajdi Puka, Michael Sey, Keyur Patel and Mayur Brahmania

Introduction: Spontaneous bacterial peritonitis (SBP) is a common complication of decompensated cirrhosis (DC) with high morbidity and mortality rate. There is a paucity of evidence regarding the incidence of SBP in asymptomatic liver cirrhosis patients undergoing routine out-patient large volume paracentesis (LVP). The aim of this study was to perform a systematic review and meta-analysis to determine the incidence of SBP among asymptomatic DC patients undergoing routine outpatient LVP. Methods: A systematic search of Ovid Medline, EMBASE, Web of Science and CENTRAL electronic

databases was performed in January 2021, along with a manual search of reference lists of retrieved articles. Data was extracted to determine the incidence of SBP (SBP; polymorphonuclear cells (PMNs) greater than 250 PMNs/mm³ with or without positive culture) and the incidence of all positive paracentesis (SBP and/or bacterascites-positive ascitic culture but no elevation in PMNs). Results: A total of 500 articles were retrieved with 16 studies being included in the review. A total of 1532 patients were included with a total of 4016 paracentesis performed. The incidence of a positive paracentesis (SBP and/or Bacterascitis) was 4% (95% CI: 3-6%). However, the incidence of definite SBP was 2% (95% CI 1-3%). Conclusion: The incidence of SBP in asymptomatic outpatients with DC requiring LVP is low. The benefit of routine analysis of all paracentesis samples in this population is questionable. Further studies are required to determine the cost-effectiveness of routine analysis and to determine if certain subgroups are at higher risk of SBP that require routine analysis.

Brandon Baer

Exogenous Surfactant as a Drug Delivery Vehicle for Budesonide in the Treatment of ARDS

Brandon Baer, Lynda McCaig, Cory Yamashita, Ruud Veldhuizen

Acute Respiratory Distress Syndrome (ARDS) is associated with overwhelming inflammation in the deeper, alveolar, areas of the lung. Consequently, the extensive branching structure of the lung, its large surface area, and associated areas of edema create substantial hurdles for adequate delivery of anti-inflammatory drugs to these remote sites. To address this, our lab utilized exogenous surfactant (BLES) to facilitate the pulmonary delivery of a glucocorticoid (budesonide). We hypothesized that BLES would enhance drug delivery and efficacy for treating pulmonary inflammation. An in vivo model of pulmonary inflammation was created by instilling either saline (control) or heat-killed bacteria (HKB) into the lungs of male and female rats. Thirty minutes after the administration of HKB either budesonide or BLES/budesonide was instilled. Animals were monitored for six hours, euthanized and a variety of inflammatory outcomes were determined using bronchoalveolar lavage and harvested lung tissue. Results showed that instillation of HKB significantly increased pro-inflammatory cytokine concentrations, inflammatory cell and neutrophil counts as well as myeloperoxidase activity compared to control. Budesonide alone significantly reduced the number of neutrophils compared to HKB. However, BLES/budesonide showed significant reductions across all markers of inflammation compared to budesonide and HKB groups. Moreover, these results were observed in both sexes. Together, this data demonstrates that administering budesonide with BLES improved its delivery and efficacy within the lung. This novel approach of utilizing a spreading agent to deliver budesonide represents a new therapy for ARDS and a novel strategy for directly delivering therapeutics to distal regions of pulmonary inflammation.

Ibrahim Balubaid

LIVER CIRRHOSIS AND VENOUS THROMBOEMBOLISM: A NATIONAL INPATIENT SAMPLE STUDY

Ibrahim Balubaid, Waleed Alghamdi, Reena Khanna, Anouar Teriakly

Background: The sequelae of decompensated cirrhosis include a reduction in both hepatic coagulation factors and platelets. While historically it was felt that patients with cirrhosis were naturally anticoagulated, recent studies have refuted this. As a result, cirrhotic patients may be a risk for development of venous thromboembolism (VTE). Conflicting data regarding VTE risks limits guidance for clinicians. Aim National Inpatient Sample (NIS) data were analyzed to compare the prevalence of VTE among hospitalized patients with and without cirrhosis. Method: NIS is a database of US inpatient admissions. The 2014 NIS database was interrogated using ICD-9-CM codes to identify adult patients with cirrhosis and VTE. Baseline characteristics for patients with and without cirrhosis were compared. Multivariate regression models identified risks of VTE adjusting for survey procedures. Data were presented with odds ratio (OR) with 95% confidence intervals (95% CI). A p-value <0.05 was statistically significant. Results: 605,825 patients with cirrhosis were included. VTE occurred in 8,940 patients with cirrhosis and 627,490 controls (1.5% and 2.2% respectively). The corresponding values for PE were 0.5% and 1.1%; and for DVT were 1.1% and 1.4%. The OR for VTE in patients with cirrhosis was 0.547 [95% CI (0.520-0.576), p <0.001] when adjusting for risk factors for VTE. Conclusion: Prevalence of VTE was lower among inpatients with cirrhosis compared to controls. Use of anticoagulation was not controlled as these data were not available, which could limit some associations. Further prospective studies are needed to overcome the limitations of retrospective analysis.

Yassmin Behzadian

The Risks of Care in a Time of COVID-19

Yassmin Behzadian, Dr. Sanjay Mehta

Case: A 77-year old female with ovarian cancer presented with hypoxemia and a 5-week history of progressive dyspnea and productive cough. She had previously been tested and was negative for SARS-CoV-2 in the community; 2 subsequent nasopharyngeal swabs during her admission were also negative. Computed Tomography (CT) of her chest demonstrated mucus plugging and left upper lobe ground glass opacities. Despite intravenous antibiotics, supplemental oxygen through high flow nasal cannula (HFNC), self proning, and fluid restriction for a diagnosis of SARS-CoV-2 pneumonia versus another respiratory infection, oxygen requirements continued to increase and repeat imaging revealed progression of upper lobe opacities, mucus plugging, and atelectasis. Diagnostic and therapeutic bronchoscopy was initially deferred because of concerns around high risk of respiratory failure and potential

transmission of SARS-CoV-2 but was eventually pursued under elective intubation. Thick, tenacious mucus plugs were extracted. The patient rapidly improved, being extubated approximately 12 hours later, weaned off of supplemental oxygen over 2 days, and discharged home. Conclusion: Severe mucus plugging was the likely key contributor to this patient's persistent hypoxemia, but treatment of a presumed diagnosis of SARS-CoV-2 delayed appropriate management. Given the pandemic proportions of SARS-CoV2, its high transmissibility and dire consequences, and valid concerns about the potentially poor sensitivity of certain methods of diagnosis, we do not present this case to criticize the patient's care or management decisions. Instead, this case emphasizes the potential adverse consequences of management decisions in patients with respiratory infection requiring hospitalization and respiratory support during the SARS-Cov-2 pandemic.

Yassmin Behzadian

When it Bleeds, it Cascades

Yassmin Behzadian, Dr. Karen Geukers

Background: Acquired Hemophilia A (AHA) is a rare autoimmune disease characterized by the presence of inhibitory autoantibodies against factor VIII (FVIII) of the coagulation cascade. This commonly manifests as subcutaneous bleeding, hematomas and bleeding from the gastrointestinal, genitourinary and respiratory tracts. While the majority of cases are idiopathic, AHA can be secondary to numerous underlying conditions, such as autoimmune disorders, pregnancy, malignancy, infection and certain drugs. Case Presentation: We present a case of a 72-year old male who presented with painless, gross hematuria that failed to resolve with conservative management and for whom a urological workup was unremarkable. His bleeding became more widespread and he developed a gluteal hematoma as well as spontaneous epistaxis and ecchymoses. Workup of his bleeding diathesis revealed an isolated elevation in his activated partial thromboplastin time (aPTT), a low FVIII activity, and a high FVIII inhibitor, which subsequently led to his diagnosis of Acquired Hemophilia A. Conclusion: This case reviews an approach to an elevated aPTT, the current recommendations in the treatment of AHA, and reinforces the importance of considering coagulopathies in all patients presenting with excessive or unexplained bleeding.

Yassmin Behzadian

The Impact of a Pandemic on COPD Program Wait Times

Yassmin Behzadian, Dr. Michael Nicholson

Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive and irreversible cause of airway obstruction that is a leading cause of morbidity and mortality worldwide. Patients with COPD can experience exacerbations of their disease necessitating visits to the Emergency Department and/or hospital admissions. The transition from hospital back home is an important aspect of a patient's care and can significantly influence their outcome. This is important as patients with COPD have one of the highest readmissions rates following hospital discharge. As such, Health Quality Ontario recommends that patients discharged from hospital following a COPD exacerbation be seen within 7 days of discharge, or 30 days of discharge for those requiring specialist care. This enables optimization of medications, reassessment of symptoms and referral to appropriate programs, such as Pulmonary Rehabilitation. At present, enrollment in Pulmonary Rehabilitation within 1 month of discharge is the standard of care for patients admitted with COPD exacerbations. Methods: Time to Appointment (TA) with a Respirology Specialist between January 2020 - September 2020 was compared for referrals received through the Rapid Access Consultation (RAC) pathway (which began in January 2020) versus other pathways. Time to Appointment through the Connecting Care to Home (CC2H) pathway was also compared. Full data is pending at this time. Conclusion: Decreasing time to appointment with a Respirology Specialist allows patients to be assessed and enrolled in appropriate programs in a more timely manner. Next steps include assessing the impact of shorter wait times on COPD exacerbations rates as well as readmission rates.

Shaily Brahmbhatt

Improving Diabetes Outcomes for Hemodialysis Patients: An Endocrinology Quality Improvement Initiative

Shaily Brahmbhatt, Julie Ann Lawrence, Paulina Bleah, Amanda Mikalachki, Kristin Clemens

Introduction: Many patients with diabetes also live with advanced kidney disease requiring hemodialysis. Diabetes support requires a multidisciplinary approach; it can be overwhelming for patients with multiple comorbidities to attend numerous physician appointments to receive care. This initiative aimed to develop and evaluate an outreach diabetes care program lead by a Certified Diabetes Educator (CDE) in the hemodialysis unit at London Health Sciences Centre. Methods: We conducted a baseline diabetes needs assessment for diabetic patients receiving in-centre hemodialysis at the Kidney Care Centre (KCC) as of August 1, 2019. Once gaps were elicited, our multidisciplinary team developed project aim statements. These included improvements to blood glucose

self-monitoring, treatment adherence, episodes of hyperglycemia and hypoglycemia, and proportion of patients receiving regular eye and foot care. We then performed a root cause analysis to identify critical drivers of gaps and conceptualized effective diabetes supports for our outreach intervention. Process, outcome and balancing measures were captured using run charts. Results: Since December 2020, our CDE has provided outreach support every 1-2 months to 51 patients with diabetes both in-person and remotely during the pandemic. Upon completing our program in the summer of 2021, we will formally analyze data using SPC software. Our outreach program appears to be improving the proportion with professional foot care, adequately self-monitoring sugars, and the mean number of blood sugars above 11. Discussion: We have successfully implemented an outreach diabetes support program at the KCC. Our program appears to be improving self-management in patients with diabetes patients undergoing hemodialysis.

Jason Chambers

The Impact of COVID-19 on Inflammatory Bowel Disease Patients Receiving Endoscopy: Preliminary Analyses

Jason Chambers, Gurpreet Malhi, Maria Mikail, Reena Khanna, Aze Wilson

Introduction: We suspect that COVID-19 impacted the care of inflammatory bowel disease (IBD) patients. We aimed to evaluate if delays in endoscopy resulted in more emergency room (ER) attendance/hospital admissions or persistently active disease for IBD patients. Methods: A retrospective cohort study was performed in IBD patients receiving outpatient endoscopies between March-August 2019 and 2020. Data pertaining to endoscopy timing, IBD activity, ER attendance/hospital admission were collected. Results: A total of 1522 endoscopies (2019, n=842; 2020, n=680) occurred during the study periods. To date, 400 events have been analyzed (2019, n=200; 2020, n=200) with delay status known for (2019, n=198; 2020, n=196). More endoscopies were delayed in 2020 than 2019 (49/196, 25% vs. 14/198, 7.1% respectively, $p=0.0195$). Median delay length: 2020=49 days, IQR=68.8 and 2019=43 days, IQR=46. More IBD patients who experienced delays in endoscopy attended the ER in 2020 versus 2019 (2019 n=1/14, 7.1%; 2020 n=10/49, 20.4%, $p=0.42$), though insignificantly. No difference was seen in IBD disease activity in patients attending endoscopy in 2019 (n=35/200, 17.5%) versus 2020 (n=34/200, 17.0%, $p=0.99$) nor was there a difference in disease activity for patients who had endoscopy delayed versus not-delayed (n=11/63, 17.4% and n=52/331, 15.7% with active disease at endoscopy, respectively, $p=0.72$). No difference in hospital admissions was observed between patients experiencing delay (n=7/63, 11.1%) versus non-delayed (n=57/331, 17.2%; $p=0.27$). Conclusion: Preliminary data fails to show that the increased delays in endoscopy seen during COVID-19 are associated with negative IBD outcomes. Completing this study will further define the extent of this impact.

Rushil Chaudhary

Improving COVID-19 vaccination appointment rates for hospitalised patients at discharge: a quality improvement effort

Rushil Chaudhary, Grace Hilton, April Mullen, Faisal Rehman

Although COVID-19 vaccination uptake in the community continues to increase, many eligible patients are unable to secure appointments due to issues of long telephone or online wait-times. Hospitalized patients form a large proportion of the eligible population in the current phase of the provincial vaccination plan due to their advanced age and comorbidities. However, due to their hospitalization, they are at a further disadvantage due to lack of access to telephones, tablets and their acute illness. An inter-disciplinary team including leadership from the mass vaccination centre, and allied health care professionals from LHSC analyzed the current vaccination booking process available to our patients in the community and identified areas of improvement. The objective of our quality improvement initiative is to measure and improve the COVID-19 vaccination booking rate using a simplified booking process initiated in hospital. The proposed initiative will involve patients admitted to the medicine floors at University Hospital over a two week period who are eligible for the COVID-19 vaccination under the current phase of the provincial plan. Proposed PDSA cycles include reminders by patient care facilitators, electronic medical record orders and facilitating a phone line at the vaccination centre. Our goal is to use quality improvement methodology to understand and mitigate the barriers associated with the COVID-19 booking process in our eligible patients.

Rushil Chaudhary

Development of a convolutional neural network to differentiate among the etiology of similar appearing pathological B lines on lung ultrasound: a deep learning study

Rushil Chaudhary, Blake VanBerlo, Thamer Alaifan, Nathan Phelps, Matthew White, Jordan Ho, Derek Wu, Robert Arntfield

Point-of-care lung ultrasound (LUS) allows for rapid diagnosis and management in numerous clinical settings. Lung ultrasound is especially beneficial in the current COVID-19 pandemic as it allows the advantage of clinical decision making without the laborious workflow and radiation of a CT. B lines are the characteristic pathological feature on LUS, created by either pulmonary edema or non-cardiac causes of interstitial syndromes including COVID-19 ARDS. The goal of our project was to identify if deep learning methodology is able to differentiate between COVID-19 illness, non-COVID ARDS or hydrostatic pulmonary edema. We designed a convolutional neural network trained on LUS images from our centre demonstrating B lines of different etiologies. We compared the performance of this model to that of POCUS experts in our centre. The

model trained on 612 LUS videos of B lines from 243 patients who had COVID-19, non-COVID ARDS, or hydrostatic pulmonary edema. The trained CNN performance on the independent dataset showed an ability to discriminate between COVID (area under the receiver operating characteristic curve (AUC) 1.0), NCOVID (AUC 0.934) and HPE (AUC 1.0) pathologies. This was significantly better than physician ability (AUCs of 0.697, 0.704, 0.967), $p < 0.01$. Our trained ML model was able to discriminate between COVID-19, NCOVID ARDS, or hydrostatic pulmonary edema significantly better than physician ability. The implication of this work could allow for eventual integration of machine learning algorithms at the bedside to achieve real-time, point-of-care diagnosis and prognosis of COVID or other respiratory illnesses.

Benjamin Chin-Yee

The Impact of SGLT2 Inhibitors on Secondary Erythrocytosis: A Review of Three Cases

Maxim Matyashin, Benjamin Chin-Yee, MD MA Alan Chin-Yee, MD FRCPC Cyrus Hsia, MD FRCPC

Background: Sodium-dependent glucose transporter 2 (SGLT2) inhibitors are a novel class of medications used in the management of diabetes, as well as renal and cardiovascular disease. As usage increases, there is a growing need to identify and manage potential adverse effects associated with this class of medications. Several case studies have highlighted secondary erythrocytosis associated with SGLT2 inhibitor use that warrant further investigation. Various mechanisms have been proposed but the exact physiological mechanisms of SGLT2-induced erythrocytosis remain to be elucidated. The Division of Hematology has experienced increased referrals of patients with erythrocytosis on SGLT2 inhibitors. This cohort of patients presents an opportunity to better describe the association between SGLT2 inhibitors and erythrocytosis. Here we describe three select cases identified in an ongoing retrospective review. Cases: Three patients were included in this series, a 78-year-old male, a 61-year-old female, and a 66-year-old male, all referred for erythrocytosis. Two individuals presented with an increase in hemoglobin values following the initiation of their SGLT2 inhibitor. All three cases showed a resolution of the erythrocytosis within 3 months after discontinuation of the SGLT2 inhibitor. Discussion: These three case, which form part of an ongoing retrospective study, demonstrate that discontinuation of SGLT2 inhibitors is associated resolution of erythrocytosis. SGLT2 inhibitor use should be considered as part of the differential diagnosis for erythrocytosis. Physicians need to be aware of this association with these commonly used class of drugs to avoid unnecessary investigation for erythrocytosis, and may consider discontinuation of SGLT2 inhibitors in individuals with elevated hemoglobin.

Lindsey Chow

Diabetes and Pregnancy in a Pandemic: Clinical Resource impacts of shifting to virtual diabetes care during the Covid-19 Pandemic

Lindsey Chow, Tamara Spaic, Ruth McManus, Amanda Berberich, Selina Liu

Our objective was to describe the impact of the COVID pandemic on care provision in the St. Joseph's Healthcare (SJHC) Endocrine Pregnancy Clinic (EPC) in London, Ontario, Canada. We performed a retrospective cohort study comparing the characteristics of diabetes in pregnancy assessments at the SJHC EPC in the 6 months pre-COVID (October 1, 2020 to March 18, 2020) and during the first 6 months of COVID (March 19, 2020 to September 30, 2020). The clinical encounter characteristics collected were: assessment type (consultation or follow-up), care delivery (in-person or virtual), and assessment reason (diabetes or endocrine). The pre- and during COVID numbers were summarized using means and SD and compared using independent student t-tests. The mean number of total assessments per month was significantly higher during COVID compared to pre-COVID (174 ± 34 vs. 115 ± 15 , $p=0.0061$), driven by the higher monthly mean diabetes follow-up assessments (109 ± 21 vs. 73 ± 12 , $p=0.0065$). There was no significant difference in monthly mean overall new consultations. The mean endocrine (non-diabetes) assessments each month was significantly lower during COVID compared to before (1 ± 1 vs. 5 ± 4 , $p=0.0237$). The average number of virtual assessments per month was significantly higher during COVID (143 ± 31 vs. 4 ± 14 , $p < 0.0001$). We demonstrated a shift in EPC care during the COVID-19 pandemic. Our results suggests that women with diabetes in pregnancy may require more intensive follow-up when followed virtually during COVID as compared to in-person diabetes follow-up pre-COVID. Further research to elucidate the reasons for this increased intensity of care is required.

Natasha Correa

Quality of Entrustable Professional Activity (EPA) feedback (EPA) in the first year Internal Medicine cohort at Western University

Natasha Correa, Jennifer T. D'Cruz, Lorenzo Madrazo, Klajdi Puka, Sheri-Lynn Kane

Background: Implementation of competence-by-design (CBD) through completion of Entrustable Professional Activities (EPA) aims to enhance resident performance by provision of meaningful feedback. We aimed to evaluate the quality of feedback received through EPAs. Methods: We assessed the quality of feedback for all PGY1 Internal Medicine Resident EPAs from July 2019 to May 2020 at Western University. Four reviewers, blinded to names of evaluators and learners, assessed feedback quality on four domains: timeliness (<7days duration from clinical encounter to EPA completion), task-oriented (yes or no), actionability (very, semi, or not actionable), and polarity (positive, negative, mixed, or neutral). Results: A total of 2,471 EPAs were

initiated, of which 1981 (80%) were completed. Of the completed EPAs, 39% were completed by faculty and 61% by residents. Forty-seven percent of EPAs were timely. Median time from EPA encounter to EPA completion was 3 days (IQR 1-10 days). Eighty-five percent of EPAs were task oriented. Eighty-three percent consisted of positive feedback, 4% mixed feedback, and 12% neutral feedback. Thirty percent of EPAs were semi- or very actionable. Timely feedback was more likely to be very actionable (26% vs. 20%, $p=.002$). Resident assessors were more likely to provide positive feedback (85% vs. 80%, $p=.07$). Conclusion: Most EPAs are task-oriented and positive. Less than half are timely and less than third are actionable. Residents bear a large burden of completing EPAs. There is a need to improve the timeliness and actionability of EPAs to improve feedback quality and achieve the goals of CBD.

Natasha Correa

Multi-centre real-world experience with epinephrine 0.5 mg dosing for anaphylaxis with allergen immunotherapy

Natasha Correa, Ariba Quidwai, Samira Jeimy, Natalie Rondilla, Harold Kim

Introduction: Epinephrine is the first line treatment for anaphylaxis. However, the optimal dose is not well studied. Anaphylaxis occurs in approximately 5% of patients receiving subcutaneous immunotherapy. The recommended dose of epinephrine for adults with anaphylaxis is 0.3 to 0.5 mg. The efficacy and safety of epinephrine 0.5 mg has never been assessed in patients reacting to subcutaneous immunotherapy. Methods: We reviewed the electronic medical records of two outpatient allergy practices for patients who received 0.5 mg intramuscular epinephrine as the initial dose for treatment of anaphylaxis secondary to subcutaneous allergen immunotherapy. Clinic notes were accessed to collect data on patient demographics, vital signs, and patient outcomes. Counts and percentages were computed to summarize the data. Means and 95% confidence intervals (CI) were calculated for vital signs. Results: Thirty-eight patients received an initial dose of epinephrine 0.5 mg intramuscularly for allergic reactions to subcutaneous immunotherapy between March 2006 to February 2020. Eleven reactions (30%) required a second dose of epinephrine. Two reactions (5%) required a third dose. Mean systolic blood pressure after administration of epinephrine was 120 mmHg (95% CI: 112-127). Mean heart rate was 98 beats per minute (95% CI 88-107). Twenty-two patients (58%) had resolution of symptoms in clinic. Sixteen patients (42%) were transferred to the emergency department with ongoing symptoms. Most patients (81%) had symptom resolution within 30 minutes. There were no adverse reactions or fatalities. Conclusion: Use of epinephrine 0.5 mg intramuscularly to treat anaphylaxis caused by subcutaneous immunotherapy is safe and effective.

Sean Cuninghame

The Effect of Inhaled Anesthetics on Cognitive and Psychiatric Outcomes Among Critically Ill Adults

Sean Cuninghame, Kevin Gorsky, Conall Francoeur, Davinia Withington, Lisa Burry, Angela Jerath, Marat Slessarev

Background: The COVID-19 pandemic has renewed interest in using inhaled anesthetics for sedation in the critically ill. Preliminary data shows inhaled anesthetics reduce lung inflammation, time to extubation, and ICU length of stay compared to intravenous sedatives. However, the impact of inhaled anesthetics on neurocognitive and psychiatric outcomes is not well described in this setting. Randomized controlled trials are underway (including at LHSC) to establish if inhaled anesthetics affect these and other patient and health system outcomes. In this systematic review, we sought to summarize the known effects of inhaled sedatives on cognitive and psychiatric outcomes. Methods: We searched MEDLINE, EMBASE, and PsychINFO to identify studies from 1970 - 2020 that assessed cognitive and psychiatric outcomes amongst critically ill adult patients sedated with inhaled anesthetics. Two independent reviewers screened each article's abstract as well as full-texts for data extraction. The Cochrane Risk of Bias tool is used to assess study bias. Results: A total of 1411 studies were identified by our initial search, with 132 that underwent full text review. Of these, 10 met full inclusion criteria and were included for data extraction which is underway. Based on study paucity and heterogeneity, we hypothesize that there will be insufficient data to conclude if inhaled anesthetics affect cognitive and psychiatric outcomes among ICU patients. Conclusion(s): Given the low number of studies available, there is insufficient evidence to conclude inhaled anesthetics affect cognitive and psychiatric outcomes among critically ill adults. Dedicated randomized controlled trials assessing these important outcomes are necessary.

Chintan Dave

Enabling Mechanical Ventilation in Resource-Limited Settings Through Frugal Innovation: A Systematic Review

Chintan Dave, Cameron, Paul MD, Basmaji, John MD, Slessarev, Marat MD, PhD

Background: Intensive care units worldwide are facing an increased need for provision of invasive mechanical ventilation during the current coronavirus disease (COVID-19) pandemic. To address the shortage of ventilators, members of the engineering and medicine faculty at Western University developed an open-source ventilator called the Western University Ventilator (WUV). To improve usability, a primary aim of the WUV ventilator design is to limit unnecessary features. To achieve this, a clear summary of various ventilator parameters that are recommended is required. Objective: The aim of our study is to systematically review the clinical practice guidelines (CPGs) for acute

respiratory failure to determine the parameters of a ventilator that confer a mortality and morbidity benefit. Methods: An information specialist will design the search strategy for Ovid MEDLINE, EMBASE, and the Cochrane Library dating back to 2010. Two reviewers will independently screen all studies for inclusion and extract eligible recommendations. To be included, CPGs must have reported at least one recommendation for mechanical ventilation. Disagreements will be resolved through consensus or involvement of a third reviewer. Results: The preparation of results is in progress. Extracted recommendations will be under the following domains: (1) levels of evidence, (2) quality of CPGs, (3) frequency of recommendation of specific interventions, (4) other treatment preferences (such as chest X-ray, elevation of head of bed), and (5) emerging themes. Discussion: The results of this systematic review will inform the basic parameters that will furnish the WUV, which will be open-source for use globally.

Jennifer DCruz

Is it Virtually Worth It? Cost-Analysis of a Quality Improvement Initiative Using Telehealth Monitoring at London Health Sciences Centre Urgent COVID-19 Care Clinic (LUC3)

Jennifer Dcruz, Natasha McIntyre, Zoe Lau, Mike Nicholson, Megan Devlin, Marko Mrkobrada, Erin Spicer

Background: Global health spending continues to rise, with unprecedented financial burden marked by COVID-19. Our system will be overwhelmed without substantial mitigation strategies to avert unnecessary emergency department (ED) visits.

Objectives: We implemented a novel telemedicine London Centre Urgent COVID Care Clinic (LUC3). This multidisciplinary quality improvement initiative provides care to COVID-19 patients without breaching quarantine. Our objectives were to identify and analyze costs associated with LUC3 when compared to in-person clinics, and evaluate for associated cost savings. Methods: A prospective observational study of COVID-19 positive patients referred to LUC3 were enrolled from April 23 - Aug 31, 2020.

Outcomes included complications from COVID-19, number of hospital admissions, unscheduled ED visits, and averted/bypassed ED visits. Cost data derived from the literature and our local hospital budgets were used to compare average costs and savings. Results: 117 patients were followed for 60-days (63% female; mean age of 47.1 [SD 16.2] years). Of the 35 probable emergency department visits, LUC3 prevented 80% of unnecessary ED visit resulting in a net cost savings of \$9,100.

Majority of the savings were attributed to avoided in-person clinic visits with \$23,460 saved, which accounts for 4% of our General Internal Medicine Fiscal year budget. Net savings, excluding LUC3 operational costs and advised ED visits, were \$25,021.

Conclusions: Majority of the cost savings accrued were from averted in-person clinic visits, followed by averted emergency department visits. LUC3 offered accessibility -

wherein patients can consult physicians on call, and be reassured by in-home monitoring of oxygen saturations.

Jennifer DCruz

Real-World Estimates of Rheumatoid Arthritis Patients at Risk for Severe COVID-19: Results from the Canadian Early Arthritis Cohort (CATCH)

Jennifer DCruz, Orit Schieir, Marie-Franc Valois, SJ Bartlett, L Bessette, G Boire, G Hazlewood, C Hitchon, EC Keystone, D Tin, C Thorne, J Pope, VP Bykerk, on behalf of CATCH Investigators

Objectives: Whether early rheumatoid arthritis (ERA) patients may have increased risks for complications from COVID-19 including severe symptomatic illness, hospitalization, and or death remains an active area of investigation. Our objective was to estimate the prevalence of individual and multiple overlapping risk factors for COVID-19 complications in a large multi-centre cohort of real-world ERA patients treated in routine practice settings. **Methods:** Identified risk factors associated with complications of COVID-19 were age (>70yrs old), males, ethnic minorities, smokers, hypertension, cardiovascular disease, chronic lung disease, cerebrovascular disease, diabetes, BMI>30, chronic renal disease, malignancy, chronic liver disease, and prednisone use >10mg/day. Based on these identified risk-factors we estimated the prevalence of these individual risk factor and cumulative risk-factor counts in patients with ERA. These patients were actively enrolled in the Canadian Early Arthritis Cohort (CATCH) at the completed assessment nearest to the onset of COVID-19 pandemic in March 2020. **Results:** Data from 1,967 CATCH patients were analyzed; the mean (SD) age was 60 (14) years and symptom duration of 69.8 (40.3) months. As a whole group, majority (90%) had >1 risk factor(s), 69% had >2 risk factors, even when stratified by age (>70 vs <70yrs). The top 3 most prevalent risk factors identified in our population were chronic lung disease (44%), hypertension (35%) and cardiovascular disease (32%). **Conclusion:** ERA patients often had multiple risk factors predisposing them to severe COVID-19 particularly due to their age(>70yrs) and multiple comorbidities. These results support the potential benefits of vaccination for ERA patients.

Jennifer DCruz

Describing characteristics of a primary care COPD population receiving Integrated Disease Management and the durability of quality of life outcomes over time

Jennifer DCruz, Anna Hussey, Madonna Ferrone, Christopher Liciskai

Introduction: Integrated Disease Management (IDM), a team-based approach to COPD, is being adopted to promote best-practice guideline concordance. Objective: To describe clinical and demographic characteristics of a primary care COPD IDM cohort, investigate baseline differences by GOLD stage and document the change in quality of life (QoL) over 36 months of follow-up. Methods: Individuals with an objectively confirmed COPD diagnosis, receiving IDM from 2012-2019 were included. Summary statistics were compared using point estimates and confidence intervals. COPD assessment test scores (CAT) were used to measure QoL over the follow-up period. Results: 5766 COPD patients were included, with a median 10month follow-up. Mean age was 68.1±10.12yrs, 53% male, 38% obese, 46% with >1comorbidity, and 26% with a high poverty index. GOLD 2017 classification distribution was, A 13%, B 44%, C 3% and D 25%. High risk, stage C/D, showed differences compared to A/B; there were more females (52% vs 45%), >3comorbidities (43% vs 33%), >2unscheduled acute health service use related to COPD (88% vs 28%). The largest sustained 3year improvements in QoL (reduced mean CAT score) were GOLD D 20.7(95%CI 19.6-21.8) to 17.1(CI 15.9-18.3), poor baseline QoL 23.6(CI 23.5-23.8) to 18.8(CI 18.5-19.2), and very poor baseline QoL 32.7(CI 32.4-33.1) to 24.5(CI 23.6-25.3). Conclusion: We characterized a large Canadian primary care IDM COPD population, specifically enriched for high-risk individuals and identified a female predominance, multiple comorbidities and urgent health services utilization with sustained QoL improvement over 3yrs.

Taylor Dear

Risk of Major Bleeding with Ibrutinib in Patients with Thrombocytopenia

Dr. Mina Dehghani, Dr. Taylor Dear, Dr. Kang Howson-Jan, Dr. Selay Lam, Dr. Joy Mangel, Dr. Chai Phua, Dr. Anargyros Xenocostas, Dr. Cyrus Hsia

Introduction: Ibrutinib, an oral Burton Kinase (BTK) inhibitor, is standard of care treatment for various patients with chronic lymphocytic leukemia (CLL). Previous studies reported an increased risk of bleeding due to impaired platelet function. Patients with CLL experience significant thrombocytopenia, which increases their risk for bleeding. This population was excluded from major trials and data is lacking to inform management in this setting. Objective: To determine the risk of bleeding in CLL patients with thrombocytopenia receiving ibrutinib. Methods: Retrospective chart review of adult patients with CLL who received single agent Ibrutinib in London, Ontario. Bleeding

events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) grading system. Results: 142 patients were included with median age 65 years (range 33-87) and 87(61%) male. There were 37 bleeding events: Mucocutaneous (13), intracranial (6), gastrointestinal (3) and genitourinary (3), and other bleeding events (12). There were 4 CTCAE grade 3 or above bleeding events, including one patient with grade 5 intracranial hemorrhage. The mean platelet count at the time of bleed was 140. 18% of the bleeding events was associated with concurrent severe thrombocytopenia (platelet count= <50). Analysis will be performed on the cohort of patients with thrombocytopenia compared to the cohort of patients without thrombocytopenia for the period of observation. Multivariate analysis will assess risk factors for predicting bleeding in this population. Conclusion: Pending final data analysis.

Mina Deghani

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

Pei Jun Zhao, Mina Deghani, Cyrus Hsia, Dervla Connaughton, Ian Chin-Yee, Joy Mangel, Chai Phua, Ziad Solh

Introduction: Post-transplant erythrocytosis (PTE) is a condition of elevated hematocrit within 8-24 months after renal transplant and is associated with complications such as hyperviscosity, thromboembolic and cardiovascular disease. Some of the factors associated with PTE include circulating erythropoietin, angiotensin II, insulin-like growth factor, and genetic polymorphisms in these genes, however data regarding effect of donor-recipient age and sex mismatch is lacking. Treatment of PTE utilizes ACE inhibitors, ARBs or phlebotomy, albeit 22% of patients are refractory to this treatment. Objectives: We aim to examine the real-world choice of treatment and clinical response in patients with PTE. We will also construct a clinical prediction rule to identify patients who are at high risk of developing PTE and to predict treatment response. Methods/Analysis: Retrospective chart review of adult patients with PTE, managed at LHSC from 2000 to 2020 will be conducted. Patients with hematocrit $> 51\%$ (or hemoglobin > 170 g/L) lasting >1 month, within the first 24 months after renal transplant will be included. Groups of PTE patients will be categorized by initial treatment choice - ACE inhibitor, ARB, phlebotomy, and other. Comparison between groups will be done using chi-square or Fisher's-exact test for categorical variables and T-tests or Mann-Whitney-Utest for continuous variables. Time-to-event analysis will be performed using Kaplan-Meier methods. Risk factors and predictors will be explored using linear and logistic regression. Using variable coefficients from the regression analyses, clinical prediction rules can be constructed to predict the risk of developing PTE and effectiveness of treatment for future patients.

Hernan Franco

ACTH dependent Cushing's syndrome in Metastatic Acinic Cell Carcinoma: A poor prognostic factor

Hernan Franco Lopez, Paul Stewart, Danielle MacNeil, Bret Wehrli, Sheereen Ezzat, Stan Van Uum

Acinic cell carcinoma (ACC) with high-grade transformation is an aggressive subtype of salivary gland neoplasm with a poor prognosis. We present a 52-year-old woman who developed overt Cushingoid features 18 months after her initial diagnosis, and one month after completing first line chemotherapy for metastatic ACC. This prompted immunohistochemical staining for ACTH of her initial pathology sample which was found to be positive despite the absence of clinical signs and symptoms of cortisol overproduction at the time of resection. Development of her Cushing's syndrome coincided with aggressive spread of her ACC, despite second- and third-line chemotherapy regimens. Although there are only a few documented cases of ACTH production in metastatic ACC, this case suggests that, in patients with ACC, the development of Cushing's syndrome correlates with the onset of aggressive progression and thereby poorer prognosis. Treatment of the Cushing's symptoms with adrenal enzyme inhibitors has been used previously with little benefit, and it is suggested that treatment should focused on the underlying malignancy. Circulating ACTH and its activity may thus serve as a useful marker of prognosis in ACC with high-grade transformation. In patients with ACC, vigilance for signs and symptoms of cortisol overproduction is warranted as this may signal dedifferentiation, disease progression and a poorer prognosis. Further retrospective analysis of immunohistochemical staining of metastatic ACCs can help establish the utility of routine ACTH staining as a prognostic marker.

Asher Frydman

Secondary prevention ICDs in patients with preserved ejection fraction - Do these patients need an ICD?

A Frydman, AC Skanes, LJ Gula

Introduction: Implantable cardioverter-defibrillators (ICDs) improve survival in patients with prior cardiac arrest without reversible cause, and those with sustained ventricular tachycardia (VT) with left ventricular ejection fraction below 30%. However, the evidence remains unclear whether patients with preserved ejection fraction and sustained, hemodynamically tolerated, VT benefit from ICD therapy. ICD implantation entails some risk, and therefore, the balance of benefit-to-risk is clinically relevant to ICD decision-making. Objectives: We describe a cohort that received an ICD for hemodynamically tolerated VT with preserved ejection fraction and assess whether they received ICD therapy for ventricular arrhythmias. Methods: Via chart review, we

identified patients who received an ICD for treatment of a hemodynamically stable VT episode with preserved ejection fraction of 35-50%. Parameters recorded include patient demographics, medications, comorbidities, and timing and nature of ICD therapy. A 7-day blanking period was applied after ICD implantation to ensure the presenting VT episode was not counted as a follow-up event. Results: Among 423 secondary prevention ICDs implanted, 64 patients met the enrollment criteria. Average age was 68 ± 12 years, and ejection fraction $40 \pm 4.4\%$. Over a mean follow-up of 961 ± 589 days, 36 (56%) patients received ICD therapy. ICD shocks were delivered to 18 (28%) patients over 370 ± 347 days. Antitachycardia pacing was delivered to 32 (50%) patients over 239 ± 277 days. Conclusion: ICD therapies were delivered to approximately half of patients over a 2.5-year period after implantation. ICD guidelines for these patients are currently unclear, and our findings suggest that expanding these guidelines to include them may be reasonable.

Dan Gillett

Improving *Pneumocystis jiroveci* pneumonia prophylaxis in immunocompromised patients requiring prolonged corticosteroids

Gillett, Daniel, Chakraborty Debarati, Dhaliwal Inderdeep, Gob Alan

Prolonged immunosuppression with corticosteroids is associated with many adverse effects. Among them, include infection with opportunistic infections such as fungal pneumonia, including *Pneumocystis jiroveci* pneumonia (PJP). Given this risk, patients on prolonged immunosuppression with corticosteroids are often prescribed prophylactic antibiotics to prevent PJP, such as trimethoprim- sulfamethoxazole, dapsone, pentamidine or atovaquone. The American Thoracic Society suggests that prophylaxis for PJP be considered in patients with hematologic and solid malignancies receiving cytotoxic chemotherapies, organ transplantation and those treated with immune-suppressive regimens for inflammatory conditions. In the case of corticosteroids, prophylaxis should be considered when prednisone doses exceed 20mg/day for greater than 1 month. Despite strong evidence that prophylaxis reduces rates of PJP in this population, rates of prescribing remain quite poor. This work looked to identify prescriber groups within our institution who had low rates of appropriate prescription for PJP prophylaxis in cases where patients received at least 20mg/day or prednisone for 4 weeks or more. We found that in our audit period, the overall rate of prescription for PJP prophylaxis was low, estimated at 21%. Using root-cause analysis, we identified several proposed interventions including provider education through posters and email, and development of a new prescriber module. Our goal is to improve the rate of prescriptions for PJP prophylaxis amongst patients discharged from clinical teaching unit teams on prolonged corticosteroid courses to 50%.

Hayley Good

Inhibition of NF- κ B Signaling in Dclk1+ Cells Promotes Colonic Inflammation and Colitis-Associated Cancer

Hayley Good, Alice Shin, Liyue Zhang, Samuel Asfaha

Background: Inflammatory bowel disease is a major risk factor for colitis-associated cancer (CAC). Despite the link between inflammation and cancer, the mechanism for this remains unknown. We previously showed that Dclk1+ tuft cells are long-lived and resistant to proliferation even upon mutation of the tumor suppressor APC. Following colitis, however, APC-mutated tuft cells initiate cancer. NF- κ B signaling is a key inflammatory pathway upregulated in colitis and linked to CRC. Interestingly, NF- κ B inhibition in intestinal epithelial cells reduced the initiation of CAC (Greten et al., 2004). Aims: Here, we aim to examine the effect of tuft cell-specific NF- κ B inhibition on CAC. Methods: Dclk1CreERT2/APC^{f/f} mice were crossed to IKK-B^{f/f} mice and administered tamoxifen to knockout APC and inhibit NF- κ B signaling in tuft cells. Mice were administered DSS to induce colitis and tumorigenesis. Fourteen weeks post-DSS, colonic tumor number and size were analyzed to determine the role of NF- κ B on tumor initiation and growth. Colitis severity was assessed by myeloperoxidase (MPO) activity, histology, and expression of inflammatory mediators. Results: Inhibition of NF- κ B signaling increased Dclk1+ cell-derived tumor number, with no change in tumor size. IKK-B^{f/f} mice had increased colitis severity as shown by elevated MPO, histologic damage, and inflammatory cytokine expression. We also detected crypt hyperplasia and increased MPO in IKK-B^{f/f} mice, suggesting that NF- κ B inhibition in Dclk1+ tuft cells may lead to basal colonic inflammation. Conclusions: Our data suggest that Dclk1+ cell-specific NF- κ B signaling is protective against colitis and CAC. Targeting this pathway may reduce colitis severity and CAC.

Angela Guo

High oncostatin-M predicts non-response to tumor necrosis factor- α antagonists in inflammatory bowel disease

Dr. Aze Wilson, Angela Guo, Ross C, Chande N, Gregor J, Ponich T, Khanna R, Beaton M, Kim RB

The cytokine Oncostatin-M (OSM) has been associated with response to tumor necrosis factor- α antagonists (anti-TNFs) in small cohorts of patients with inflammatory bowel disease (IBD). We aimed to further evaluate the association between plasma OSM concentrations and response to anti-TNFs (infliximab and adalimumab) in addition to other clinical outcomes in both ulcerative colitis (UC) and Crohn's disease (CD). A retrospective cohort study was carried out in patients with IBD with a history of anti-TNF exposure. Blood samples, collected prior to anti-TNF exposure, were analyzed by enzyme-linked immunosorbent assay for the presence and quantity of OSM. The

primary outcome evaluated was clinical remission at 1-year based on the Harvey Bradshaw Index (HBI, remission, HBI<5) for CD and the Partial Mayo Score for UC (remission, Partial Mayo Score<2). 114 patients with IBD (CD, n=73; UC, n=40) seen at a tertiary care centre in London, Ontario Canada, were included in the analyses. Patients received one of infliximab (n=61) or adalimumab (n=53). For those with UC achieving clinical remission at 1-year (n=24), the mean OSM concentration was 84.5±119.7pg/ml versus those not achieving clinical remission (n=16) where the mean OSM concentration was 1064.0±958.8pg/ml (p<0.0001). For those with CD, the mean OSM concentration was 116.3 ± 222.3pg/ml in those achieving clinical remission (n=52) versus those who did not (n=22) where the mean OSM concentration was 1220.0 ± 1274.0pg/ml (p<0.0001). In conclusion, OSM plasma concentrations were associated with response to anti-TNFs at 1-year in IBD.

Brook Hadwen

Baseline Characteristics Associated with Hypertension in an Early Rheumatoid Arthritis Cohort

Brook Hadwen, Saverio Stranges, Neil Klar, Bindee Kuriya, Janet E. Pope, Susan Bartlett, Gilles Boire, Louis Bessette, Carol A. Hitchon, Glen Hazlewood, Edward C. Keystone, Orit Schieir, Carter Thorne, Diane Tin, Marie-France Valois, Vivian Bykerk, Lillian Barra

Background: It is not well understood why hypertension (HTN) is more common in rheumatoid arthritis (RA) patients than in the general population. **Objective:** This study explored the prevalence of HTN at time of RA diagnosis and which demographic, behavioural and clinical characteristics were associated with HTN. **Methods:** Data from the Canadian Early Arthritis Cohort (CATCH) were used to analyze baseline characteristics associated with HTN. Univariate and multivariate logistic regression models were conducted. Variables included age, sex, race, body mass index (BMI), education, smoking, alcohol servings, seropositivity, disease activity and comorbidities. **Results:** In total, 2052 subjects were included with mean(±SD) age of 55(±14) years and symptom duration mean(95%CI) was 5.60(5.47, 5.73) months, 71% of subjects were female and 85% were Caucasian. HTN was reported in 26% of subjects at baseline. In univariable analysis, older age, being male, lower education, ever smoking, high BMI, diabetes, hyperlipidemia, worse RA disease activity, longer duration of RA symptoms, being seronegative, using NSAIDs and corticosteroids were associated with having HTN. In multivariable analysis [OR(95%CI)] HTN was associated with older age [2.26(1.65, 3.11)], overweight BMI [1.63(1.10, 2.43)], diabetes [3.20(1.99, 5.15)], hyperlipidemia [2.80(1.94, 4.02)], and being seronegative [0.64(0.44, 0.92)]. **Conclusion:** Early in the RA disease course, approximately 1 in 4 had HTN. At the time of RA diagnosis, those with traditional cardiovascular risk factors were most likely to also have

HTN. Characteristics associated with HTN later in RA disease course will be further explored.

Fahad Hannan

Brain structure and function in patients with Thrombotic Thrombocytopenic Purpura (TTP)

Fahad Hannan, Drs. Susan Huang and Jonathan Thiessen

Immune-mediated Thrombotic Thrombocytopenic Purpura (iTTP) affects an individual's hemostasis, the process of preventing bleeding in a damaged blood vessel. A patient with iTTP have the protein a disintegrin-like and metalloprotease with thrombospondin type 1 repeats 13(ADAMTS13), which regulates blood clotting, inhibited. This leads to spontaneous blood clotting which deprives tissues of oxygen. While, studies have shown patients in remission suffer from neurological impairment, the exact effects iTTP has on the brain are not well known. In an effort to understand these effects, two pilot studies have been conducted. One including Computed Tomography (CT) Perfusion and another involving a comprehensive Magnetic Resonance Imaging (MRI) study along with an online cognitive test and a depression assessment. Early results indicate patients have an increase in blood brain leakage, lesions in the brain, a decrease in myelin and experience mild depression. This research aims to develop advanced analysis techniques and comparisons of quantitative MRI sequences. These techniques include Myelin Water Imaging (MWI) and their depression scores and cognitive changes. This pilot study will include 10 patients with iTTP. Measurements will be taken after their iTTP episodes and 6 months after. In the long run, the technique we develop will help determine what impairments can be caused by iTTP, how do they progress, and how they affect the cognitive state of an individual. Notably, these techniques will efficiently determine changes in brain function and structure, allowing for prevention methods to be investigated.

Emily Heath

A comparative analysis of drug therapy, disease phenotype, and health care outcomes for men and women with inflammatory bowel disease

Emily Heath, Richard B. Kim, Aze Wilson

Background: Sex and gender refer to biological and social differences between men and women. While well-evaluated in other disciplines, roles of sex and gender in inflammatory bowel disease (IBD) are not well-defined. This study aimed to characterize differences in healthcare outcomes in men and women with IBD. Methods: A retrospective single-centre cohort study was conducted to evaluate differences between

men and women receiving care for Crohn's disease (CD) and ulcerative colitis (UC) at the Western University Personalized Medicine Clinic from March 2012 to September 2019. Primary endpoint was the proportion of IBD drugs used for all drug classes. Secondary outcomes included adverse drug reactions (ADRs). Student's t-test and Fisher's exact test were used to assess differences. Results: 1015 total participants were included (CD=656; UC=359). In UC 47.9% were women, in CD 59.0% were women. Overall, women were more likely to be prescribed budesonide (23.6% vs. 13.4%; $p<0.0001$), while more men were exposed to prednisone for IBD management (73.5% vs. 67.4%; $p=0.04$). Immunomodulator use was higher in men with CD versus women (86.6% vs. 78.3%; $p=0.008$) and of those exposed, women more commonly experienced ADRs (29.5% vs. 21.2%; $p=0.01$). Though no sex-related difference was found, age was a predictor of biologic exposure in women with CD and men with UC, with those >55 less likely to receive biologics. Conclusion: These findings highlight differences in disease course and treatment approaches between men and women with IBD and support the consideration of sex and gender when researching disease outcomes.

Zaid Hindi

NO EVIDENCE OF A FRIDAY EFFECT ON COLONOSCOPY QUALITY OUTCOMES

Zaid Hindi, Cassandra McDonald, Leonardo Guizzetti, Sarah cocco, Mayur Brahmania, Aze Wilson, Brian Yan, Vipul Jairath, Michael Sey

Background: Colonoscopy quality may be influenced by operator fatigue. Prior studies have shown lower adenoma detection rates for procedures performed at the end of the day. However, it is unknown if colonoscopy quality is impaired at the end of the work week. Aims: We investigated whether colonoscopy quality-related metrics differ at the end of the work week. Methods: Between April 2017 to October 2018, 45,510 consecutive colonoscopies from 20 academic and community hospitals in our region were captured to form the cohort. The primary outcome was adenoma detection rate (ADR), and secondary outcomes were sessile serrated polyp detection rate (ssPDR), polyp detection rate (PDR), and failed cecal intubation. Outcomes were presented as unadjusted and adjusted risk ratios adjusting for physician-level clustering, and characteristics of the patient, procedure and physician. Results: During the observation period, 9,132 colonoscopies were performed on the last day of the work week compared to 36,378 procedures during the rest of the work week. After adjusting for potential confounders, there were no significant differences in the ADR (RR 1.01, 95% CI [0.88, 1.15], $p=0.94$), ssPDR (RR 0.90, 95% CI [0.70, 1.14], $p=0.38$), PDR (RR 1.00, 95% CI [0.92, 1.09], $p=0.94$), or failed cecal intubation (RR 0.92, 95% CI [0.72, 1.18], $p=0.51$) for colonoscopies performed on the last day of the work week compared to the rest of week. Conclusions: Colonoscopy quality metrics, including ADR, ssPDR, PDR, and failed cecal intubation are not significantly different at the end of the week.

Nisha Howarth

Transjugular intrahepatic portosystemic shunt for refractory ascites: liver-transplant free survival rate in the London Health Sciences Centre cohort

Nisha Howarth, Sebastien Robert MD, Mitali Chaudhary BSc, Mayur Brahmania MD MPH, David Peck MD, Amol Mujoomdar MD, Derrick Cool MD PhD, David Hocking MD, Anouar Teriaky MD MPH, Karim Qumosani MD, Ephraim Tang MD Msc, Anton Skaro MD PhD

Background: Refractory ascites (RA) is a complication of portal hypertension bearing significant morbidity for patients. Classically, RA is treated with diuretics and serial large volume paracentesis (LVP), however recent randomized control trials have demonstrated that transjugular intrahepatic portosystemic shunts (TIPS) have improved control of RA compared to serial LVP. A database of patients who received a TIPS at LHSC between the years of 2014-2020 was created. Our objective was to observe the liver transplant-free survival rate in our cohort of patients who received TIPS for RA. **Methods:** We conducted a retrospective, observational study investigating adult patients who underwent a TIPS procedure for RA. Patients were eligible for inclusion if they had the TIPS between 2014-2020. This time frame was chosen as it was when our centre began performing TIPS with ePTFE-covered stents. Liver transplant-free survival was assessed using Kaplan-Meier curves. **Results:** 152 patients had TIPS at LHSC between 2014 and 2020. Of this group, 72 patients had TIPS for RA. [The remainder of the results will be included prior to Resident Research Day]. **Conclusion:** TBD

Stella Iankov

Prevalence of Bundle Branch Block in Heart Failure Patients

Stella Iankov, Anthony Tang

Heart Failure (HF) is an epidemic in the developed world and will continue to increase in prevalence. HF patients are classified as HF with reduced EF (HFrEF), mid-range EF (HFmrEF) and preserved EF (HFpEF) based on their Left Ventricular Ejection Fraction (LVEF). Bundle Branch Block (BBB) has a known prognostic significance in the HFrEF population, however little is known of its role in HFmrEF and HFpEF. The goal of the present study is to retrospectively determine the prevalence of Left and Right BBB (LBBB and RBBB, respectively) in patients with HFpEF, HFmrEF, and HFrEF attending the Saint Joseph's HF clinic prior to August 2020. Data collected from each patient will include: age, sex, LVEF, comorbidities (atrial fibrillation, COPD, TI/TI+DM, sleep apnea, hypertension, coronary artery disease, prior stroke, prior MI, coronary artery bypass graft, percutaneous coronary intervention, anemia, chronic kidney disease), baseline and subsequent electrocardiograms, health care utilization (hospitalizations, ER visits), and mortality. Of the 238 patients enrolled thus far in the study, 112(47%) have HFrEF, 50(21%) have HFmrEF and 76(32%) have HFpEF. Of the HFrEF, HFmrEF and HFpEF

patients 23(20.5%), 5(10%) and 5(6.57%) have LBBB respectively. Of the HFrEF, HFmrEF and HFpEF patients, 9(8%), 6(12%) and 6(7.89%) have RBBB, respectively. In the future, the prevalence of co-morbidities and the prognostic impact of BBB on HF patients will be examined. This research will provide insight into the prevalence and prognostic implications of BBB in HF patients in a local context.

Gabriella Jacob

The association between orthostatic hypotension and gait in cognitively impaired elderly adults

Gabriella Jacob, Malcolm Sherwood, Shahbaz Malik, Jacquie Baker, Jaspreet Bhangu

Orthostatic hypotension (OH) is associated with increased fall risk; however, the associations between gait and OH in patients with cognitive impairment (CI) remains unclear. The purpose of this study was to test the hypothesis that gait speed and dual task gait speed were slower in CI patients with concomitant OH. A retrospective analysis of a sample of participants from the Canadian Consortium of Neurodegeneration and Aging (n=246) was performed. To confirm a diagnosis of OH, heart rate and blood pressure was measured supine and after 3 minutes of standing. Single factor ANOVA was used to compare patients with (n=39) and without OH (n=207). A secondary analysis was performed comparing those with CI+OH to healthy controls (HC+OH). Patients with OH demonstrated slower mean gait speed (5.8 ± 1 seconds) compared to patients without OH (5.6 ± 1.5 seconds; $p=0.55$). Patients with OH also demonstrated slower mean dual task gait speed (6.9 ± 1.7 seconds) compared to those without (6.5 ± 2.3 seconds; $p=0.26$). There were no statistically significant differences detected between patients with CI+OH compared to HC+OH. Patients with OH demonstrated slower mean gait and dual task gait speed. These parameters failed to reach statistical significance; however, this may be due to small sample size. OH remains an important clinical risk factor in individuals with cognitive impairment; however the factors that may pre-dispose an individual to increased fall risk remains unclear. We have demonstrated important signals that warrant further analysis with a larger cohort.

James Jae

Vasodilatory shock from rilmenidine and doxazosin overdose

James Jae, Daniel Ovakim & George Dresser

Rilmenidine is a centrally acting antihypertensive agent with significant affinity for the Imidazoline (I1) receptors in the lateral reticular nucleus of the brainstem. This results in reduced sympathetic tone and total peripheral resistance. It may also bind selectively to I1 receptors in the kidneys and inhibit the sodium-hydrogen antiporter in the proximal convoluted tubule, leading to a reduction in sodium and water retention. In the recommended dosage range (1 to 2 mg daily), the drug is safe and well tolerated. To date, there have been no cases of overdoses reported in the literature, likely due to limited availability of this agent in many parts of the world. The objective of this review is to describe a case of rilmenidine overdose associated with profound vasodilatory shock. This patient survived a massive overdose of rilmenidine and doxazosin, presenting as profound shock and CNS depression. Attentive support care of airway, breathing, and circulation as well as gastric decontamination on initial presentation was vital in her improvement. Although she was dialyzed for anuric renal failure, we do not believe this intervention played a major part in her recovery as rilmenidine is poorly dialyzed. This review should serve as a caution to clinicians of the significant effects of rilmenidine overdose.

James Jae

Posterior reversible encephalopathy syndrome (PRES) from acetaminophen-induced hepatorenal failure

James Jae, Constance Mackenzie & Daniel Ovakim

Massive acetaminophen overdose is an established cause of acute hepatic and renal failure. However, literature linking acetaminophen-induced hepatorenal failure to posterior reversible encephalopathy syndrome (PRES) is sparse. PRES is a condition characterized by reversible, acute cortical and subcortical vasogenic edema, mainly in the parieto-occipital regions. Afflicted patients present with encephalopathy, seizures, and visual disturbances. The objective of this review is to describe a case of PRES associated with acetaminophen-induced hepatorenal failure. The patient experienced status epilepticus in the context of a medication error involving acetylcysteine wherein the 4-hour loading dose (60 mg/kg/hr) was given continuously for a total of 14 hours. She received a total of 44.5 grams (840 mg/kg) of IV acetylcysteine instead of 19.1 grams (360 mg/kg) over 14 hours. Acetylcysteine overdose was initially considered a potential culprit. But her subsequent MRI showed hyperintensity in the posterior parietal and occipital lobes suggestive of PRES, which may be incited by acetaminophen-induced hepatorenal failure. Acetylcysteine was resumed as she developed acute liver failure. Seizures were treated with anticonvulsants; blood pressure was controlled with

labetalol. Despite her delayed presentation and administration of acetylcysteine, this patient experienced a tremendous improvement of her hepatic and neurologic function after a week, although she remains on dialysis. This case highlights the need to consider PRES when patients with acetaminophen overdose experience acute neurologic deterioration. We believe addressing underlying causes, blood pressure control, and fluid restrictive strategy are vital in treatment of these patients.

Atul Jaidka

In-Plane, Dynamic Ultrasound Guided Pericardiocentesis with Micropuncture Kit is a Safe and Practical Technique: Case and Tutorial

Atul Jaidka, Pavel Antiperovitch, Rachel Green, Elizabeth King, Sabe De

Case Eighty-two year old male with a history of gastroesophageal adenocarcinoma presented with 2 weeks of progressive shortness-of-breath. The patient had stable vitals, elevated JVP and mild peripheral edema. Investigations revealed unremarkable blood work and enlarged cardiac silhouette on chest x-ray. Imaging Transthoracic echocardiography showed a large circumferential pericardial effusion with early signs of tamponade, with largest pocket in the lateral/posterior regions. POCUS with a linear probe revealed the apical window as the most superficial approach while avoiding the lungs. Micropuncture needle was used to access the effusion under dynamic ultrasound guidance and confirmed with bubble study. Discussion Ultrasound guided pericardiocentesis has become the standard of care for pericardiocentesis. Our goal is to show that in-plane, dynamic ultrasound guided pericardiocentesis with micropuncture (MPT) kit is a safe and practical technique and provide a high-quality educational demo on its performance. Full study available at www.cardioguide.ca/pericardiocentesis. Dynamic ultrasound guided pericardiocentesis has been studied and shown to be potentially safer by reducing myocardial puncture and avoiding other structures. It may be beneficial in accessing small effusions as the needle is dynamically guided into the fluid. There has been limited generalizability given requirements of needle holders and multiple operators. With the proliferation of POCUS, new studies have shown that a single operator technique without needle holders is possible. In addition, MPT provides several potential benefits: decreased risk of complications, given the smaller 21-gauge needle, and convenient performance of the bubble study, which can be performed through MPT sheath.

Tyler James

Ring Sideroblast Quantification in Patients with SF3B1 Mutation and Myelodysplastic Syndrome: A Retrospective Chart Review

Tyler James, M.D., Benjamin Chin-Yee, M.D. Ian Chin-Yee, M.D. Bekim Sadikovic, PhD. Ben Hedley, PhD. Cyrus Hsia, M.D.

Introduction: Myelodysplastic syndrome (MDS) occurs when impaired hematopoiesis causes dysplastic cytopenias potentially causing blood transfusion dependency. MDS with ring sideroblasts (MDS-RS) is a subtype diagnosed on bone marrow aspirate showing either i) $\geq 15\%$ of erythroid precursors with ring sideroblasts or ii) 5-14% ring sideroblasts and the SF3B1 mutation. In 2020, the MEDALIST trial showed patients specifically with MDS-RS subtype have decreased transfusion dependency with use of a novel medication, Luspatercept, that reduces late stage erythropoiesis inhibition. However, ring sideroblasts are routinely only reported when $\geq 15\%$ and the SF3B1 mutation is not routinely tested. Therefore, patients with SF3B1 mutations and 5-14% ring sideroblasts are commonly not identified for eligibility for Luspatercept. Unlike other Canadian centers, London Health Sciences Centre completes genetic testing on all bone marrow specimens for MDS which includes the SF3B1 mutation. We are uniquely poised to identify all MDS patients that have the SF3B1 mutation. Methods: The Next Generation Sequencing (NGS) database will be used to select MDS patients from 2018-2020 that possess the SF3B1 mutation. The bone marrow aspirates will be reviewed by two independent hematologists to enumerate ring sideroblasts. Results: Eighty-seven of the 2023 patients in the NGS database have the SF3B1 mutation. Of which, 46 had a diagnosis of MDS with 30 patients already having $\geq 15\%$ ring sideroblasts. We will next enumerate ring sideroblasts for the remaining 16 patients. Conclusion: This work aims to quantify patients currently being missed by Canadian laboratory reporting practices that may benefit from Luspatercept to reduce blood transfusion dependency.

Devika Jayawardena

The role of the TIMP/metalloproteinase balance in human septic PMVEC barrier dysfunction

Devika Jayawardena, Lefeng Wang, Cynthia Pape, Sanjay Mehta, Sean Gill

Sepsis, a life-threatening human disease characterized by excessive inflammation. During sepsis, endothelial cells, especially pulmonary microvascular endothelial cells (PMVEC), become injured leading to loss of barrier function and organ damage. Metalloproteinases, including matrix metalloproteinase (MMP) and disintegrin and metalloproteinase (ADAM), are capable of cleaving cell surface proteins. Metalloproteinase activity is regulated by tissue inhibitors of metalloproteinases (TIMPs). Recently, we demonstrated that expression of metalloproteinases and TIMPs in mouse PMVEC changes under septic conditions. We hypothesize that human septic

PMVEC permeability will be reduced by the application of synthetic metalloproteinase inhibitors. Isolated human PMVEC were stimulated with PBS (basal) or cytomix (septic; equimolar tumour necrosis factor alpha, interferon gamma, and interleukin 1beta). RNA was isolated, gene expression examined by RNA-Seq, and data analyzed using Partek Genomics Suite. Trans-PMVEC macromolecular flux was assessed. The role of metalloproteinases in PMVEC permeability was assessed by treatment with synthetic metalloproteinase inhibitors. RNA-seq identified more than 3300 genes differentially expressed in cytomix-treated PMVEC. Functional enrichment analysis revealed multiple pathways that were significantly enriched. ADAMTS family appeared to have significantly altered. Septic conditions were also associated with disruption of junctional proteins and increased permeability. The application of synthetic metalloproteinase inhibitors reduced the permeability and disruption of junctional protein degradation. Changes in metalloproteinase expression was associated with disruption of junctional protein localization and loss of barrier function. This suggests that metalloproteinases are critical mediators of barrier dysfunction. Inhibition of metalloproteinase activity reduced the permeability. These studies suggest that inhibition of metalloproteinase activity may promote PMVEC barrier function.

Nessika Karsenti

Diagnostic Accuracy of Laboratory Assays for SARS-CoV-2: A Systematic Review and Narrative Synthesis

Nessika Karsenti, Sameer Elsayed

This systematic review was conducted to determine the performance characteristics of currently available commercial and in-house laboratory diagnostic assays for SARS-CoV-2 by evaluating accuracy, sensitivity, and specificity in relation to validated RT-PCR assays and/or radiological methods. We searched Medline® and Embase® databases from January 1, 2020 to June 23, 2020. Two-stage screening of retrieved papers (title and abstract, then full text) was independently performed by two investigators, as was extraction of information from the full text of each included paper. We also conducted QUADAS-2 risk of bias assessments for included papers, performed independently by two investigators. A total of 84 papers were retained for this review after exclusions. Overall, the risk of bias for the patient selection, index test, reference standard, and flow and timing domains was low in 6/84 (7.1%), 13/84 (15.5%), 66/84 (78.6%), and 13/84 (15.5%) of the studies, respectively. Median accuracy, sensitivity, and specificity across each RT-PCR method ranged from 84.2% to 100%, 76.4% to 100%, and 85.0% to 100%, respectively. For each component immunoassay, median accuracy, sensitivity, and specificity during the first week of illness ranged from 41.2% to 89.4%, 4.1% to 56.1%, and 91.7% to 100%, respectively. We noted significant heterogeneity in patient selection, choice of reference standard, and index test interpretation across all types and technologies. Although molecular diagnostic methods

appear to be superior to immunodiagnostic assays for early diagnosis of COVID-19, higher quality studies assessing the performance characteristics of laboratory diagnostic assays for the diagnosis of COVID-19 are required.

Shayan Kassirian

Effect of Needle Size on Diagnostic Sensitivity of Endobronchial Ultrasound-Transbronchial Needle Aspiration (EBUS-TBNA) in Sarcoidosis: A Systematic Review and Meta-analysis

Shayan Kassirian, Stephanie N. Hinton; Alla Iansavitchene; Kayvan Amjadi; Alex Chee; Inderdeep Dhaliwal; Michael A. Mitchell

Background: Sarcoidosis is a multisystem disease characterized by non-caseating granulomatous inflammation that most commonly involves the lungs. Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) has become an invaluable tool in the assessment of patients with mediastinal and/or hilar lymphadenopathy. It has been hypothesized that use of the larger 19-gauge (G) needle with EBUS-TBNA improves diagnostic sensitivity in sarcoidosis. However, it is unclear whether the existing literature supports this supposition. Methods: A literature search of EMBASE, MEDLINE, Cochrane Library, and Google Scholar was performed by two reviewers. Included articles were evaluated for bias using the QUADAS-2 tool. For quantitative analysis, we performed a meta-analysis using a binary random-effects model to determine pooled sensitivity. Subgroup analysis was performed based on needle size, use of ROSE, study design, and prevalence of sarcoidosis in study group. Results: Sixty-five studies with a total of 4242 patients were included in the meta-analysis. Overall pooled sensitivity for diagnosis of sarcoidosis was 83.99% (95% CI 81.22 - 86.53) among all studies. The 19G subgroup had a significantly higher sensitivity (93.73%; 95% CI 89.72% - 97.74%; I² 0.00%; p<0.01) compared to 21G subgroup (78.52%; 95% CI 66.89% - 90.15%; I² 93.05%), 22G subgroup (84.07%; 95% CI 80.90% - 87.24%; I² 85.21%) or unspecified 21G/22G subgroup (78.85%; 95% CI 70.81% - 86.90%; I² 84.47%). There were no significant differences with use of ROSE, prevalence of sarcoidosis or by study design. Conclusion: The use of 19G needles during EBUS-TBNA appears to improve diagnostic sensitivity and should be considered in patients with suspected sarcoidosis.

Nadine Khalil

The Association Between Individual Drugs Injected Intravenously and the Development of Right vs Left-sided infective Endocarditis

Nadine Khalil, MD, Rochelle Johnstone, MD; Esfandiar Shojaei, MD; Lise Bondy, MD; Sharon Koivu, MD; and Michael S. Silverman, MD, FRCP

Objectives: The development of infective endocarditis in persons who inject drugs (PWID) is associated with significant morbidity. Many studies have suggested that endocarditis in PWID is predominantly right sided while other studies suggest left sided. We hypothesized that the differences in results may be related to the type of drug most commonly injected. Stimulants can have marked impact on hemodynamics and may predispose to left sided valvular damage. Injection of opiates is associated with poor solubility with large particles leading to tricuspid valvular damage and predisposition to right sided disease. **Design:** This case series studied PWID for first episode of endocarditis from April 2007 - March 2016. Participants were adults (age >18) admitted to hospitals in London, ON. Main outcomes measured were valvular site of endocarditis, survival among PWID, causative organisms, cardiac and non-cardiac complications, referral to addiction services, and medical vs. surgical management. **Results:** There were 370 cases of first episode IEs, 261 (54.6%) of which were in PWID. From those who injected only opioids, 48 (70%) developed right sided IE, 17 (25%) developed left sided IE, and 4 (6%) had bilateral IE. From those who injected only stimulants, 11 (46%) developed right sided IE, 11 (46%) developed left sided IE, and 2 (8%) had bilateral IE. **Conclusions:** This study demonstrates an association between right and left sided infection and type of drug use. As the epidemic of crystal methamphetamine injection continues to grow the rate of left sided disease with its attendant higher morbidity and mortality may also grow.

John Krakovsky

The lipid profile of individuals with the APOE c.T137C:p.L46P mutation

Krakovsky J, McIntyre AD, Hegele RA

BACKGROUND: Certain variants of apolipoprotein E, encoded by the APOE gene, have been associated with lipid disorders. Previously, there has been contradictory evidence regarding the association between the rare pL46P substitution and dyslipidemia. The purpose of this study is to analyze the lipid profile of patients with the APOE cT137C:pL46P missense mutation to identify an association with a specific phenotype. **METHODS:** Next generation sequencing was performed on patients seen in the Lipid Genetics Clinic in London, Ontario since 1998. Patients heterozygous for the APOE cT137C:pL46P mutation were identified. Untreated lipid profiles were imputed and compared with healthy controls. **RESULTS:** A total of 9 patients met the inclusion/exclusion criteria. Mean total cholesterol, triglycerides, HDL-C and LDL-C in

mutation-positive subjects were 6.83 ± 1.84 , 2.91 ± 1.67 , 1.03 ± 0.28 and 4.30 ± 1.90 mmol/L, respectively. In controls, the mean values were 4.81 ± 0.82 , 1.05 ± 0.37 , 1.27 ± 0.41 and 3.18 ± 0.83 mmol/L, respectively ($P < 0.05$ for all except HDL-C). The pL46P allele frequency in patients with dyslipidemia was 0.74% compared with 0.25% in the general population (odds ratio, 2.96; 95% CI, 2.06 to 4.24; $P < 0.05$). 55.6% of mutation-positive individuals had clinical evidence of coronary artery disease with an average age of onset of 62.2 ± 12.9 years. **CONCLUSIONS:** Individuals with this mutation were found to have elevated LDL-C and triglycerides, suggesting an association with combined hyperlipidemia. Patients referred with dyslipidemia were significantly more likely to have this mutation compared with the general population. This rare mutation can be considered in diagnostic genetic screening in patients with hypertriglyceridemia and hypercholesterolemia.

Catherine Lang

Right-sided infective endocarditis: A review of demographics, risk factors, imaging and complications in this unique population

Catherine Lang, Dr. Michael Silverman

Traditional research has focused on left-sided infective endocarditis (IE), however as risk factors for right-sided disease, such as intravenous drug use, continue to grow, an increased focus on this unique disease entity is warranted. This study aims to describe a large cohort of patients meeting modified Dukes criteria for definite IE. Five-hundred and seventy-seven patients with 685 unique episodes of IE were identified, including 297 (43.4%) episodes involving purely right-sided IE (RSIE). For pure RSIE, the average age at admission was 36.2 years and 54.9% were females. The main risk factors were intravenous drug use (90.1%) and history of previous endocarditis (29.6%). *Staphylococcus aureus* was the main microorganism implicated (59.9% MSSA, 22.6% MRSA); however fungal (2.4%) and polymicrobial (7.4%) infections were increasingly clinically important pathogens. There were 301 episodes initially identified as RSIE-only via transthoracic echocardiogram (TTE). Of these, 114 went on to have a transesophageal echocardiogram (TEE). Only 4 (3.5%) ultimately showed missed left-sided disease on TEE, thus suggesting that a 2-week course of appropriate antibiotics is likely sufficient when TTE identifies only RSIE. Finally, pure RSIE was not only associated with respiratory findings (77.4%) but also with systemic findings (19.6%). Systemic findings were thought to arise from either bacterial seeding (69.5%), embolic phenomenon (10.2%) or both (20.3%). For pure RSIE with systemic findings thought to arise from embolic phenomenon, although 55.6% had TEEs confirming no left-sided disease, it may still be reasonable in this subset to complete a full 6-week course of antibiotics for presumed left-sided disease.

Frederikke Larsen

Hypomethylation of Dclk1+ tuft cells inhibits colitis-associated colorectal cancer

Frederikke Larsen, Hayley Good, Alice Shin, Liyue Zhang, Samuel Asfaha

Background: Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the intestine. A major complication of IBD is colitis-associated cancer (CAC). We previously showed that upon deletion of the Apc gene, tuft cells, a rare epithelial cell type, can serve as the cellular origin for CAC in the presence of colitis. The mechanism by which colitis leads to the transformation of tuft cells, however, is unknown. Interestingly, IBD and CAC are characterized by epigenetic changes that modulate gene expression. Specifically, changes in DNA methylation are described to occur in both diseases, but if and how these changes contribute to tuft cell transformation is not known. In this study, we investigated the role of DNA methylation in CAC. Methods: Dclk1CreERT2/Apcf/f mice were treated with tamoxifen to induce APC-loss, followed by 2.5% dextran sodium sulfate (DSS) to induce colitis and the DNA demethylating agent 5-AZA-2'-deoxycytidine (5-AZA-CdR) or vehicle weekly for six weeks. Sixteen weeks after tamoxifen, colonic tumors were quantified, and histology examined. Additionally, Dclk1CreERT2/Apcf/f/Dnmt1f/f mice were treated with tamoxifen followed by 2.5% DSS. Sixteen weeks after tamoxifen, tumors were quantified. Results: Mice receiving 5-AZA-CdR or with DNMT1 loss in DCLK1+ cells had significantly reduced colonic tumor number and tumor size when compared to control mice. Discussion and conclusions: Our findings suggest that inhibition of DNA methylation inhibits colonic tumor formation arising from Dclk1+ tuft cells. These data suggest that DNA methylation plays an important role in inflammation-associated tumorigenesis and may provide a novel strategy for the prevention of CAC.

SiuYuZoe Lau

Dyspnea in a patient with asthma, interstitial lung disease, and dermatomyositis

Siu Yu Zoe Lau, Lawrence Jacobs

We describe the case of a 32 year old woman with interstitial lung disease (ILD) secondary to dermatomyositis and severe asthma who presented with 2 months of progressive dyspnea and hypoxemia while on rituximab, prednisone, and omalizumab. She had presented to care multiple times before and several investigations revealed no clear cause. Most recently, she was treated for an ILD flare with higher doses of prednisone but still became further dyspneic and hypoxemic. Repeat CT chest revealed bilateral cystic lung changes, and thus the top differentials were Pneumocystis jirovecii pneumonia (PJP) and lymphangiomyomatosis (LAM). Bronchoalveolar lavage (BAL) subsequently confirmed PJP. She had been trialed on PJP prophylaxis before but developed adverse reactions to sulfamethoxazole-trimethoprim and dapsone, and thus was ultimately treated with methylprednisolone and atovaquone. Clinicians should

consider PJP as a cause of progressive dyspnea and hypoxia in patients with rheumatologic conditions and immunosuppression.

Sharon Lee

Suboptimal glycemic control and pregnancy outcomes in emerging adults 18-25 years old with diabetes

Sharon Lee, Selina Liu, Ruth McManus, Tamara Spaic

Background: Pre-existing diabetes is associated with increased pregnancy complications, including fetal malformations, hypertension, perinatal mortality, preterm delivery, and macrosomia. Optimal glycemic control before and during pregnancy is paramount. "Emerging adulthood" , a developmental stage between ages 18-25 is a challenging period for diabetes care, associated with worse health outcomes, that can be further complicated by pregnancy Objective: To characterize pregnant emerging adult-age women with pre-existing diabetes followed by the SJHC Endocrine Pregnancy Clinic (EPC) and describe their antenatal diabetes management and pregnancy outcomes. Methods: Pregnant women aged 18-25 with pre-existing type 1 or 2 diabetes who attended the SJHC EPC from January 1, 2012 - December 31, 2016 were included. Clinical characteristics of their pregnancy care and outcomes were collected. Descriptive statistics were summarized. Results: There were 66 pregnancies among 58 women, including 1 twin pregnancy. Of the 66 pregnancies, there were 53 (80.3%) documented live births, 10 (15.2%) miscarriages and 2 (3.0%) pregnancies terminated for severe congenital anomalies. Mean duration of diabetes was 8.1 years. Mean A1c at initial EPC visit was 8.1%. Mean A1c at last EPC visit was 7.6%. Folic acid use was documented in 57.6% of pregnancies. Mean GA at delivery was 36.4 weeks. 22.7% had preterm deliveries. 31.9% had macrosomia. 22.7% had pregnancy-induced hypertension/pre-eclampsia. Conclusion: Emerging adults with diabetes have suboptimal glycemic control in pregnancy. Although there is some improvement with close follow-up, there is a high prevalence of adverse outcomes. More studies are needed to determine if education programs for pregnancy planning may be useful.

Anna Liu

A rare case of prolactin-secreting pituitary carcinoma with epidural and thecal metastases

Anna Liu, Stan Van Uum, Donald Lee, Robert R. Hammond, Maria MacDonald, Shereen Ezzat, Kristin K. Clemens

Introduction: Pituitary carcinomas are rare (only 0.2% of pituitary tumours), but important due to their related morbidity and mortality. In this case, we highlight the signs and symptoms that should prompt a higher index of suspicion for this condition and review the treatment of prolactin-secreting pituitary carcinomas. Case: A 56-year-old man presented with erectile dysfunction and binocular vertical diplopia. He was found to have central hypogonadism, secondary adrenal insufficiency, and central hypothyroidism. His serum prolactin was 1517 (reference range 4-15) mcg/L and sellar MRI showed a 2 x 2.2 x 3.1 cm pituitary lesion. Pathology showed a prolactin-secreting tumour with a Ki-67 proliferation index of 20-25% and methylguanine-DNA methyltransferase (MGMT) of <10%. Despite treatment with high dose cabergoline, two transsphenoidal resections, and one course of radiation, prolactin levels continued to rise. Three years after diagnosis, he presented with lower extremity weakness and urinary incontinence. He had metastases to the epidural space and thecal sac extending from thoracic to sacral spine, and a 5.5 mm suspicious nodule inferior to the cerebellar tonsil. He received twelve cycles of temozolomide chemotherapy with initial clinical and biochemical response followed by relapse with continued disease progression. Discussion: We describe a rare case of pituitary carcinoma. Features that may suggest possible future malignant transformation include presentation in males >50 years old, progressive increase in prolactin despite dopamine agonist and surgical therapy, macro-tumour at presentation, and a high Ki-67 proliferation index. Low MGMT on pathology might predict initial response to temozolomide, with uncertainty on optimal treatment durability.

HsinYen Liu

Regression analysis in quality improvement: identifying waste to reduce length of stay in patients with heart failure

Hsin Yen Liu, Joseph Carson, Tim Rice, James Calvin

Background: A prolonged length of stay (LOS) leads to increased health care costs and is difficult for patients and families. For patients with congestive heart failure (CHF), research shows that LOS can be decreased without increasing 30-day readmission rates. Objectives: To conduct a root cause analysis for increased LOS and hospital costs in CHF patients and identify factors amenable to intervention using quality improvement methods. Methods: A retrospective chart review was performed on 1997 CHF hospitalizations at London Health Sciences Center (LHSC), between April 2017-April

2019. Increased costs was defined as exceeding the government-allocated payment. Univariate and multivariate logistic regressions were used to determine risk factors for increased LOS (>9 days) and costs. Sensitivity analyses used 6 or 7 days as the threshold for increased LOS. Statistical analyses were conducted using R 3.4.1. Results: The mean LOS was 9.6 days and median was 6 days. Among hospitalizations with LOS > 9 days, 93% had increased costs. Patients with increased LOS were more likely to be male, and have comorbidities, laboratory derangements, and inpatient procedures. In multivariate analysis, male sex, age, elevated urea, renal impairment, atrial fibrillation, echocardiography and cardiac catheterization were independent risk factors for prolonged LOS. Among 1244 hospitalizations with an echocardiogram ordered, having a delayed procedure (>48 hours) was independently associated with an increased LOS (P=0.001, OR= 1.6 [1.2-2.1]). Conclusions: This root cause analysis identified that delayed echocardiography was associated with increased LOS. Next steps involve designing and implementing a quality improvement project to reduce these delays.

Russell MacMillan

Does patient pancreatitis risk level determine selection of prophylactic interventions for post-ERCP pancreatitis?

Russell MacMillan, Erika Heckendorn, Terry Ponich

Post-ERCP pancreatitis (PEP) is a common complication of ERCPs leading to significant patient morbidity. ASGE/ESGE guidelines recommend pancreatic duct stent placement, rectal indomethacin (IND), and/or fluid hydration with lactated Ringer's (RL) or normal saline (NS) to prevent PEP. Recommendations regarding which intervention to use are based on patient's estimated PEP risk level and relevant patient comorbidities. We developed a patient PEP risk screening tool based on ASGE/ESGE guidelines and analyzed this with regards to PEP prophylactic interventions given in clinical practice. Retrospective chart reviews of ERCP patients were performed in a single clinician's practice at LHSC, between 2016-2019 to: 1) assess the PEP rate for different PEP prophylactic interventions; and 2) determine whether PEP interventions were given according to PEP risk level. Five hundred sixty-one patients who underwent ERCP were assessed using the PEP risk screening tool with 6.6% (37/561) developing post-ERCP pancreatitis. PEP rates were highest in patients who underwent pancreatic stenting (16.7%) or received IND (8.8%) +/- RL (11.2%). Using the risk screening tool, all patients receiving pancreatic stenting were deemed high risk. High PEP risk patients were roughly twice as likely to receive IND (OR 2.09, [CI] 1.36-3.21) compared to low PEP risk patients. Overall, using our PEP absolute risk screening tool, patients with a higher risk level generally were given pancreatic stents, rectal indomethacin +/- lactated Ringer's as expected. The observed elevated post-ERCP pancreatitis rates in patients

receiving these interventions might be partially explained by higher average PEP risk level among these patients.

Russell MacMillan

Developing and validating a patient risk assessment tool to predict post-ERCP pancreatitis

Russell MacMillan, Erika Heckendorn, Terry Ponich

Post-ERCP pancreatitis (PEP) is a common complication of ERCP, leading to significant patient morbidity. ASGE/ESGE guidelines emphasize assessing PEP risk among ERCP patients to initiate appropriate prophylactic measures. An ideal risk assessment tool has not yet been developed that accurately predicts PEP risk and most sensitively identifies patients likely to benefit from PEP prophylactic measures. Retrospective chart reviews of ERCP patients were performed within a single clinician's practice at the LHSC, Victoria Hospital, between 2016-2019. We developed a patient PEP risk screening tool based on ASGE/ESGE guidelines (patient and procedure, definite and likely, risk factors) and analyzed its accuracy predicting PEP rates in our clinical practice. We then identified the absolute risk score using that tool that most accurately identified high PEP risk patients. Five hundred sixty-one ERCP patients were assessed using PEP risk screening tool with 6.6% (37/561) developing PEP. Using the screening tool, 79.5% (446/561) were identified as high risk, using a cut-off score of 1. A cut-off score of 1 was associated with the best combination of sensitivity (95%) with specificity (22%). High PEP risk patients using a risk score of 1 was significantly linked to increased PEP rates in ERCP patients ($X^2 = 5.5$; $df = 1$, $p < .05$). Using our PEP risk screening tool with cut-off score of 1, the PEP risk screening tool was very sensitive at identifying patients who went on to develop PEP. We hope that, high-risk patient identification can be improved, to provide more targeted PEP prophylaxis.

Lorenzo Madrazo

"I'm not gaining anything out of this so why don't I just take a nap?": Insights on residency education during the COVID-19 pandemic

Lorenzo Madrazo, Grace Zhang, Kristen A. Bishop, Andrew Appleton, Mala Joneja, Mark Goldszmidt

Background: The COVID-19 pandemic has created unprecedented changes in the delivery of residency education. Gaining insight into how these changes have impacted resident learning experiences is an important step in adapting residency training to the ongoing pandemic. Methods: We conducted semi-structured group interviews with Ontario Internal Medicine (IM) residents between November 2020 and March 2021.

Interviewees were asked to describe their learning experiences as residents during the pandemic. Constructivist grounded theory guided the iterative data collection and analyses. Results: We interviewed 15 Ontario IM residents. Overall, participants perceived a decrease in the quality of their learning. As IM programs transitioned their in-person teaching sessions to virtual ones, participants felt the virtual sessions to be comparably inferior--perceiving loss in both education quality and socialization that come with in-person learning. While participants recognized the need to promote efficiency and safety in the clinical setting, they also lamented lost opportunities for direct observation and bedside teaching. Despite the perceived decrease in the quality of their education, only a few participants found alternative means of supplementing their learning. Conclusions: While disruptions to residency education and the urgent shift to virtual platforms were necessary measures to mitigate the health risks of the COVID-19 pandemic, our study suggests that our current adaptations are not feasible long-term solutions. We, therefore, need to properly adapt--rather than relocate--teaching for the virtual platform and find avenues to re-introduce bedside teaching safely as the pandemic remains a present reality.

Gurpreet Malhi

Invisible Colonic Malignancy and Possible Idiosyncratic Drug-Induced Liver Injury from Vedolizumab in a Patient with Ulcerative Colitis, Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome

Gurpreet Malhi, Matthew Cheah, Karim Qumosani, Aze Wilson, Reena Khanna

A 32-year-old Caucasian female with Ulcerative Colitis (UC) on vedolizumab (VDZ) with Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis (AIH) had multiple colonoscopies performed demonstrating multifocal low-grade dysplasia. However, she remained resistant to surgery. She presented to clinic with tea-coloured urine, fatigue, and scleral icterus. Investigations revealed conjugated hyperbilirubinemia with elevation in hepatocellular liver enzymes. Imaging was consistent with large duct PSC, and liver biopsy showed grade 2 chronic hepatitis raising the possibility of large bile duct obstruction. She underwent liver transplant assessment and VDZ was held. Her bilirubin and liver enzymes recovered. Given multiple colonoscopies showing multifocal dysplastic changes and the patient declining other biologics, she would ultimately undergo total proctocolectomy with end ileostomy. Pathology demonstrated mucinous adenocarcinoma with a signet ring component. Both mucinous adenocarcinoma and signet ring carcinoma are more aggressive malignancies associated with poor prognosis. Found more often in younger patients, they are often diagnosed in later stages with lymphovascular invasion. Here, there was no evidence of metastases in any of the 40 lymph nodes examined, which indicated more favourable prognosis. The mechanism by which VDZ potentially causes liver injury is unknown. Multiple therapies for PSC-AIH overlap and IBD were entertained as causative agents. However,

significant improvement in clinical symptoms and serologic parameters following cessation of VDZ was temporally suggestive. This case simultaneously highlights the importance of both timely colectomy in IBD patients with high-risk features during surveillance and early recognition and cessation of potential causative medications which induce liver injury.

Gurpreet Malhi

The impact of COVID-19 on the provision of care for patients with Inflammatory Bowel Disease: A cross sectional survey

G. Malhi, M. Mikail, J. Chambers, R. Khanna, A. Wilson

Background: The COVID-19 pandemic has shifted healthcare resource allocation toward treating those affected by the virus. We aimed to survey IBD patients to determine how they have been affected by changes to the provision of care due to the pandemic. Methods: A mixed methods survey was conducted with IBD patients who received care since March 17, 2019 in Canada. Results: 135 complete or partial responses were received, of which 90 responses were included. The majority of respondents were from Ontario, with a mean age of 42 years, and over 75% being female. 67% had Crohn's Disease, and 69% were on a biologic. Three percent of respondents stopped taking all IBD-related medications without the advice of their gastroenterologist due to pandemic-related concerns while 8% reported difficulty obtaining their medications. Thirty-eight percent reported a delay in being able to see their gastroenterologist, with a majority reporting a delay >4 weeks (n=21). twenty-three percent visited the emergency department for IBD-related concerns. Thirty-eight percent reported receiving poorer care since the pandemic began, while 36% reported no change. 76% of respondents used Telehealth for their appointments. Thirty percent preferred telehealth appointments to in-person visits. Half reported no change with their quality of interaction with their gastroenterologists. Conclusion: Preliminary data suggests patients experienced significant delays in IBD care during the pandemic, with more than one third reporting a reduction in the quality of that care. Further studies will help define whether there were a significant change in the number of hospitalizations due to this delay.

Gurpreet Malhi

Pivoting in a pandemic: The impact of COVID-19 on the provision of care for patients with Inflammatory Bowel Disease - A retrospective study

G. Malhi, J. Chambers, G. Minhas, M. Mikail, R. Khanna, A. Wilson

Background: COVID-19 was declared a worldwide pandemic in March of 2020. While the effect of COVID-19 has been felt amongst many patient populations, those with Inflammatory Bowel Disease (IBD) have been particularly impacted. We aimed to determine how the COVID-19 pandemic has affected IBD patients. Methods A retrospective cohort study was carried out in patients with an IBD diagnosis comparing patients admitted to two tertiary care centres affiliated with Western University in London, Canada between March 17 and August 31 2019 (2019 cohort or pre-pandemic), to patients admitted between March 17 and August 31 2020 (2020 cohort or pandemic). Patients were reviewed to assess any differences in care utilization and IBD-related outcomes. Results: A total of 863 patients were reviewed in 2019, and 554 in 2020. Of those, 184 (CD, n= 125; UC, n= 59) and 172 (CD, n= 109; UC, n= 62) were included. The length of stay in hospital was shorter in 2020 (6.88 days vs 9.63, p=0.045). Significantly fewer patients were initiated on Infliximab in hospital in 2020 (2020, 3.50 per month; 2019, 6.83 per month, p=0.001). Fewer in-patient surgeries were performed in 2020 (2019, 76; 2020, 57; p=0.112). Conclusion: Preliminary data demonstrate there was a significant reduction in the length of stay for patients with IBD as well as fewer patients initiated on infliximab while in hospital during the COVID-19 pandemic. These differences may reflect an effort to minimize contact between patients and health care facilities as well as reduce the introduction of further immunosuppression.

Aminmohamed Manji

The role of caspases in septic pulmonary microvascular endothelial cell barrier dysfunction

Aminmohamed Manji, Sanjay Mehta, Lefeng Wang, Cynthia M. Pape, Sean E. Gill

Sepsis, defined as multiple organ dysfunction due to a dysregulated host response to infection, contributes to 11 million deaths per year globally. Within the lung, septic organ dysfunction is associated with injury to pulmonary microvascular endothelial cells (PMVEC), leading to microvascular barrier dysfunction and accumulation of protein-rich edema fluid. Barrier dysfunction can arise through disruption of inter-PMVEC junctional proteins, such as vascular endothelial (VE)-cadherin. Previous studies identified a potential role for caspases in inducing endothelial barrier dysfunction. Caspases are multifunctional proteases that are known to cleave β -catenin, an adapter protein for VE-

cadherin. Pilot data from our lab demonstrated caspase-dependent cleavage of β -catenin in septic human PMVEC in vitro. Based on this, we hypothesize that septic endothelial barrier dysfunction is due to caspase-dependent cleavage of inter-PMVEC junctional proteins. Control (receiving PBS) and septic (receiving sepsis-relevant cytokines) mouse PMVEC will be treated with or without a broad-spectrum caspase inhibitor. Western blots and immunofluorescence will be performed to quantitatively and visually assess abundance and cleavage of inter-PMVEC adherens junction and tight junction proteins, including VE-cadherin and occludin, as well as associated adapter proteins, β -catenin, α -catenin, γ -catenin, and zona occludens 1-3. We will correlate these findings with macromolecular leak across the PMVEC monolayer, as assessed using Evans blue-labelled albumin. We anticipate septic PMVEC barrier dysfunction to be associated with increased cleavage of junctional proteins, which will be abrogated when treated with the caspase inhibitor. Our results may elucidate the mechanisms of sepsis-induced endothelial barrier dysfunction and may highlight a therapeutic target for treatment.

Eman Mansory

Venous Thromboembolism in Hospitalized critical and non-critical COVID-19 Patients: a systematic review and meta-analysis

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Introduction: Venous Thromboembolism has been observed as a frequent complication in patients with severe COVID-19 infection requiring hospital admission. Aim: To evaluate the epidemiology of venous thromboembolisms in hospitalized intensive care (ICU) and non-ICU patients. Materials and Methods: PubMed was searched up to 13th of Nov 2020 and updated in December 12th, 2020. We included studies that evaluated the epidemiology of VTE, including PE and/or DVT, in patients with COVID-19. Results: A total of 91 studies reporting on 35,017 patients with COVID were included. The overall frequency of VTE in all patients, ICU and non-ICU was 12.8% (95% CI 11.103 to 14.605), 24.1% (95% CI 20.070 to 28.280), and 7.7% (95% CI 5.956 to 9.700), respectively. PE occurred in 8.5% (95% CI 6.911 to 10.208), and proximal DVT occurred in 8.2% (95% CI 6.675 to 9.874) of all hospitalized patients. The relative risk for VTE associated with ICU admission was 2.99 (95% CI 2.301 to 3.887, P value <0.001). DVT and PE estimates in studies that adopted some form of systematic screening were higher compared to studies with symptom-triggered screening. Analysis restricted to studies in the 5th quintile of sample size reported significantly lower VTE estimates. Conclusion: This study confirmed a high risk of VTE in hospitalized COVID-19 patients specially those admitted to the ICU. Nevertheless, sensitivity analysis suggests that previously reported frequencies of VTE in COVID-19 might have been overestimated.

Leonardo MartinCalderon

Healthcare Utilization and Economic Burden in Scleroderma

Leonardo Martin Calderon, Mitali Chaudhary, Janet E. Pope

Background: Scleroderma (SSc) is a multi-system autoimmune disease, characterized by vasculopathy and fibrosis of internal organs and skin, associated with substantial morbidity and disability. Patients with SSc commonly require considerable healthcare resources resulting in significant economic impact. **Objective:** This systematic review aims to provide a narrative summary of the economic impact and healthcare resource utilization associated with SSc. **Methods:** MEDLINE and EMBASE were searched without language restriction from inception to January 20th, 2021. Studies were included if they provided information regarding total, direct, and indirect medical costs including medication, diagnostic test, and assistive devices costs. Costs of common SSc complications was additionally collected. Included observational studies had risk of bias assessments through the Joanna Briggs Institute cross-sectional and case series checklists, and the Newcastle-Ottawa Cohort and Case-Control study scales. **Results:** The search retrieved 1777 studies, of which 37 were included representing 19 cross-sectional, 13 cohort, 3 case series, and 2 case-control studies. Studies used various methods of calculating cost including bottom-up cost, humanistic approach, and health resource units cost analyses. Total annual medical cost ranged from €3017 to €22,459 in Europe, USD \$7478 to \$23,268 in North America, and AUD \$7060 to \$11,607 in Oceania. Annual cost for SSc associated with interstitial lung disease, pulmonary arterial hypertension was USD \$7336 to \$55,446 and \$7822 to \$63,320, respectively. Additional cost secondary to digital ulcers was \$4259 to \$8680. **Conclusions:** Globally, SSc represents high patient and systemic economic burden. Governmental policies should emphasize prevention of SSc complications.

Zahra Merali

Why do residents create? Using a podcast project to explore resident motivation and engagement during creation of scholarly activities.

Zahra Merali MB BCh BAO, Kallirroï Laiya Carayannopoulos MD, Daniel Brandt Vegas MD FRCPC, Alison Lai, MD FRCPC

Introduction: Scholarly activities such as journal clubs or grand rounds are commonly mandated within internal medicine training programs. However, there is little data exploring the resident experience during the creation process. This qualitative study examines the creation experiences of residents who voluntarily developed a podcast for “The Intern at Work,” a learner-generated podcast series, in comparison to mandated scholarly activities. **Methods:** Purposive sampling was used to recruit residents who wrote a podcast for “The Intern at Work”. Focus groups were completed using semi-structured interviews and were recorded, transcribed, and coded by two researchers.

Constructivist grounded theory was used to analyze the data. Results: Three focus groups were conducted. Residents (n=12) described three key factors of the podcast project that fostered learner motivation and engagement: (1) Intrinsic Motivator: Residents were excited to use a novel, creative outlet to teach near peers. (2) Self-Directed Process: The opportunity to collaborate with attending physicians, flexibility in topic selection and production timeline were cited as favourable aspects of the podcast process. (3) Tangible Benefit: Residents described appreciable self-gains, including strengthening their teaching skills, direct mentorship and a widely-disseminated product. Some factors were paralleled in the residents' experiences creating mandated scholarly activities, but most were unique to this novel initiative. Conclusion: Our framework of intrinsic motivator, self-directed process and tangible benefit represents key factors that increase learner motivation and engagement when creating a podcast for "The Intern at Work ". Future research should be directed to see whether this framework applies to existing or new scholarly projects.

Maria Mikail

The impact of the COVID-19 pandemic on gastroenterologists providing care to inflammatory bowel disease patients in Canada: preliminary data of a cross-sectional survey

Maria Mikail, Principal Investigators: Dr. Reena Khanna, Co-Investigators: Dr. Maria Mikail, Dr. Gurpreet Malhi & Dr. Aze Wilson

Background: We aim to explore the impact of COVID-19 pandemic-related restrictions on gastroenterologists providing care to inflammatory bowel disease (IBD) patients in Canada. Methods: We invited Canadian gastroenterology societies, academic centres, community hospitals and private clinics to have their gastroenterologists engage in an online mixed methods survey from December 2020 - March 2021. Results: 59 gastroenterologists participated in our study. Mean age was 43.7 years with 62.7% practising primarily at an academic centre. Respondents primarily were from Ontario, Quebec and British Columbia. 93.2% of respondents reported their practice was affected by the pandemic. 44.6% noted a reduction in the number of total consultations completed. 87.3% reported a reduction in the total endoscopies performed during the pandemic, with 43.8% of those individuals noting a minimum reduction of 25% of previous volumes. The following barriers attributed to the decrease in endoscopies performed: institutional-imposed restriction on daily allowed endoscopies, indication for endoscopy was non-urgent and patient-requested cancellation due to a fear of contracting COVID-19. Respondents noted outpatient diagnostic imaging and laboratory investigations were delayed during the COVID-19 pandemic. When advancing drug therapy in IBD patients before versus during the pandemic, respondents reported the following factors as playing a crucial role in clinical decision making: patient symptomatology (87% vs. 79.3%), laboratory investigations (94.8% vs. 96.6%),

diagnostic imaging (89.7% vs. 81%) and endoscopy findings (89.7% vs 72.4%).
Conclusion: We illustrate that Canadian gastroenterologists have been affected by the pandemic, with decreases in endoscopy performance related to access and patient preference and less decision-making guided by endoscopy.

Shara Nauth

Improving Delirium Screening in the Geriatric Rehabilitation Setting

Shara Nauth, BHSC MD and Luxey Sirisegaram, BSc MD, Carson, Joseph MSc., Thain, Jenny. MHPE, MD, FRCPC, Taabazuing, Mary Margaret. MD, FRCPC

Objective: To improve the identification of patients who are delirious upon admission to the Geriatric Rehabilitation Unit (GRU). Aim: To increase the proportion of documented delirium screening on GRU admission to 70%. Design and Setting: A prospective cohort study for geriatric patients admitted to the Geriatric Rehabilitation Unit in Parkwood Hospital. Population: All patients admitted to the Geriatric Rehabilitation Unit in Parkwood Hospital from August 1, 2020 - April 2021 (data collection ongoing). Strategy: Change was implemented through Plan-Do-Study-Act cycles. The first PDSA cycle involved adding a fillable section for the 4AT Delirium tool in the pre-printed Admission template for the GRU. Dictated admission notes were then reviewed for the inclusion of delirium screening. Results: The average percentage of 4AT Delirium screening on the GRU prior to the intervention was 16.9%, and PDSA Cycle 1 improved delirium screening to 44%. Lessons Learnt: Implementation of delirium screening can be improved using a validated tool in the rehabilitation setting. This may ultimately improve delirium management and intervention, patient therapy and patient outcomes. Future Directions: Future PDSA Cycles will include educational interventions such as posters, instructive video during GRU orientation, and in-person teaching facilitated by Geriatric medicine fellows.

Leah Nicoletti

Components of junior and senior learners' daily patient assessment on CTU

Leah Nicoletti, Alan Gob

The Medicine Clinical Teaching Unit (CTU) is the backbone of the inpatient medicine learning experience for medical students and Internal Medicine residents, but very little research has been done into how learners assess patients while on CTU. This Quality Improvement study used a survey to evaluate what senior residents (PGY2s and PGY3s) believe to be important aspects of a daily patient assessment for patients admitted to CTU. This information was compared to survey data from junior learners (medical students and PGY1s). Both senior residents and junior learners included

documenting vital signs, reviewing lab and imaging results, and speaking with the patient in their list of the most important components of a daily patient assessment. However, senior residents also placed importance on reviewing medications and active orders, while junior learners emphasized reading previous progress notes. The identification of this difference allows for future investigation into why this difference exists and how best to educate learners about assessing and caring for patients admitted to CTU.

Laurent Perrault-Sequeira

Discharging the Complex Patient - Changing our Focus to Patients' Networks of Care Providers

Laurent Perrault-Sequeira, Jacqueline Torti, Andrew Appleton, Maria Mathews, Mark Goldszmidt

Background: A disconnect exists between the idealized model of every patient having a family physician (FP) who acts as the central hub for care, and the reality of health care where patients must navigate a network of different providers. This disconnect is particularly evident when hospitalized multimorbid patients transition back into the community. These discharges are identified as high-risk due to lapses in care continuity. Exploring the networks of care providers for these complex patients could help identify novel approaches to improve discharge planning. Methods: This was a prospective cohort study with data collection and analysis informed by constructivist grounded theory methodology. Data included interviews from 30 patients admitted to LHSC - University Hospital's Clinical Teaching Unit (CTU). Analysis and data collection proceeded iteratively with sampling progressing from purposive to theoretical. Results: We identified network of care configurations commonly found in complex patients admitted to hospital. FPs and specialists form the network's scaffold. The involvement of physicians in the network dictated not only how patients experienced transitions in care but the degree of reliance on social supports and personal capacities. The ideal for the multimorbid patient is an optimally involved FP that remains at the centre, even when patients require more subspecialized care. However, in cases where a rostered FP is non-existent or inadequate, increased involvement and advocacy from specialists is crucial. Conclusions: Our results have implications for transition planning in hospitalized complex patients. Recognizing salient network features can help identify patients who would benefit from enhanced discharge support.

Sonya Ramondino

Physician perceptions of nephrology virtual care clinics

Sonya Ramondino, Seung Heyck (Alex) Lee, Kerri Gallo, Dr. Louise Moist

Keywords: Virtual care, Telenephrology, COVID-19, Provider satisfaction, Survey, Canada **Background:** The COVID-19 pandemic required rapid adoption of virtual modalities to provide care for patients with chronic disease. The objective of this study is to describe physician perceptions and preferences of virtual care in a Nephrology chronic kidney care clinic. This study will focus on 2 of the 6 domains of health care quality: timeliness and efficiency. **Methods:** The survey development engaged key stakeholders to identify measurements of important physician facing outcomes and the survey was distributed by email to nephrologists who provide virtual care. The survey focused on time management, completeness of assessment, job satisfaction, technology, cost, challenges and strengths of virtual chronic kidney disease clinics. Once completed, the data will be collected and organized through RedCap. Content analysis will be performed to evaluate physician experiences with virtual chronic kidney disease clinics in comparisons to experiences with in-person clinics. **Results:** Currently pending.

Sonya Ramondino

Patient perceptions of nephrology virtual care clinics

Seung Heyck (Alex) Lee, Sonya Ramondino (PGY2), Kerri Gallo, Dr. Louise Moist

Background: The COVID-19 pandemic required rapid adoption of virtual modalities to provide care for patients with chronic disease. The objective of this study is to describe patient perception and preferences of virtual care in a Nephrology chronic kidney care clinic. This study will focus on 3 of the 6 domains of healthcare quality: patient centered, timeliness, and efficiency. **Methods:** Survey development engaged key stakeholders and was piloted with patients to identify measurements of important patient outcomes. Surveys were distributed by mail or email to 332 participants. Surveys were redistributed 4 weeks after the initial distribution. Description statistics summarized effective communication and transfer of knowledge. Content analysis was performed to evaluate the qualitative responses. The study was approved by the Ethics Board. **Results:** 200 responses were collected (response rate of 60%). 79% of patients were ≥65 years old and 82% were not in the labour force. 49% preferred phone consultations over face-to-face visits while 67% felt very comfortable with phone consultation. 27% preferred face-to-face visits. Although 65% perceived no changes in access to healthcare, 67% reported spending less resources on transit and parking while 73% spent less time to receive the same level of care. Improving virtual care by including video conferencing was most commonly suggested. **Conclusion:** Patient experiences with phone consultations was generally favourable. However, further study will be

needed to assess the characteristics and preferences of those who prefer a face-to-face visit. Further study on the quality of care delivered by phone consultation is being pursued.

Sonya Ramondino

Quality Improvement Project to Improve Physician-Nurse Communication on General Medicine Wards

Sonya Ramonidino, MD, Robbie Sparrow, MD; Alan Gob, MD

Objective: On general medicine wards, communication between nurses and physicians is important to providing high-quality medical care. Previously, many nurses reported that the quality of communication was suboptimal, and a recent Plan-Do-Study-Act (PDSA) cycle that aimed to provide residents with nurse phone numbers failed to improve communication. This quality improvement project sought to further identify residents' and medical students' perceived barriers to speaking with bedside nurses. Methods: Using a PDSA quality improvement (QI) methodology, a team of physicians designed a qualitative research survey that outlined barriers to communication. This survey was reviewed by a qualitative research specialist and was distributed electronically to internal medicine residents and medical students working on the Clinical Teaching Unit in London, Ontario. Results: Overall, 22 medical students and 34 residents completed the survey, and 88% of respondents agreed that significant obstacles to communication existed. Of these, the most frequently cited barrier was nurses taking breaks when medical team members were assessing patients at bedside (71%). Nurses being busy with another task was also reported as a barrier by 45% of respondents. Conclusions: This QI project identified that a conflict in nursing break schedules and the time of day resident/medical students assess patients may be a communication barrier. However, given that past QI initiatives failed to improve communication when this barrier was removed, a disconnect may also exist between perceived and actual barriers to communication.

Omar Raslan

Impact of Next Generation Sequencing in Patients with Lower Risk Myelodysplastic Syndrome on Clinical Outcomes

Omar Raslan, Ben Hedley, Ian Chin-Yee, Mohammed Abu Farhaneh, Pratihba Bhai, Bekim Sadikovic, Cyrus Hsia

Myelodysplastic syndromes (MDS) are clonal stem cell malignancies characterized by cytopenias, inefficient hematopoiesis, dysplasia in one or more myeloid cell lineages and increased risk of development of acute myeloid leukemia (AML). MDS can be

classified broadly into low risk and high risk MDS using calculated risk scoring systems. Based on the clinical, morphologic, immunophenotypic, and cytogenetic findings, diverse risk stratification models such as the 1997 International Prognostic Scoring System (IPSS) and the updated Revised IPSS (IPSS-R) were created. However, these scoring systems do not account for genetic mutation as they do for karyotypic changes. This results in misclassifying patients as low risk while being high risk, and vice versa. This greatly impacts the clinical outcomes and choice of treatment in clinical practice. In our study, we aim to assess the impact of mutational analysis on clinical outcomes using Next Generation Sequencing (NGS) panels in patients with lower risk MDS. We are conducting a retrospective cohort study involving all patients with MDS who received both cytogenetics and molecular studies. We will include patients over a 3-year period. Our primary outcome is to measure the prevalence of discordant test results between cytogenetics and molecular studies. Our secondary outcomes are to measure the effects of discordant test results on overall survival (OS), treatment-free interval (TFI), divided into different subgroups based on time to first transfusion, lenalidomide, erythropoietin stimulating agents, immunosuppression and hypomethylating agents. We aim to highlight the clinical importance in including molecular testing to the risk scoring systems.

Hani Rjoob

Paroxysmal headache and high blood pressure triggered by micturition in a patient with urinary bladder paraganglioma: a case report

Hani Rjoob, Dr. Stephen Pautler, Urologist, Dr. Brendan Wallace, Urology Fellow, Dr. Jose A. Gomez, Pathologist, Dr. Tayyab Khan, Endocrinologist, Dr. Stan Van Uum, Endocrinologist

Introduction: Paraganglioma of urinary bladder is a very rare neuroendocrine tumor accounting for less than 1 % of all pheochromocytomas and less than 0.05% of bladder tumors. These paragangliomas may be functioning or non-functioning and present with variable manifestations. Case description: A 49-year old female patient presented with a 5 year history of episodes of headache and hypertension triggered by urination. The episodes lasted about 30 minutes, and blood pressure increased to 250/120 mmHg, with systolic blood pressure being 95-115 mmHg outside of the episodes.

Normetanephrine was elevated in 24-hour urine at 4.1 (Normal <3.4) umol/day and in plasma at 2.84 (Normal <0.89) nmol/L. MIBG scan showed increased focal activity on the right side of urinary bladder, consistent with a complex mass of 3.5 cm seen on MRI of the pelvis. She underwent a robot-assisted laparoscopic partial cystectomy. No significant intraoperative instability was noted. The patient did not require ICU admission or vasopressors. Pathology showed a completely resected paraganglioma. Upon follow up, she reported significant improvement of her symptoms. Repeat 24-hour urine collection, 3 months after surgery, was within normal range for catecholamines

and metanephrines. Genetic testing for paraganglioma panel was negative. Discussion: This patient presented with adrenergic symptoms with micturition, which may be the initial manifestations of bladder paraganglioma. Patients can also be asymptomatic or present with microscopic hematuria. Surgical resection of paraganglioma is the initial treatment modality, and can be curative. This case report highlights the important role of careful history in diagnosing bladder paraganglioma.

Michael Sattin

Incident atrial fibrillation and cardiovascular risk increases in patients with increased burden of atrial ectopy

Michael Sattin, Zhe Li, Marko Mrkobrada, Erin Spicer

INTRODUCTION: Atrial fibrillation (AF) is a major risk factor for cerebral ischemia. Atrial ectopy (AE) is associated with incident AF and increased stroke risk on short-duration continuous ECG monitoring (CEM). **OBJECTIVE:** Characterize the relationship of AE on extended CEM with future cardiovascular events including incident AF and stroke. **METHODS:** Retrospective, observational study enrolling adult patients referred from TIA clinic for 7- or 14-day CEM. Binomial logistic regression utilized to determine odds ratio (OR) of developing primary composite outcome (AF, TIA/stroke, ACS, death), with adjustment for age and CHA₂DS₂-VASc. Secondary analysis evaluated each outcome individually. OR reported with 95% confidence intervals. **RESULTS:** 1124 patients included in the study and followed for 1 year. Population was high-risk with mean CHA₂DS₂-VASc of 4.0 (\pm 1.8). Primary outcome occurred in 115 (10.2%) patients. There was increased odds of developing incident AF with > 5 PAC runs/day (aOR 4.308, 1.363-13.621). PAC runs/day as a continuous variable was associated with increased odds for the composite outcome (aOR 1.251, 1.099-1.425) and incident AF (aOR 1.670, 1.349-2.069). Percentage of PACs as a continuous variable was associated with increased odds for the composite outcome (aOR 1.254, 1.111-1.414) and incident AF (aOR 1.199, 1.050-1.370). Longest PAC run as a continuous variable was associated with increased odds for the composite outcome (aOR 1.372, 1.159-1.624) and incident AF (aOR 1.718, 1.346-2.193). **CONCLUSION:** Increased burden of AE on extended CEM is associated with increased odds of developing AF and a composite of cardiovascular events.

Alice Shin

F4/80+Ly6Chi macrophages contribute to colon cancer initiation in colitis

Alice E. Shin, Hayley J. Good, Yodit Tesfagiorgis, Liyue Zhang, Steven M. Kerfoot, Philip M. Sherman, Timothy C. Wang, Christopher J. Howlett, Samuel Asfaha

Colorectal cancer is the second leading cause of cancer death with a major risk factor being chronic inflammation. However, the mechanism by which colitis leads to cancer is not known. Our previous studies showed that the type of colonic injury, rather than the simple presence of inflammation, is most important for tumorigenesis. Thus, we aim to compare various colitis models with respect to their ability to initiate tumor formation. We hypothesize that dextran sodium sulfate (DSS)-induced colitis leads to the infiltration of specific immune cell populations that contribute to tumorigenesis. Following injection of the carcinogen azoxymethane (AOM), mice were treated with the colitis-inducing agents DSS, trinitrobenzene sulfonic acid (TNBS), oxazolone, *Citrobacter rodentium*, or Doxorubicin (Doxo), and colonic tumorigenesis were compared. DSS administration led to colonic tumors, whereas TNBS, oxazolone, *C. rodentium*, and Doxo did not lead to tumorigenesis even up to 52 weeks following colitis induction. Flow cytometry analysis of immune cells in the colonic tissue revealed increased levels of Ly6G+ neutrophils and F4/80+Ly6Chi macrophages in the DSS-treated mice versus other models of colitis. Additionally, analyses of the RNA-seq data from 206 UC patients revealed increased expression of genes associated with myeloid cells. Depletion of Ly6G+ neutrophils did not affect tumorigenesis, whereas depletion of F4/80+Ly6Chi macrophages significantly reduced the number of colonic tumors. Our data suggest that infiltration of F4/80+Ly6Chi macrophages unique to DSS-induced colitis leads to colonic tumor formation. These findings demonstrate that specific myeloid cells are critical to the initiation of colitis-associated cancer.

Luxey Sirisegaram

THE ROLE OF SEX IN MOTOR AND COGNITIVE TRAJECTORIES BEFORE DEMENTIA

Luxey Sirisegaram, Yanina Sarquis-Adamson, Manuel Montero-Odasso

Slowing of gait and cognitive declines are common in older-adults. Older adults with motor and cognitive decline (dual-decliners) have a higher risk of progressing to dementia than individuals who have either decline alone. Our aim in this study is to examine the role of sex in these cognitive and motor trajectories before dementia. Data was used from Gait and Brain Study, a prospective cohort study in community-dwelling older-adults free of dementia at baseline. Participants were assessed biannually for 5 years, using gait velocity and MoCA testing. Incident dementia using DSM-IV criteria was used. The risk of progression to dementia was done using Cox-regression models, stratifying by sex and adjusting by age and comorbidities. From 207 older adults, 18%

progressed to dementia, where 43% were males and 57% females. Among dual-decliners, males had a higher risk for progressing to dementia when compared with females (Males $p=0.046$; Females $p=0.155$). In males, the association becomes stronger after adjusting for comorbidities ($p=0.039$), whereas in females, the risk for progressing to dementia lowers when adjusting for comorbidities ($p=0.590$). Male dual-decliners showed a stronger and statistically significant association with progression to dementia when compared with females in adjusted and unadjusted models. Older adults that are dual-decliners have the highest risk to progress to dementia, particularly if they are male. These findings suggest that number of comorbidities might be driving the association with dementia in females. Sex differences in motor and cognitive trajectories before dementia may increase accuracy of dementia risk prediction.

Gavasker Sivaskandarajah

Quality improvement for assessing the demand for diagnosing and treating primary aldosteronism (PA) with an adrenal vein sampling (AVS) and adrenal surgery in London, Ontario

Gavasker Sivaskandarajah, George Dresser, Angela Rutledge, and Stan VanUum

Background: Primary aldosteronism (PA) is emerging as an important factor in resistant hypertension, but diagnosing PA and confirming with adrenal vein sampling (AVS) is technically challenging since it requires consistent referrals to maintain expertise to continue providing this service in London, Ontario. **Objective:** To determine the number of patients screened and treated for PA in London, Ontario in the past four years to determine if there is a sufficient referral base for standardizing testing and allocating resources to make St. Joseph's Health Centre London (SJHC) a centre of excellence for PA diagnostics. **Methods:** This Quality Improvement (QI) project assesses LHSC/SJHC patients who had ARR testing from January 1, 2016 to December 31, 2020. A retrospective chart review will be done for each patient on whether they met guideline recommendations for: screening, confirmatory testing, adrenal imaging, AVS, and adrenalectomy. A descriptive analysis will be done with the goal of comparing the incidence of PA managed at LHSC/SJHC to the published literature; and the proportion of patients who received AVS or adrenal surgery following positive confirmation and those lost to follow-up. **Significance:** In London, PA screening is being done by the LHSC/SJHC and we believe there may be an emerging need for local expertise for AVS. By determining the proportion of patients diagnosed and treated with PA over a four-year period we aim to develop a centre of excellence at SJHC that standardizes the clinical pathway for confirmatory diagnosis, AVS, and definitive treatment.

Robbie Sparrow

Racial, Ethnic and Socioeconomic Disparities in Patients Undergoing Left Atrial Appendage Closure

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Objective: This paper aims to explore the impact of race/ethnicity and socioeconomic status on in-hospital complication rates after left atrial appendage closure (LAAC).

Methods: The United States National Inpatient Sample was used to identify hospitalizations for LAAC between October 1st, 2015 and December 31st, 2018. These patients were stratified by race/ethnicity and quartiles of median neighborhood income. The primary outcome was the occurrence of in-hospital major adverse events, defined as a composite of post-procedural bleeding, cardiac and vascular complications, acute kidney injury (AKI), and ischemic stroke. **Results:** Of 6478 hospitalizations for LAAC, 58% were male and patients of Black, Hispanic, and "Other" race/ethnicity each comprised approximately 5% of the cohort. Adjusted by the older Americans population, the estimated number of LAAC procedures was 69.2/100,000 for White individuals, as compared to 29.5/100,000 for Blacks and 47.2/100,000 for Hispanics. Black patients were ~5 years younger but had a higher comorbidity burden. The primary outcome occurred in 5% of patients and differed significantly between racial/ethnic groups ($P < 0.001$) but not across income quartiles ($P = 0.88$). After multilevel modelling, the rate of in-hospital major adverse events was higher in Black patients as compared to Whites (OR: 1.60, CI: 1.22-2.10, $P < 0.001$) and the incidence of AKI was higher in Hispanics (OR: 2.19, CI: 1.52-3.17, $P < 0.001$). **Conclusion:** In this study assessing racial/ethnic disparities in patients undergoing LAAC, minorities are underrepresented, specifically patients of Black race/ethnicity. Compared to Whites, Black patients had higher comorbidity burden and higher rates of in-hospital complications.

Robbie Sparrow

Racial, Ethnic and Socioeconomic Disparities in Patients Undergoing Transcatheter Mitral Edge-to-Edge Repair

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Objective: To assess the impact of race/ethnicity and socioeconomic status on in-hospital complications after Transcatheter mitral edge-to-edge repair (TEER). **Methods:** Cohort-based observational study using the National Inpatient Sample between October 2013 and December 2018. The population was stratified into 4 groups based on race/ethnicity and quartiles of neighborhood income levels. The primary outcome was in-hospital complications, defined as the composite of death, bleeding, cardiac and vascular complications, acute kidney injury, and ischemic stroke. **Results:** 3795 hospitalizations for TEER were identified. Patients of Black and Hispanic race/ethnicity comprised 7.4% and 6.4%, respectively. We estimated that Whites patients received TEER with a frequency of 38.0/100,000, compared to 29.7/100,000 for Blacks and 30.5/100,000 for Hispanics. In-hospital complications occurred in 20.2% of patients and no differences were found between racial/ethnic groups (P=0.06). After multilevel modeling, Black and Hispanic patients had similar rate of overall in-hospital complications (OR: 0.84, CI:0.67-1.05 and OR: 0.84, CI:0.66-1.07, respectively) as compared to Whites patients, however, higher rates death were observed in Black patients. Individuals living in income quartile-1 had worse in-hospital outcomes as compared to quartile-4 (OR: 1.19, CI:0.99-1.42). **Conclusions:** In this study assessing racial/ethnic disparities in TEER outcomes, aged-adjusted race/ethnicity minorities were less underrepresented as compared to other structural heart interventions. Black patients experienced a higher rate of in-hospital death and similar overall rate of post-procedural adverse events as compared to Whites patients. Lower income levels appear to negatively impact on outcomes.

Wajahat Syed

Decision-making patterns in patients requesting medical assistance in dying: A scoping review

Wajahat Syed, Andrew Appleton

OBJECTIVE: A primary role of physicians is to educate and guide their patients so that they may make informed decisions regarding their own care. Knowing decision-making patterns in requesting medical assistance in dying (MAiD), something largely unexplored, can help physicians better guide their patients in making decisions about

their care in the context of MAiD. **METHODS:** Using a scoping literature review, we sought to explore current evidence (both qualitative and quantitative) to identify if decision-making patterns exist in patients requesting MAiD worldwide, and if so, what those patterns are. **RESULTS:** Our initial search yielded a total of 635 citations relating to patient decision-making patterns in MAiD and alternative descriptors of the process. Among these, 11 studies met all inclusion criteria and were subjected to further analysis. Unfortunately, none of these studies ultimately commented on reasons for patient's decision-making regarding this topic. **CONCLUSIONS:** Much of the literature reviewed explores physician perspectives or patient demographics with regards to MAiD, however none were able to explicitly identify patient insight. This topic remains largely unexplored and would benefit greatly from primary research. Insight of this nature could serve to benefit physicians who work with these patient populations in personalizing care and ensuring informed consent when patients request MAiD.

Maria Tauqir

The Association between Vedolizumab and the Development of New-Onset Spondyloarthritis in Patients with Inflammatory Bowel Disease: A Pilot Study

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Background: Vedolizumab is a humanized IgG1 monoclonal antibody to alpha-4 beta-7 integrin approved for treatment of inflammatory bowel disease (IBD). Case series suggested that vedolizumab may induce new-onset spondyloarthritis (SpA). However, it is unclear whether the arthritis developed after vedolizumab initiation, was present previously and under-investigated, or was masked by pre-existing therapy including tumour necrosis factor inhibitors (TNFi). **Objective:** To evaluate the association between vedolizumab and development of de novo features of SpA in TNFi-experienced and TNFi-naive IBD patients. **Methods:** We performed a prospective observational study of 13 TNFi-naive and 11 TNFi-experienced IBD patients. Patients were assessed prior to vedolizumab initiation and 8 and 24 weeks after by a rheumatologist for historical and physical features of SpA, biochemical inflammatory markers, and clinical outcome measures for SpA and IBD. MRI of the sacroiliac joints was performed at each visit using a SpA protocol and centrally read by a blinded radiologist. **Results:** Twenty-four patients were recruited. One patient had evidence of burn-out sacroiliitis on MRI at baseline while another could not tolerate MRI; both were withdrawn. Five patients were lost to follow-up although one developed worsening joint pain and swelling after vedolizumab initiation. Sixteen of 17 patients (9 TNFi-naive, 8 TNFi-experienced) did not demonstrate new clinical or radiological signs of SpA. One TNFi-experienced patient developed a worsening hip effusion at 24-weeks. **Conclusions:** The majority of patients treated with vedolizumab did not develop new manifestations of SpA which does not

support the hypothesis that vedolizumab induces inflammatory arthritis. Larger studies are needed.

Aaron Teel

The role of myositis specific autoantibodies in idiopathic inflammatory myopathy associated interstitial lung disease

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Idiopathic inflammatory myopathies (IIM) are a group of inflammatory disorders including polymyositis, dermatomyositis, and anti-synthetase syndrome. They can be associated with extra-muscular manifestations including interstitial lung disease (ILD), the predominant driver of mortality in IIM. These manifestations can vary based on myositis specific autoantibodies (MSA's). The aim of this study was to evaluate the role of MSA's in ILD and management of IIM associated ILD. A systematic review was performed examining how MSA's relate to ILD manifestations and comparing treatment outcomes among MSA groups and IIM patients on varying immunosuppressive regimens. Outcomes of interest included ILD manifestations such as presence or absence of ILD, acuity of ILD, pulmonary function tests, radiographic findings, and clinical manifestations; as well as treatment responses including mortality, recurrence rates, glucocorticoid dependence, and adverse events. Patients with anti-synthetase antibodies and anti-MDA5 antibodies had consistently higher rates of ILD than other MSA groups. Anti-ARS positive patients had higher rates of chronic ILD whereas anti-MDA5 positive patients had higher rates of rapidly progressive ILD. Small sample sizes, a lack of head-to-head trials, and non-randomized designs prevented drawing meaningful conclusions with respect to immunosuppressant management. Clear relationships exist with regards to the ILD manifestations of certain MSA's. However, the management of IIM associated ILD in general and as it pertains to each MSA subgroup remains unclear. Further studies comparing specific immunosuppressants as well as comparing glucocorticoid monotherapy to multi-drug therapy would aid in guiding management in IIM associated ILD.

Shivani Upadhyaya

Prevalence of Primary Biliary Cirrhosis in Systemic Sclerosis and Sjögren's Syndrome Over Time: A Systematic Review

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Primary biliary cirrhosis (PBC) is known to coexist together with rheumatological conditions such as Sjögren's syndrome (SS) and systemic sclerosis (SSc); however, the exact prevalence rates remain unclear. The objectives were to determine the

prevalence of: 1) PBC in patients with SS and SSc (and the subsets of limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc)), 2) SSc and SS in patients with PBC, and 3) to analyze changes in frequency over time. A systematic review of the literature was performed using Medline, EMBASE, CINAHL, and the Cochrane Library databases up till June 2020 and we included only full text English articles with at least 40 patients. Of 2876 citations identified, 67 were included in the analysis (n=33 for PBC, 15 for SSc, 18 for SS and 1 for SSc/SS). The prevalence of PBC was 5% in patients with SSc. Within the subsets, the prevalence of PBC in lcSSc was 8% and in dcSSc was 1%. In patients with SS, the prevalence of PBC was 4%. The prevalence of SSc overall in those with PBC was 5% and, within the subsets was 6% in lcSSc and 0% in dcSSc. The prevalence of SS in PBC was 18%. There was no significant association between year of publication and prevalence. PBC is increased in SSc but mostly in the lcSSc subset. SS in PBC is common at nearly 1 in 5. Over the years, there was no change in the prevalence of PBC in SSc indicating stability over time.

Kathleen Winger

SALMONELLA MENINGITIS IN SOLID-ORGAN MALIGNANCY PATIENT

Kathleen Winger, Nikesh Adunuri

Introduction: Salmonella meningitis is a rare manifestation of an enteric organism reported more commonly in the neonatal population. In rarer circumstances, it has affected immunocompromised adults with HIV or patients receiving immunosuppressive therapy. Here we report the first case of a patient with a solid organ malignancy developing Salmonella meningitis. Case: A 72-year-old female with Stage 4 lung adenocarcinoma undergoing cycles of Pemetrexed presented to hospital with Salmonella meningitis. Her presentation was remarkable for a white blood cell count of $2.8 \times 10^9/L$ (absolute neutrophil count of $2.3 \times 10^9/L$). Cultures from blood and cerebral spinal fluid grew salmonella enteritidis. She was treated with a 21-day course of Ceftriaxone, only to develop recurrence shortly thereafter despite no evidence of seeding identified on further investigations. Discussion: This case is the first to identify Salmonella meningitis in an adult patient with a solid-organ tumour. Previously, Salmonella meningitis had been identified in two other case reports in which both patients had lymphoma where defects in cellular immunity predisposed them to the infection. This patient's increased susceptibility to Salmonella meningitis was likely related to the use of Pemetrexed disrupting the integrity of the gastrointestinal epithelial barrier. Conclusion: This case expands the spectrum of adult patient populations that may be predisposed to developing Salmonella meningitis and demonstrates that laboratory markers of immunosuppression such as neutropenia do not need to be present. This case also poses the question as to what is considered adequate treatment duration as this patient developed recurrence despite no identifiable source.

Laura Xu

Mechanism of AIF-Regulated Nuclei Damage

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Introduction: Necroptosis is a caspase-independent necrotic pathway sharing features with accidental cell death. Necroptosis is regulated by receptor-interacting protein kinases 1 and 3, forming a necrosome complex and phosphorylating MLKL (mixed lineage kinase domain-like). MLKL oligomerizes, opens membrane pores, and releases danger-associated molecular patterns. We have demonstrated that necroptosis is a key therapeutic target in organ injury and transplantation. The downstream mechanism of cell death is still unknown. Mitochondrial apoptosis-inducing factor (AIF) translocates to the nucleus, potentially participating in necroptosis through DNA fragmentation.

Methods: Isolated murine microvascular endothelial cells (MVECs) were treated at physiological and acidic pH (7.4, 6.0, and 6.5) with the following: TNF-alpha, second mitochondrial activator of caspase (SMAC), IETD, and necrostatin-1s.

Immunocytochemistry was performed to detect nuclear translocation of AIF and DNA fragmentation was characterized via agarose gel staining. MVECs were silenced with siRNA targeting AIF and confirmed using qPCR and western blots. Results: TNF-alpha and SMAC led to apoptosis. IETD inhibited caspase-mediated apoptosis but cell death remained at a high level. RIPK1 inhibitor Nec-1s blocked necroptosis. AIF translocation was absent at physiological pH but visible at acidic pH during necroptosis. AIF siRNA inhibited AIF expression, preventing cell death. Our study suggested that environmental conditions can alter the mechanism of necroptosis. Discussion: In Canada, over 200 patients underwent heart transplants and 2300 Canadians were living with a transplanted heart in 2019. Cardiac allograft vasculopathy contributes to post-transplant failure so this work may help improve cardiac transplantation outcomes. Keywords: necroptosis, AIF, endothelial cells, cell death
