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Abdelhady, Abdalla

Rare Variant Associations in Individuals with Neurodegenerative Diseases

Abdalla Abdelhady Allison Dilliott, Sali M. K. Farhan, Adam McIntyre, John Robinson, Henian Cao, Sandra E. Black, Morris Freedman, Lorne Zinman, Elizabeth Finger, Maria Carmela Tartaglia, Anthony Lang, Richard Swartz, Ekaterina Rogaeva, The ONDRI Investigators, Robert A. Hegele

Millions of individuals around the world suffer from the effects of neurodegenerative diseases. Currently, there are limited treatment options, as well as challenges with effective diagnoses of the diseases. However, identifying genetic markers that affect the presentation of these diseases may improve diagnosis, prognosis, and treatment. As part of the Ontario Neurodegenerative Disease Research Initiative (ONDRI), over 500 DNA samples from individuals with various neurodegenerative diseases were collected and sequenced using a custom next-generation sequencing gene panel, called ONDRISeq. Over 180 DNA samples from elderly, cognitively normal individuals were also sequenced as controls. Rare variant association analysis (RVAA) was performed on the sequencing data to identify specific genes covered by ONDRISeq with an increased frequency of nonsynonymous, rare variants (Minor allele frequency (MAF) < 1%) in the disease cohorts. We identified three genes (DAO, PARK2, and VCP) that harboured significantly more nonsynonymous, rare variants (P-value < 0.05) in one of two disease cohorts (FTD and ADMCI) compared to the control cohort, suggesting that they may contribute to disease presentation. On the other hand, two other genes (CHMP2B and NEFH) were found to have significantly more nonsynonymous, rare variants in the control cohort, suggesting possible protective effects. Domain clustering in the identified genes was also considered. The results provide a step towards the discovery of potential therapeutic targets, as well as new biomarkers for neurodegenerative diseases diagnosis and prognosis.

Akman, Olgun

Patients,' Descriptions of Their Last Bowel Movement Before Colonoscopy, Converted to a Standardized Score, Shows Strong Correlation with Boston Bowel Preparation Scale (BBPS) Score.

Olgun Akman, MD James C. Gregor; MD, Nilesh Chande, MD.

INTRODUCTION: Early detection of adenomatous polyps and adenocarcinoma by colonoscopy reduces colorectal cancer mortality. Inadequate bowel preparation limits the utility of colonoscopies. This study assesses the correlation between a patient,'s description of their last bowel movement and the quality of their bowel cleansing. METHODS: This is a cross-sectional study performed at LHSC. Prior to their colonoscopies, 121 outpatients were asked to describe their last bowel movement. The description was converted to a standardized score: "fully solid", "liquid with solid pieces", "brown liquid", and "clear / yellow liquid", assigned scores of 0, 1, 2, and 3 respectively. Subsequently, each patient,'s total and segmental Boston Bowel Preparation Scale (BBPS) score was determined and recorded by the clinician performing the colonoscopy; clinicians performing the procedure were blinded to the patient,'s description.Bivariate Pearson,'s Correlation was used to assess the correlation between the patients,' description and their BBPS scores. RESULTS: There was a strong correlation ($r = 0.738$; $p < 0.001$) between the patients' descriptions of the last bowel movement and total BBPS scores. Patients' descriptions versus segmental BBPS scores showed: strong correlation with Left Colon BBPS score (r =

0.702; p < 0.001); moderate correlation with Transverse Colon BBPS score (r = 0.632; p < 0.001); and moderate correlation with Right Colon BBPS score (r = 0.667; p < 0.001). DISCUSSION: A patient,'s description of their last bowel movement shows a strong correlation with BBPS score. Identifying patients with inadequate preparation before colonoscopy may allow for extra time and medication for colon cleansing.

Almaghrabi, Majed

Sensitivity and specificity of lower gastrointestinal bleeding scores to predict adverse outcomes: systematic review and meta-analysis

Majed Almaghrabi Gandhi, M, Iansavitchene, A, McDonald, C, Jairath, V, Sey, M

Introduction: Risk prediction scores are important to stratify patients at presentation with lower gastrointestinal bleeding (LGIB). We aim to perform a systematic review and meta-analysis comparing LGIB risk prediction scores. We provide a summary effect measure of their predictive values for 30-day mortality, safe discharge, rebleeding, need for blood transfusion, and need for endoscopic therapy/IR/surgery.Methods: Electronic search for relevant publications after 1990 was conducted in PubMed, EMBASE, Web of Science, Cochrane Central Register of Controlled Trials, NIH ClinicalTrials.gov, and Cochrane Database of Systematic Reviews. We also searched relevant published conference abstracts over the past 5 years. Studies with a primary goal of deriving or validating a LGIB risk score were included. Title and abstracts were reviewed by two independent reviewers and then full text review was done by both reviewers. Results: Our search identified 1,832 citations for review. After title and abstract review, 68 publications were selected for full text review. Thus far, we identified 15 risk scores and algorithms from 11 studies (See figure).Two of the risk scores are UGIB risk scores that were assessed for LGIB. Of these studies, 4 were validation studies, one derivation study and six for both validation and derivation.The scores assessed safety of discharge (n=3), mortality (n=9), need for therapy (n=9), severe bleeding (n=8) and rebleeding (n=7).Conclusion: We conducted a systematic review of LGIB risk scores, with a meta-analysis to follow if appropriate, for use to predict 30-day mortality, safe discharge, rebleeding, required blood transfusion, endoscopic therapy/IR/surgery.

AlObaid, Sarah

Polyp to adenoma conversion factor as a surrogate for adenoma detection rate.

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University10Department of Epidemiology and Statistics, Western University11Robarts Clinical Trials, Western University

BACKGROUND:Adenoma detection rate(ADR) is one of the main quality indicators of a colonoscopy but can be difficult to calculate in all centers, as it requires a combination of endoscopic and histologic findings.We attempted to calculate a examine the correlation between polyp and adenoma detection ratios to identify if an average adenoma to polyp detection rate quotient (APDRQ) could serve as a surrogate for an ADR. AIMS:To validate the use of a conversion factor as a surrogate for ADR.METHODS:We examined the correlation between the polyp and adenoma detection rate using data that was prospectively collected by Cancer Care Ontario from all colonoscopies performed for any indications across 20 hospitals in Southwestern Ontario between April 2017 and February 2018. The data collected includes patient demographics, endoscopist demographics, procedural indication, quality of bowel preparation, cecal intubation, and histology of polyps removed. Procedures performed in patients less than 18 years of age, by endoscopists who perform <50 colonoscopies/year were excluded. Cases that did not have histology records were also excluded.RESULTS:During the 18 month observation period, 35,955 colonoscopies were performed by 52 physicians, and the total number of polyps records were 20,353. 9722 of which were revealed to be adenomas, as identified by pathology.The vast majority of these adenomas were tubular adenomas making up 71% of the total adenomas, as compared to tubulovillous(17%), villous(0.9%) and traditional serrated adenoma(1.08%) Analysis -Pending

Ayoub, AbdulRahman

Safety and Efficacy of Biologic Therapy in Elderly Patients with Inflammatory Bowel Disease: A Retrospective Case Series

Abdul Rahman Ayoub Vipul Jairath, Saleh Al Draiweesh, James Gregor, Reena Khanna, Nilseh Chande

Background: The aims of this study were to evaluate the safety and efficacy of biologic therapies (infliximab, adalimumab, vedolizumab) in IBD patients 80 years or older since limited studies in this population exist.Methods: In our retrospective single-centred study, we collected data from IBD patients age 80 years or older treated with a biologic agent between January 1, 2010 and November 15, 2018. Patients were grouped based on biologic therapy received. Response and prior biologic rates were compared between groups for the efficacy analysis. Mild infections, serious infections, mortality, and malignancy were compared between groups for the safety analysis.Results:A total of 32 patients treated with biologic therapy were included (infliximab n=13, adalimumab n=4, vedolizumab n=15). There was no significant difference between groups in the efficacy and safety analysis. Response was defined in terms of whether or not remission was achieved by patients according to physician opinion of patient symptoms. 68.75% of patients achieved remission (p=1.0) and 7.7% were on a prior biologic (p=0.144). Adverse events included mild infections 9.4% (p=0.24), serious infections 15.6% (p=0.824), malignancy 9.4% (1.0), and mortality 9.4% (p=0.725).Conclusion:Overall, no significant differences were found regarding the safety or efficacy of infliximab, adalimumab and vedolizumab in IBD patients 80 years or older. However, incidence of biologic cessation and adverse events were slightly higher than reported in previous studies of elderly patients 65 or older. Further study is warranted to clarify biologic use in very elderly patients as IBD rates are rising in this population.

Aziz, Salman

Recurrent Hepatocellular Carcinoma post-liver transplant: Evaluation of Results of external validation of 8 post-transplant scoring systems on a cohort of 150 patients

Salman Aziz Anouar Teriaky, Karim Qumosani

Introduction: Recurrence of hepatocellular carcinoma (HCC) after liver transplantation is a major cause of morbidity and mortality. Discordance between pre-transplant imaging and post-transplant pathology affect risk of recurrence. Several post-transplant risk assessment tools have been developed, although to date, there is no widely accepted tool to predict recurrence. The aim of the current study is to determine which pathologic risk assessment score has the best predicative ability. Methods: We retrospectively evaluated 150 patients over a twelve-year period that underwent liver transplantation for HCC. Using explanted pathology reports, each patient was stratified according to the pathologic risk score and followed over time for HCC recurrence. Predictive ability was assessed the area under the receiver operating characteristic curve (AUROC).Results: Out of 150 consecutive liver transplants for HCC, recurrence occurred in 23 patients (15.3%) with a mean follow-up of 53.7 months. 66% of patients were within Milan criteria prior to transplant. According to explant pathology, microvascular invasion was seen in 29 (19.3%) patients, with majority of the tumors being moderately differentiated (54%). The RETREAT score had the highest predictive ability (AUROC 0.80; 95% CI, 0.70-0.91) while the “up-to-seven” criteria had the least predictive ability (AUROC 0.66; 95% CI, 0.54-0.78). Conclusions: Our data suggests that the RETREAT score may have the best predictive ability among the eight risk assessment tools analyzed in this study. This scoring system may be used to help tailor surveillance strategies for potential early detection or early adjuvant therapy to improve long-term survival.

Baer, Brandon

Exogenous Surfactant as a Pulmonary 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 of inflammation. 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.

Balubaid, Ibrahim

CELIAC DISEASE IS A RARE CAUSE OF BENIGN DUODENAL STRICTURE

Ibrahim Balubaid Nitin Khanna

BackgroundBenign duodenal strictures are an uncommon problem encountered by gastroenterologists. The most common cause is peptic ulcer disease (PUD). We present the case of a man with a refractory web-like stricture in the second part of the duodenum (D2) caused by Celiac disease (CD)Case presentationA 64 year old male was referred for consideration of duodenal stenting of a refractory stricture in D2. The patient had a 1 year history of abdominal pain, early satiety and weight loss. CT scan of the abdomen which showed a stricture at the level of proximal D2 described as a “duodenal band”. Previous attempts at balloon dilation had not resulted in prolonged symptomatic or endoscopic improvement. Testing for H. Pylori was negative and he did not use NSAIDs. Repeated upper endoscopy showed a tight web-like stricture in proximal D2 which was balloon dilated up to 16.5 mm, enabling the endoscope to pass beyond it. The mucosa in D2 was atrophic with flattening of the folds and scalloping. Biopsies from D2 revealed villous blunting and intraepithelial lymphocytosis. Celiac serology testing was abnormal, with an anti-tTG Ab level of 32 RU/ml. The balloon dilation and gluten-free diet resulted in resolution of his symptoms. Follow up endoscopy revealed normalization of his duodenal folds, biopsies. In addition, anti-tTG Ab level was normalized.DiscussionBenign duodenal stricture is a very uncommon complication of CD. The likely pathophysiology involves inflammation and potentially ulceration. We recommend to biopsy D2 and check anti-tTG Ab in cases of duodenal stricture.

Blaszak, Michael

Practice Patterns of Emergency Department Physicians Administering Naloxone for Patients with Suspected Opioid Overdose

M.A. Blaszak SN Chilton, S Knezevic, JW Yan, KP Van Aarsen, S Detombe, & MAA Riggan

Background: There is wide variability in emergency department (ED) practice patterns regarding naloxone use, dosing, and observation time post-administration. Objective: Describe the naloxone practice patterns of ED physicians managing suspected opioid overdose patients. Methods: This is a single centre retrospective chart review of 113 patients (>/= 18 years) presenting with suspected opioid overdose administered naloxone in the ED (January 1 ,Äì December 31, 2017). This study was performed at an academic tertiary care centre. Patients were identified electronically. Clinical information

regarding apparent indications for naloxone administration, response to therapy, and adverse effects were abstracted. Data were analyzed using standard descriptive statistics.Results: Indications for naloxone administration were: level of consciousness (50.5%), respiratory depression (4.0%), miosis (1.0%), a combination of these factors (19.8%), or undocumented (24.8%). Median initial dose was 0.40 mg (IQR: 0.20-0.40 mg). Median total naloxone administered in the ED was 0.48 mg (IQR: 0.35-1.2 mg). The initial dose resulted in a response in 43.1%, with 36.0% of responders later experiencing subsequent respiratory depression. Four patients experienced emesis following naloxone. Median length of ED stay was 7.0 hours (IQR: 4.0-9.5 hours), and median hospital admission was 3.0 days (IQR: 1.0-5.0 days). Median observation time prior to discharge was 4.0 hours (IQR: 2.0-8.0 hours). Ultimate disposition home, the ward, or the intensive care unit was 47.1%, 42.2%, and 9.8% respectively. Conclusion: The dose and usage of naloxone by ED physicians in this study is variable. Further prospective studies are needed to determine the effective naloxone dosing strategy.

Chaudhary, Rushil

PeffNet: Creation of a convolutional neural network that distinguishes between epicardial fat and pericardial fluid on point-of-care echocardiography.

Blake VanBerlo Matt White, Jordan Ho, Rushil Chaudhary, Derek Wu, Michael Blaivas, Rob Arntfield

Background:Point-of-care ultrasound (POCUS) is a goal-directed application of ultrasound at the bedside to answer time-sensitive clinical questions. In a resuscitative setting, the timely identification of pericardial fluid can lead to life-saving interventions in patients with circulatory collapse.¬π Conversely, epicardial fat represents a normal anatomic finding that may mimic pericardial fluid, leading to false positives and adverse patient outcomes. Previous studies have shown that even attending physicians exhibit poor sensitivity and specificity distinguishing between these entities.¬≤Artificial intelligence is increasingly being used in medical domains to produce automated systems that perform as well as human experts.??? A reliable automated classifier for distinguishing pericardial effusions from epicardial fat pads could have important clinical implications for patients and providers.Methods:In this project, we built a convolutional neural network (CNN) to distinguish between pericardial effusions and epicardial fat on POCUS. We extracted nearly 100000 frames from subcostal views of the heart and partitioned them into training, validation, and test sets. Our CNN architecture consisted of three convolutional blocks each consisting of a convolutional layer, a Leaky ReLU activation function, and a maxpool layer. The network was trained using optimal values through a hyperparameter search.Conclusion:Our study demonstrates that deep learning can differentiate between epicardial fat from pericardial effusion. We achieved a peak area under the receiver-operator-curve of 0.985, well above previous models. Such a system has the potential to improve the efficiency in diagnosis by expediting care in life-threatening circumstances and decreasing the need for unnecessary procedures.

Cheah, Matthew

IGA-MEDIATED WARM AUTOIMMUNE HEMOLYTIC ANEMIA IN A PATIENT WITH CROHN,'S DISEASE ON VEDOLIZUMAB.

Matthew Cheah Reena Khanna

Iron deficiency anemia and anemia of chronic disease are relatively common manifestations of Crohn's disease. Autoimmune hemolytic anemia, however, is quite rare with few reported cases. Warm hemolysis due solely to to IgA autoantibodies is an even rarer and less understood entity.Vedolizumab is a humanized monoclonal IgG antibody specific for the ?4?7 integrin used in both induction and maintenance of remission in patients in both Ulcerative Colitis (UC) and Crohn,'s Disease (CD). Vedolizumab exerts selective activity in reduction of inflammatory leukocytes and ?-lymphocytes in intestinal tissue. There is no high-quality study to date that has shown that Vedolizumab induces hematologic abnormalities when compared to placebo.Here we report a both rare and challenging case of IgA-mediated, DAT positive autoimmune hemolytic anemia in a patient with Crohn's disease on Vedolizumab.A 21-year-old male with a recent diagnosis of Crohn,'s disease on Vedolizumab presents to infusion clinic with generalized weakness, coke-colored urine and weight loss. Physical examination was remarkable for tachycardia and jaundice. Laboratory investigations revealed profound anemia with IgA-mediated DAT positivity. The patient remained admitted in hospital for a prolonged period. Bone marrow biopsy, CT imaging and infectious workup were negative. Vedolizumab was held and treatment with both high-dose corticosteroids and rituximab was required. Eventually, the anemia would stabilize and Vedolizumab was safely resumed as an outpatient.

Ching-Johnson, Justin

Personalized assessment of thoracic aortic aneurysm stability by diffusion tensor magnetic resonance imaging

J. Ching-Johnson P. McCunn, C. O'Neil, H. Yin, R. Bartha, G. Pickering

IntroductionIndividuals with thoracic aortic aneurysms are at risk of catastrophic rupture and dissection. Currently, measuring aortic diameter is the primary means of gauging this risk and the need for surgical replacement. However, registry data has established that more than half of type A aortic dissections are not prevented using current guideline thresholds. Missing is information on organization and degeneration of the aortic wall itself. Recently, magnetic resonance-diffusion tensor imaging (MR-DTI) has emerged as a strategy to delineate tissue micro-structure in the brain. A role for vascular disease is unknown.MethodsWe developed an ex vivo model of aortic wall degeneration, based on micro-injecting porcine aorta with elastase and collagenase. We next developed aorta MR-DTI imaging protocols using high-field (9.4 Tesla) MR scanning. Micro-architecture was quantified by tract analysis, fractional anisotropy and mean diffusivity.ResultsHistology of micro-injected aortas revealed localized elastin breakdown and smooth muscle cell disarray and loss that mimicked human aortopathy. DTI scans revealed a remarkably organized array of circumferentially oriented diffusion tracts, that disassembled at the site of the micro-injury. The degenerated zone was associated with a 1.9-fold increase in water diffusivity and 4.3-fold decline in fractional anisotropy ($p<0.0001$). Co-registration of histology and MR-DTI images revealed that reduced fractional anisotropy predicted the loss in smooth muscle cells and

elastin content (R2=0.676; R2= 0.838 p<0.0001, respectively).ConclusionMR-DTI provides an entirely new window into the integrity of the aortic wall and thus holds promise for defining the risk of individuals with otherwise silent thoracic aneurysms.

Chretien, Marc L

Drug disposition in celiac disease - A study with fexofenadine.

ML Chretien DG Bailey, L Asher, J Parfitt, D Driman, J Gregor, GK Dresser

Introduction ,Äì Fexofenadine is a non-metabolized hydrophilic antihistamine with oral absorption dependent upon transporters. These include uptake by organic anion transporting polypeptides (OATPs) and efflux by ABC transporter (P-glycoprotein). Celiac disease is an autoimmune illness caused by gluten-containing foods in genetically susceptible individuals that injures intestinal mucosa. Hypothesis - Celiac patients have altered fexofenadine bioavailability dependent on degree of duodenal mucosal damage. Materials and Methods ,Äì Celiac disease patients (n=41) were stratified into Group A (n=15, normal histology), B+C (n=14, inflammatory cell invasion with/without mild villous blunting) and D (n=12, moderate to severe villous blunting). Single dose oral pharmacokinetics of fexofenadine (120 mg) were assessed over 8 hours. Negative control was a group of healthy volunteers (n=48) from previously reported fexofenadine interaction studies with comparable pharmacokinetic testing. Results ,Äì Celiac patients in Group A, B+C and D and negative control had fexofenadine AUCs of 2038+304, 2259+367, 2128+410 and 1954+138 ng.h/ml (p>0.05, mean + SEM) and Cmaxs of 440+73, 513+96, 523+104 and 453+32 ng/ml (p>0.05), respectively. Linear trend for greater duration for fexofenadine tmax was observed among celiac patient groups with increasing severity of disease (2.0+0.3, 2.7+0.4. 3.1+0.5 h; p<0.05).Discussion and Conclusions ,Äì Celiac disease severity based on duodenal histopathology did not alter fexofenadine bioavailability. Increasing fexofenadine tmax with greater disease severity supported better absorption further along the small intestine (jejunum) where histology is more normal. Celiac patients may not require alternative drug management for this class of drugs.

Cocco, Sarah

What is the impact of trainee participation on colonoscopy quality ,Äì Findings from the Southwest Ontario Colonoscopy Cohort

Cocco, S McDonald C, Hindi Z, Rahman H, Chakraborty D, French K, Alsager M, Siddiqi O, Blier M, Markandey B, Al Obaid S, Wong A, Siebring V, Brackstone M, Brahmania M, Gregor J, Khanna N, Ott M, Qumosani K, Teriaky A, Vinden C, Wilson A, Guizzetti L, Yan B, Jairath V, Sey M

BACKGROUND: Trainees participate in colonoscopy as part of their curriculum yet their impact on the quality of the procedure is unknown. Our objective was to determine the impact of trainee participation on colonoscopy quality outcomes in a population-based cohort.METHODS: The Southwest Ontario Colonoscopy cohort captures all colonoscopies between April 2017 and Oct 2018 at 21 hospitals in Southwest Ontario. Procedures performed on patients <18 years or by endoscopists who perform <50 colonoscopies/year or who do not supervise trainees were excluded. The primary outcome was

adenoma detection rate (ADR). Secondary outcomes included sessile serrated adenoma (SSA) detection rate, polyp detection rate (PDR), cecal intubation (CI) rate, and perforation rate.RESULTS: 35,955 colonoscopies were performed, of which 6,055 involved trainees. Colonoscopies involving trainees were more likely to be performed for symptoms (58.2%, 53.8%, p<0.001), involve an inpatient (12.7%, 2.5%, p<0.001), occur at academic centres (88.1%, 48.3%, p<0.001), and less likely to utilize propofol (17.4%, 32.9%, p<0.001). With trainee involvement, the ADR (29.0%, 30.5%, p=0.025), SSA detection rate (4.4%, 5.2%, p=0.009), and PDR (39.2%, 42.0%, p<0.001) were lower but not the CI (96.7%, 97.2%, p=0.069) or perforation (0.05%, 0.06%, p=0.823) rates. On multi-variable analysis, trainee involvement had no significant impact on ADR (RR0.94, [0.88-1.01], p=0.08), polyp (RR0.98, [0.93-1.04], p=0.47), or failed CI (RR0.93, [0.78-1.10], p=0.38) but the risk of detecting a SSA was lower (RR0.79, [0.64-0.98], p=0.03). CONCLUSION: Trainee involvement reduced SSA detection rates but not other outcome measures.

Cuninghame, Sean

Diagnosing Polycythemia Vera: Are we ordering too many JAK2 tests?

Sean Cuninghame Eri Kawata, Bekim Sadikovic, Hanxin Lin, Ian Chin-Yee

Background: Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by an elevated red blood cell mass, neurologic phenomena, and thrombosis. A JAK2 mutation is identified in almost all patients with PV. In 2016, the WHO diagnostic criteria for PV changed to include a lower hemoglobin threshold of >165 g/L (men), or >160 g/L (women) in hopes of capturing previously undiagnosed PV. We investigated whether this change in diagnostic criteria is associated with increased testing, and capturing more people with PV. Methods: All JAK2 tests ordered between 2015 and 2018 at LHSC were collated, and the corresponding complete blood count, EPO level, and other relevant parameters were collected. Results: There was a total of 1950 JAK2 tests ordered between 2015 and 2018 at LHSC. The overall trend to increase testing observed over these four years was associated with a decrease in the percentage of positive tests. In 2015 and 2016, 88 of 428 (21%) and 92/448 (21%), of tests were positive, respectively. Thereafter, in 2017 and 2018, there was a decrease in positive results to 107/590 (18%) and 65/484 (13%), respectively.Conclusion: The change in WHO criterion for a lower hemoglobin threshold for diagnosis of PV was associated increase in JAK2 tests ordered at LHSC with a reduction in the percentage of positive tests. This suggests more indiscriminate test utilization without capturing more patients with undiagnosed PV. Next steps will be to develop a JAK2 clinical prediction tool for JAK2 positivity based on patient,'s laboratory parameters.

Dehghani, Mina

Risk of Major bleeding with Ibrutinib in patients with Thrombocytopenia

Mina Dehghani

Ibrutinib is an irreversible inhibitor of Bruton,'s tyrosine kinase (BTK) that is an effective treatment agent for multiple lymphoproliferative disorders including chronic lymphocytic leukemia (CLL). Ibrutinib, however is associated with increased bleeding risk. Previous trials of Ibrutinib have reported bleeding

rates between 30-60%, majority of these bleeding events are grade 1-2, most commonly mucocutaneous bleeding. Risk of grade 3-4 bleeding varies between 4-8%, including subdural hematoma, gastrointestinal bleeding and hematuria. Pathophysiology of ibrutinib associated bleeding is complex, it has been established that BTK has a role in collagen and von willebrand factor dependent platelet functions through its involvement in GP1b and GPVI downstream signaling pathways, respectively. Previous studies have not shown a significant association between bleeding risk and platelet count, however considering the mechanism of bleeding related to ibrutinib, thrombocytopenia is a clinical factor that its role in increased risk of bleeding is still debatable. The primary objective of this study is to investigate risk of major bleeding associated with significant thrombocytopenia in patients with CLL on treatment with ibrutinib. A retrospective chart review of patients >18 years with CLL who are treated with single agent ibrutinib between Jan 2014 to Dec 2019, at LHSC will be conducted. Patients will be excluded if they have a known bleeding disorder. Rate of grade 3-4 bleeding associated with platelet count < 50 will be compared to bleeding rate in patients with higher platelet counts. Secondary objective is to investigate bleeding risk associated with anticoagulation and antiplatelet agents in patients on ibrutinib.

Desai, Karishma

Clinical Course and Characteristics of Patients with COVID-19: Preliminary Results of a Single-Centred, Prospective Observational Study

Karishma Desai, MD Kyle Fiorini MD, Debarati Chakroborty MD, Daniel Gillet MD, Kimia Honarmand MD MSc, John Basmaji MD, on behalf of the CORAL investigators

Abstract:Purpose: To our knowledge, there has been no published data describing the Canadian experience of COVID-19 patients. We seek to describe the clinical course, characteristics, and outcomes of hospitalized patients with COVID-19.Methods: This is a prospective observational study of hospitalized patients with COVID-19 from March 23rd 2020 to present. Demographic data, comorbidities, clinical symptoms, laboratory values, therapies, and clinical outcomes were collected. Data were compared between patients admitted to the ward versus ICU.Results: We enrolled 42 patients. The mean age of patients was 72 years (SD 14.3), 20 were male (48%), and 13 reside in long-term care (31%). The most common symptoms at presentation included dyspnea (76.2%), fatigue (54.8%), diarrhea (40.5%), and myalgias (33.3%). On initial presentation, 19 patients (45.2%) required oxygen therapy and 8 (19%) required ICU admission. Compared to patients admitted to the ward, Patients admitted to the ICU were younger (57.3 years (10.0) vs 75.2 years (13.0), p = 0.001), had a higher C-reactive protein (307.90 mcg/L (81.3) vs 99.51 mcg/L (19.2), p = 0.02), and a higher white blood cell count (11.5 x 109 (11.4) vs 6.6 x 109 (3.3), p = 0.03). Five patients have died, 4 have been discharged, with the remaining 33 patients still admitted in hospital.Conclusions: Our preliminary results highlight differences between patients admitted to the ICU and those admitted to the ward, and could inform the design of a clinical prediction tool to identify ward patients at risk of clinical deterioration.

Desai, Karishma

The impact of Point-of-care ultrasound guided resuscitation of shock on clinical outcomes: A systematic review

Karishma Desai, MD Robert Arntfield, MD, Ian M Ball, MD MSc, Phil Jones , MD MSc, John Basmaji, MD; on behalf of the CRIXUS Investigators

Purpose: We performed a systematic review of the literature to determine the effect of point-of-care ultrasound (POCUS) guided resuscitation of shock on patient-important outcomes inpatients with shock.Source: We searched MEDLINE and EMBASE from inception to December 2019 for studiesthat evaluated the use of POCUS to guide resuscitation of shock patients. A two-step reviewprocess with three independent reviewers was employed. We assessed the risk of bias andapplied Grading of Recommendations Assessment, Development, and Evaluation (GRADE)methodology to evaluate the certainty of the evidence by outcome.Principal Findings: Nine studies were included in our final analysis (n= 7096). Three studieswere randomised controlled trials while six studies were observational cohort studies. Only threestudies showed an association between POCUS guided resuscitation of shock and mortality,none of which were randomized controlled trials. Overall, the identified studies had serious riskof bias.Conclusion: There is no evidence that POCUS guided resuscitation improves patient importantoutcomes of patients with shock, however the certainty in evidence is very low. Several studieshave identified patient populations that may benefit from POCUS guided resuscitation of shock.Further randomized interventional studies are required to address this question.

Deschner, Emilie

An Unusual Cause of Acute Myocardial Infarction

Emilie Deschner Anthony Glanz

Background: Unusual and extra-cardiac presentations are hallmarks of atrial myxomas.The variety of clinical presentations often leads to delays in diagnosis. Unexplained constitutional symptoms, especially if accompanied by a new murmur should trigger consideration of atrial myxoma as a potential diagnosis. We present a case of acute myocardial infarction preceded by constitutional and neurologic symptoms that was ultimately diagnosed as atrial myxoma. Presentation: A 50 year old female with a 6-month history of difficulty with ambulation due to leg cramps, weakness, paresthesia and an unintentional 30-40 pound weight loss developed acute chest pain and an altered level of consciousness. CT head and CT angiography of the cerebral vessels were unremarkable. Her ECG demonstrated ST elevation in the inferior leads with anterolateral ST depression. Emergency cardiac catheterization demonstrated an abrupt cut off of the intermediate artery and OM1 branch with moderate left ventricular systolic dysfunction, apical dyskinesis and moderate hypokinesis of the anterior and inferior wall. No stents were placed. Echocardiography demonstrated a large 63X24 mm left atrial tumour ball-valving and partially obstructing mitral valve flow. Persistent hypotension necessitated emergency surgery to remove the myxoma. Ultimately her STEMI was felt to be secondary to an embolus from her myxoma. Removal of the myxoma resulted in complete resolution of her neurological and constitutional symptoms.Conclusion: Atrial myxomas are rare benign tumours of the heart which may present in

insidious ways causing delays in diagnosis. Atrial myxoma should be considered in patients presenting with constitutional symptoms and an abnormal cardiac exam.

Deschner, Max

Giant calcified left ventricular aneurysm with calcified thrombus following remote myocardial infarction

Max Deschner MD Patrick Teefy, MD, Anthony Glanz, MD, MSc

Background: Left ventricular (LV) aneurysms may develop after transmural myocardial infarctions (MI). In the era of percutaneous coronary intervention (PCI), LV aneurysms and complications including mural thrombi and aneurysm calcification are rare. We describe a case of an asymptomatic giant calcified LV aneurysm and calcified apical thrombus.Presentation: A 60-year-old hyperlipidemic male smoker presented with two months of stable angina. After suffering an anterior MI seventeen years earlier, he underwent diagnostic angiography but did not receive reperfusion therapy. He took aspirin only. Recent angiography demonstrated triple-vessel coronary artery disease, left anterior descending artery (LAD) occlusion and apical akinesis with a giant LV aneurysm and calcified thrombus. Because surgical revascularization was considered too high-risk, our patient underwent stenting of the left circumflex and first diagonal and staged percutaneous coronary intervention (PCI) to the right coronary artery. At three months, he was angina-free.Discussion: Calcified aneurysms and thrombi are rare today due to prompt revascularization and medical therapy including anticoagulation. Afterload reduction using angiotensin-converting-enzyme inhibitors prevents infarct expansion, ventricular re-modelling and aneurysm enlargement. Treatment for persistent thrombi despite anticoagulation is less clear. Generally, anticoagulation may be discontinued if a thrombus is organized and old. Aneurysmectomy may be considered in select patients with heart failure, ventricular arrhythmias or recurrent thromboembolism. We feel that PCI in our patient led to functionally-complete revascularization, as the left anterior descending artery was ostensibly supplying scar tissue.Conclusion: Calcified LV aneurysms are unique, and now rare, sequelae of ST elevation myocardial infarctions.

Deschner, Max

When donor T cells attack: liver transplant-associated acute graft-versus-host-disease and the value of the hematopoietic stem cell transplant team

Max Deschner Max Deschner, Ziad Solh, Karen Bosma, Wael Haddara, Ping Yang, Robert Broadbent, Aaron Haig, Jonathan Keow, Mayur Brahmania, Anargyros Xenocostas, Uday Deotare

We describe a 54-year-old male patient who underwent liver transplantation for alcohol use disorder related cirrhosis and developed acute graft-versus-host disease. Initial clinical presentation included dermatitis, bone marrow failure and enteritis. Results of skin biopsy and cytogenetic studies were consistent with liver transplant-associated acute graft-versus-host disease. Clinical features of graft-versus-host-disease are non-specific, which may lead to delayed diagnosis as more common conditions including infections or drug reactions are considered. The importance of this case is to highlight to transplant physicians and surgeons the challenges of diagnosing graft-versus-host-disease. We argue

that early involvement of hematopoietic stem cell transplant physicians can facilitate timely identification and treatment of this complication of transplantation. In our case, pre-existing partnerships among the liver and hematopoietic stem cell transplant teams, transfusion medicine specialists, critical care specialists and members of the cytogenetics laboratory facilitated timely communication relevant to confirming graft-versus-host disease. We propose an algorithm to assist in the work up of suspected graft-versus-host disease. Because this condition is characterized by high mortality, a high index of suspicion is imperative for prompt diagnosis and optimal management of the donor-recipient immune interaction when patients present with classic clinical features.

Deschner, Max

The Impact of Red Blood Cell Transfusion on Mortality and Treatment Efficacy in Oncology Patients Treated with Radiation: A Systematic Review of the Literature

Max Deschner Lakshman Vasanthamohan, Sondos Zayed, Alejandro Lazo-Langner, David Palma, David D'Souza, Syed Omar Gilani, R. Gabriel Boldt, Ziad Solh

Introduction: Red blood cell (RBC) transfusion practices for patients undergoing radiotherapy (RT) vary due to low-quality retrospective data suggesting anemic patients may respond sub-optimally to RT. Our systematic review investigated whether maintaining higher hemoglobin (Hb) levels using RBC transfusions in radiation oncology patients leads to improved outcomes.Design and Methods: We performed a systematic review using the PubMed (Medline), EMBASE and Cochrane Library databases queried from inception-January 2019. We included randomized controlled trials (RCT), cohort studies and large case series comparing RBC transfusion for lower versus higher Hb thresholds for patients undergoing RT. The primary outcome was overall survival. Secondary outcomes were locoregional disease control, number of transfusions and transfusion-related adverse events.Results: Our search yielded 6172 titles. One study met inclusion criteria; therefore, a meta-analysis was not performed. The study pooled results from two RCTs stratifying patients with head and neck squamous cell carcinoma with low pre-radiation Hb levels (females <130 g/L and males <145 g/L) to RBC transfusion versus no transfusion. The study found no statistically significant differences between groups in overall survival or locoregional disease control, despite increased Hb levels in the transfused group. We conducted a narrative review on relevant trials not meeting inclusion criteria (n=10). These retrospective cohort studies had inconsistent results regarding effects of anemia and transfusion on survival and disease control.Conclusions: Optimal transfusion practice in radiation oncology is controversial with no high quality evidence. Well-designed prospective studies are needed given the unique radiobiology of cancer histologies and potential variability in hemoglobin targets.

Deschner, Emilie

Naltrexone initiation for alcohol use disorder during an inpatient admission: A systematic review

Emilie Deschner Max Deschner, Alla Iansavitchene, Marko Mrkobrada

Background: Patients suffering from alcohol use disorder (AUD) are frequently admitted to hospital for complications of alcohol use. Oral naltrexone and long-acting injectable naltrexone are effective pharmacological treatment options for AUD. We performed a systematic review of the literature evaluating naltrexone-based interventions for AUD in the inpatient setting.Methods: We completed a systematic search in Medline and EMBASE (from inception to February 2020) for trials examining counselling about and/or initiation of naltrexone for AUD during hospital admissions. Independently and in duplicate, we screened titles and abstracts, evaluated full-texts for inclusion, extracted data and assessed references for additional relevant trials.Results: 1112 citations were assessed for relevance and 19 articles were selected for full-text review. Three articles with 748 patients met inclusion criteria. They demonstrated significantly decreased rates of hospital re-admission after patients were counselled about or prescribed naltrexone compared to standard of care. Espiridion found a decrease in re-admission rates for patients treated with intramuscular naltrexone (2.86% vs 25.7%). In subgroup analysis, Stephens et al. found a decrease in 30-day emergency department revisits (9.7% vs 35.7%) and readmissions (2.8 vs 26.2%) among patients counselled about naltrexone. Wei et al. found reductions in 30-day emergency department re-visits (6.1% vs. 18.8%) and re-admissions (8.2% vs 23.4%) among patients who were counselled and/or treated with naltrexone.Conclusion: Hospital-based interventions including counselling and/or treatment with naltrexone have been associated with decreased hospital utilization among patients with AUD. Well-designed prospective studies are needed to inform broader use of naltrexone in the inpatient setting.

Dilliott, Allison

White matter hyperintensity burden in PD patients harbouring rare NOTCH3 genetic variation.

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is caused by heterozygous pathogenic mutations in the Notch Receptor 3 gene (NOTCH3). Patients present with ischemic strokes, cognitive impairment, and white matter hyperintensities (WMH); however, rare cases present with late-onset parkinsonism. We aimed to investigate the association between NOTCH3 variants and WMH in Parkinson,'s disease (PD) patients.We used a next-generation sequencing gene panel to sequence 139 PD patients and identified 13 (~9%) harbouring rare, non-synonymous NOTCH3 variants. Patients were also imaged using magnetic resonance imaging (MRI; 3T) and underwent robust clinical characterization. Using a Bayesian linear model, we observed a doubling of WMH volume between the NOTCH3 variant negative patients and the NOTCH3 variant positive patients, with a multiplicative effect of ~2.2 (between 1.2 and 3.7, 95% probability), accounting for conventional vascular risk factors. Interestingly, no differences in cognition or motor phenotypes were identified between the groups, yet suggested relationships were observed between WMH volumes and

cognition (r=-0.19, C.I: -0.32, -0.02) and motor phenotypes (r=0.14, C.I.: -0.03, 0.30), across all PD patients. This is the first report suggesting that rare, non-synonymous NOTCH3 variants may have a role in WMH burden in cases of idiopathic PD. Although cognition and motor phenotypes were not different between NOTCH3 variant positive and negative patients, this may have resulted from limited sample size. It is recommended that future studies examining WMH volumes in PD are complimented with genomic analysis for NOTCH3 variation.

Edgerley, Sarah

Literature Review of Peanut Oral Immunotherapy with Maintenance Doses Equivalent to 1 Peanut

Sarah Edgerley Harold Kim

Background: Approximately 3% of the general population have an IgE mediated food allergy. Current guidelines recommend total avoidance of allergens as well as proper identification and treatment of allergic reactions. However, these recommendations do not mitigate the severity of a reaction after an accidental exposure. One emerging treatment method is oral immunotherapy (OIT). This involves daily consumption of a food allergen beginning at doses below the amount that causes a reaction, with dose increases over time. The goal of OIT is to increase tolerance to an allergen in order to improve clinical outcomes after accidental exposures. Objectives: This literature review aimed to determine the percent of patients starting OIT that are able to tolerate a maintenance dose equivalent to 1 peanut as well as the severity of adverse events related to therapy.Methods: A literature search was conducted on PubMED. Initial search results were narrowed down to studies with peanut OIT maintenance targets equivalent to approximately 1 peanut (250-400mg of peanut protein [PP]). 6 studies were included.Results: Of 741 participants enrolled 617 (83%) were able to complete OIT up to their targeted maintenance dose. Over 86% of participants experienced an adverse event during the study period. Most events were mild in nature and only 25 reactions were documented as severe. Conclusions: Most patients are able to tolerate maintenance PP doses equivalent to 1 peanut. Despite common mild adverse reactions during therapy, OIT may prevent more severe reactions after accidental peanut ingestion in comparison to allergen avoidance alone.

Fanous, Yehia

What are patients reading?Sudden Cardiac Arrest in Athletes: Assessing the Quality of Online Resources

Yehia Fanous Paul Dorian

Background: Sudden cardiac arrests (SCA) in athletes attract attention and controversy. No studies have explored the quality of online content aimed at the lay public regarding SCA in athletes.Methods: The first 200 hits of the search “sudden cardiac arrest in athletes” on Google were analyzed. Reading difficulty was evaluated using validated reading indices. Content quality was assessed with scoring systems established by expert opinion. An accuracy score was calculated by allocating points (/15) based on accuracy and comprehensiveness on the domains of epidemiology (/1), etiology (/9), screening (/3) and treatment (/2). A comprehensibility score was calculated (/5), based on clarity of lay explanations of

5 concepts: SCA, cardiac disease, resuscitation, defibrillation, and screening (1 point/category).Results: A total of 115 unique web-domains were analyzed, of which 53.9% were from educational institutions. Mean accuracy-score was 6.5¬±3.9 (/15); mean comprehensibility-score: 1.9¬±1.2 (/5); and mean school grade-reading level: 13.3 ¬± 2.9 years (i.e. post-secondary). No website met reading level recommendations set by national health organizations. The majority of websites had poor lay appropriate explanations of concepts; 68.7% failed to mention over half of common etiologies associated with SCA or differentiate age specific causes; only 59.1% correctly cited incidence in young athletes; 28.7% mentioned treatment options beyond immediate resuscitation; 46.1% listed the value of history, physical exam and ECG in screening. Higher reading difficulty correlated with higher accuracy scores (? 1.1, p<0.001).Conclusion: There is a paucity of accurate, comprehensive and lay language appropriate online health information on SCA in athletes.

Fatima, Safoora

Health Assessment Questionnaire at One Year Predicts All-Cause Mortality in Patients with Early Rheumatoid Arthritis

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Objective: Higher HAQ (health assessment questionnaire) disability has been associated with hospitalizations and mortality in established RA (rheumatoid arthritis) patients but associations in early RA are unknown. Methods: RA patients (symptoms <1 year) enrolled in the Canadian Early Arthritis Cohort(CATCH) who initiated DMARDs and had completed HAQ data at baseline and 1 year follow-up were eligible. Discrete-time proportional hazards models were used to estimate crude and multi-adjusted associations between HAQ at baseline and 1 year with all-cause mortality.Results: 1724 patients with early RA; mean age 55 years and 72% female were included. Over 10 years, 62 deaths (2.4%) occurred. Deceased patients had higher HAQ scores and DAS28(disease activity) scores at baseline and 1 year versus the non-deceased group. Age, male sex, lower education, smoking, more comorbidities, higher baseline disease activity and steroid use were associated with mortality in unadjusted survival models. Contrary to HAQ at baseline, the association between all-cause mortality and HAQ at 1 year remained significant even after adjusting for age, gender, comorbidities, disease activity, smoking, education, seropositivity, symptom duration and steroid use in adjusted survival models. HAQ baseline unadjusted hazard OR was 1.46 (CI 1.02-2.09) and adjusted 1.25 (CI 0.81-1.94) vs. HAQ at 1 year unadjusted hazard OR was 2.58 (CI 1.78-3.72) and adjusted 1.75 (CI 1.10-2.77).Conclusion: Higher HAQ at 1 year was significantly associated with all-cause mortality in a large early RA cohort suggesting poorer disease control and function in first year of RA contributes to higher mortality.

Findlay, Ryan

The Diagnosis and Management of a Functional Paravertebral Paraganglioma

Ryan Findlay Angela Rutledge, PhD; Sonja Payne, MD; Richard Inculet, MD; Sachin Pandey, MD; Stan Van Uum, MD,PHD, FRCPC.

A 32-year-old male presented with a 4-year history of palpitations, diaphoresis, and orthostatic hypotension. One year prior, he began experiencing severe headaches and neck pressure. Work-up included an MRI head/neck/spine, identifying a 2.4 x 2.0 cm left posterior mediastinal lesion adjacent to the T5 vertebrae. A community center attempted VATS resection, which was aborted intraoperatively from hypertensive crisis, with SBP increasing above 325 mmHg. Evaluation revealed a 24-hour urine norepinephrine of 6117 nmol/d (normal <575) and normetanephrines of 16.6 umol/d (normal <3.4). An MIBG showed tracer avidity in the left paraspinal lesion and minimal uptake in the adrenals. A functional paraganglioma was diagnosed and the patient was initiated on alpha and beta-blockade. Spinal angiography confirmed a hypervascular paraspinal tumor. Trans-arterial particle embolization was performed with minimal residual tumor blush present post. Successful VATS excision of the tumor was completed one week after embolization. Pathology revealed an intact tumor that stained diffusely positive with synaptophysin with a few foci of coagulative necrosis. Peri-procedural plasma metanephrine and cathecholamine levels were collected. Normetanephrine (normal <=0.89 nmol/L) was 4.66 before embolization, >6.25 after embolization, 3.70 the day after embolization, 4.10 before VATS, and 0.69 after VATS. Norepinephrine (normal 0.8-3.4 nmol/L) was 24.3, 111.7, 61.1, 19.6, and 4 respectively.Discussion: Functional neuroendocrine tumours may be difficult to diagnose from the wide variety of presentations and must be considered when investigating vascular mediastinal tumors. In our case, pre-operative embolization did not normalise catecholamines, likely from incomplete arterial embolization, but helped reduce intra-operative bleeding risk.

Good, Hayley

Aspirin Prevents Tuft Cell-Derived Colitis-Associated Cancer in a PGE2 and Phospho-Akt Dependent Manner

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Introduction: Inflammatory bowel disease is a major risk factor for colorectal cancer (CRC). Despite the link between inflammation and cancer, the mechanism for this remains unknown. Dclk1 expression marks tuft cells. We previously showed Dclk1+ cells are quiescent, long-lived, and resistant to proliferation even upon mutation of the tumor suppressor APC. Following colitis, however, APC-mutated tuft cells become cancer-initiating cells. Interestingly, Dclk1+ cells highly express cyclooxygenase (COX)-1 and -2, the direct enzyme targets of Aspirin, a chemopreventative drug against CRC. Therefore, we aimed to determine the effect of Aspirin on Dclk1+ cell-derived colitis-associated cancer (CAC).Methods: Dclk1CreERT2/APCfl/fl/R26mTmG mice were administered tamoxifen to induce APC-loss and GFP expression in Dclk1+ cells, followed by DSS to induce colitis and daily treatment with Aspirin or vehicle. Sixteen weeks post-tamoxifen, colonic tumors were examined. Colonic tissue was analyzed acutely for prostaglandin levels by LC-MS. To investigate how Aspirin influences tumorigenesis, we focused on

PGE2, a key prostaglandin in CRC, and its downstream mediator, phospho-Akt. Misoprostol (PGE analogue) and SC-79 (Akt activator) were tested on Dclk1+ cell-derived tumorigenesis. Colonic tissue was collected acutely post-DSS and analyzed for GFP+ cells by fluorescence microscopy.Results: Aspirin reduced Dclk1+ cell-derived colonic tumor number. LC-MS revealed that prostaglandins were elevated in DSS and reduced upon Aspirin treatment. Treatment with vehicle, Misoprostol, or SC-79 during DSS resulted in GFP-traced crypts with normal morphology, however, co-treatment with Misoprostol and SC-79 showed GFP-traced dysplastic lesions.Conclusion: Our data suggest that Aspirin prevents CAC by inhibiting PGE2 and phospho-Akt signaling during colitis.

Hadwen, Brook

The Presence of Autoantibodies in Males Versus Females with Rheumatoid Arthritis: A Systematic Review and Meta-analysis

Brook Hadwen Lillian Barra

Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic inflammation in joints. Approximately 75% of RA patients test seropositive for the autoantibodies rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA). While it is understood that women develop RA more often and more aggressively than men, it is unknown whether sex plays a role in seropositivity. The purpose of this systematic review and meta-analysis was to investigate whether autoantibodies are more often found in women than men with RA. Secondarily, are there any other factors that may influence seropositivity? Databases were searched and studies of RA (n ?100) were included if they reported proportion of seropositive RA patients by sex. Meta-analyses and meta-regression were conducted using the random effects model. Covariates regressed were smoking, age, body mass index, a functional score and disease activity score. Twenty studies were included; 90% were conducted in Western countries, the mean age ranged from 47,Äì65 years and 48,Äì79% of subjects were female. Results indicated that women were less likely than men to be positive for RF (logOR of ,Äì0.16[95%CI:¬¨,Äì0.31, ,Äì0.02]). ACPA seropositivity was not different by sex (logOR of ,Äì0.13[95%CI: ,Äì0.31, 0.05]). Meta-regression determined smoking and age to have a statistically significant relationship with RF and ACPA seropositivity, p=0.03 and p<0.001, respectively. In conclusion, despite women having more severe disease and seropositivity predicting worse outcomes, women were less likely seropositive than men. The relationships between other factors and seropositivity require further study.

Haghbayan, Hourmazd

Adenosine Diphosphate Receptor Inhibitor Monotherapy with Ticagrelor or Clopidogrel Following Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Hourmazd HAGHBAYAN Daniel P. DUROCHER; Eric A. COOMES; Shahar LAVI

In patients undergoing percutaneous coronary intervention (PCI), current practice is to treat patients with at least 6 months of dual antiplatelet therapy (DAPT); however, prolonged DAPT is associated with

heightened bleeding risk. Limiting DAPT to a shorter period after PCI, followed by adenosine diphosphate receptor inhibitor (ADPri) monotherapy, may optimize the balance of risks.We undertook a systematic review and meta-analysis of randomized trials assessing abbreviated DAPT followed by ADPri monotherapy post-coronary stenting, examining clinically important bleeding, major adverse cardiovascular events (MACE), and all-cause mortality. Data were pooled at one-year using the inverse variance method with random effects models. Sub-group analyses were undertaken according to the primary ADPri employed.Four trials (n=29084) were eligible, with 51.5% of patients recruited in the context of acute coronary syndrome. Following meta-analysis, clinically significant bleeding events were lower in patients receiving ADPri monotherapy (RR=0.60; 95%CI, 0.43-0.83; I2=73%), with no significant difference in all-cause mortality (RR=0.87; 95%CI, 0.71-1.06; I2=0%) or MACE (RR=0.90; 95%CI, 0.79-1.03; I2=1%). In subgroup analysis, trends toward lower rates of all-cause mortality (RR=0.81; 95%CI, 0.65-1.01; I2=0%) and MACE (RR=0.90; 95%CI, 0.79-1.03; I2=25%) were seen in the studies employing ticagrelor; however, neither analysis reached statistical significance (p-values=0.06 and 0.19, respectively).Overall, an abbreviated course of DAPT followed by ADPri monotherapy significantly reduces rates of bleeding post-PCI with no difference in MACE or all-cause mortality. Future studies are required to conclusively determine whether ticagrelor in this setting also reduces all-cause mortality compared to clopidogrel.

Haghbayan, Hourmazd

Temporal Trends in the Complexity of Novel Drug Nomenclature

Hourmazd HAGHBAYAN Shahrzad SAIF; Ahmed M. BAYOUMI

In contemporary drug nomenclature, commercial drug names may vary across manufacturers, languages, or time whilst generic names are usually constant and should therefore be preferred. However, patient and clinician preferences for commercial names may lead to use of bioequivalent but more expensive brand-name medicines. Word length may be one reason that commercial names are preferred as syllable counts above three correlate with perceived word complexity and longer names are harder to remember and pronounce.We assessed temporal trends in generic and commercial name syllable counts for all pharmaceuticals approved by the FDA from 2002/01-2019/02. We extracted generic and commercial names for all New Molecular Entities and Biologic License Applications (biologics) and counted drug name syllables, excluding terms specifying a salt, ester, concentration, or mode of administration. We linearly regressed syllable count over time and compared differences between slopes using seemingly unrelated estimation.We identified 551 drugs, of which 132 (24%) were biologics. Mean (standard deviation) syllables for generic and commercial drug names were 5.5 (2.5) and 3.1 (0.8), respectively; 97% of generic and 14% of commercial names contained more than three syllables (p<0.001). A difference between commercial and generic names was apparent in 2002 (1.41 syllables, 95%CI 1.04-1.77, p<0.001) and increased over time (0.098 syllables/year, 95%CI 0.062-0.13, p<0.001).Overall, this study identified a large and increasing difference in the number of syllables between generic and commercial drug names, indicting the need for additional approaches to help clinicians associate generic and commercial drug names.

Hatam, Erfun

Rate of Prescription of Oral Anticoagulation in patients presenting with new onset Atrial Fibrillation/Flutter in the Emergency Department

Erfun Hatam Gauri GhateKristine VanAarsenMelanie ColumbusChiana Garvida

IntroductionThe goal of this study was to identify whether the ED patient population presenting with new onset AF/AFL with CHADS65 ?1 are appropriately initiated on OAC by ED physicians.MethodsThis was a retrospective chart review (Jan-Dec 2017) of ED visits at two academic hospitals in London Ontario. ResultsA total of 1272 charts were reviewed. 1124 were excluded. 148 charts were identified as patients with new onset AF/AFL presenting to the ED who were discharged by ED physicians. 24/148 (16%) were appropriately prescribed OAC. 124/148 (84%) were not prescribed OAC. Of these 40/124 (32%) were CHADS65 0 while the other 84/124 (67%) were CHADS65?1 who should have been considered for OAC. Further review determined that 78/84 (92%) were referred to outpatient clinics for the decision regarding OAC with the mean (SD) number of days to follow up being 11(¬±15). Importantly 1/84 (1.2%) returned prior to their scheduled appointment with a stroke. Only 6/84 (7%) had no follow up arranged. ConclusionsOverall, we found that the rate of OAC prescription by ED physicians for patients being discharged with a new diagnosis of AF/AFL with a CHADS65 score ?1 was 16%. This is despite the CCS 2014 recommendation of starting OAC for all patients with a CHADS65 score ?1. It appears that ED physicians are continuing to defer the decision to prescribe OAC to outpatient clinics. Further projects can explore barriers to application of the CCS guidelines and create knowledge translation tools.

Hu, Amanda

Pulmonary arterial hypertension in systemic sclerosis is nearly always accompanied by a low diffusing capacity

Amanda Hu Tatiana Nevskaya, Murray Bacon, Janet Pope

Background:Scleroderma (systemic sclerosis; SSc) has high morbidity and mortality. Pulmonary arterial hypertension is common with a high mortality. SSc patients are screened with pulmonary function tests (diffusing capacity of the lung for carbon monoxide; DLCO).Objectives:The DLCO % predicted was analyzed comparing patients with and without PAH to determine if it is always low at time of PAH diagnosis. Methods: The Canadian Scleroderma Research Group (CSRG) database was used containing more than 1300 SSc patients with a mean disease duration of 8 years. All patients with at least one follow up visit and DLCO recorded at least twice were eligible for enrolment into this nested case control study. Diagnosis of PH was verified using several algorithms within the database including R heart catheterization, use of PH medications and physician response of ‚Äòyes,' to question has this patient been diagnosed with pulmonary hypertension.Results At time of PH diagnosis, the mean DLCO% predicted was 47% (N=30) vs no PH 73% (N=960) P<0.0001, and proven documented PAH also showed the differences (PAH, N=22 DLCO% predicted 51% vs. PAH negative (N=968) DLCO% pred 72%, P<0.0001).ConclusionDLCO <50% is associated with a high odds of PH/PAH

Iablokov, Vadim

HopX Labels a Colonic Stem Cell That Contributes to Colonic Regeneration But Not Colonic Tumors

Vadim Iablokov H. Good, A.E. Shin, E.N. Fazio, J. Loggie, L. Zhang, S. Asfaha

Background: Colorectal cancer is the 2nd leading cause of cancer death in Canada. In rapidly dividing tissues such as the colon, only long-lived, multipotent, self-renewing stem cells have longevity to accumulate mutations and serve as the cellular origin of cancer. In the small intestine, there are at least two principal stem cell pools: actively cycling, crypt base cells expressing Lgr5, and quiescent cells situated above the crypt base. Lgr5-expressing cells can give rise to cancer upon mutation. We examined whether the atypical homeobox protein Hopx marks stem cells in the colon and whether these cells can give rise to colon cancer.Methods: Hopx lineage tracing in the absence and presence of colonic damage was quantified in mice. Hopx+ cells were selectively ablated in the mouse colon to determine their role in injury. To test whether Hopx expressing cells can serve as a cellular origin for colon cancer the APC gene was selectively disrupted in Hopx+ colonic cells.Results: Consistent with the labeling of a stem cell, Hopx+ cells expanded to lineage trace full colonic crypts. Interestingly, ablation of Hopx+ cells did not alter histological damage or survival during normal homeostasis, however, Hopx+ cell ablation in the presence of colonic damage resulted in increased histological damage. Surprisingly, loss of APC in Hopx+ cells did not induce colonic adenomas even after 8 months.Conclusions: Hopx expressing cells identify a novel colonic stem cell pool but do not have the capacity to give rise to colorectal adenomas upon loss of the APC gene.

Isen, Marly

Non Convulsive Seizures in Delirium: A systematic review of the literature

Marly Isen Monidipa Dasgupta

Background and objectives: Nonconvulsive seizures (NCS) are difficult to diagnose due to their varied presentations. Most frequently they present with altered mental status (AMS), and can resemble delirium. We conducted a systematic review to determine the prevalence of NCS in acutely confused adults; secondary goals were to ascertain whether certain variables are associated with NCS. Methods: PubMed, Embase, and PsycINFO databases were searched from inception to February 21 2019, using the terms ("Status epilepticus" OR "Seizures" OR "Epilepsy") AND ("Nonconvulsive" OR "Petit mal" OR "Subclinical seizure" OR "Absence seizure") AND (Delirium OR Encephalopathy OR Altered mental status OR Confusion). English studies on adults, reporting prevalence of NCS in acutely confused or delirious persons, with at least 10 participants were included. Studies done mainly in the ICU, palliative or pediatric settings were excluded. Two reviewers took part in study selection and analysis. Findings:Our search yielded 358 abstracts and another 12 were reviewed from references of included studies. Fourteen met inclusion criteria. Prevalence of NCS ranged from 1.2% to 37% in participants with AMS. Studies varied in populations enrolled and criteria used to diagnose NCS. Most studies were felt to have some referral bias. Variables associated with NCS in at least 2 studies included older age, female sex, and the presence of abnormal ocular movements. Conclusion: NCS should be considered as a frequent contributor to delirium in adults. Few variables for NCS were consistently identified. More research is needed to evaluate the utility of EEG in working up delirium or AMS.

Jacob, Gabriella

Standardizing the discharge process for COVID19-positive inpatients: a quality improvement initiative.

Gabriella Jacob Erin Spicer

At London Health Sciences Centre, recovered inpatients with COVID-19 are being discharged, but currently there is no standardized process to ensure patients are discharged safely and efficiently. We aim to create a standardized discharge process for hospitalized patients with COVID-19 with use of an essential discharge checklist. Our target is for 90% of patients with COVID-19 or suspected COVID-19 to be discharged from hospital with a complete discharge checklist. The first developmental PDSA cycle involved input from physicians about barriers to discharge of COVID-19 patients including a paucity of reference material, guidance around public health notification, and instructions about how long to self-isolate. A discharge checklist was developed to address these items, including a streamlined process for Public Health notification, standardized discharge documents including Public Health handouts, and referrals to London Urgent COVID Care Clinic (LUC3). The outcome measure is defined as the percentage of patients discharged with a discharge checklist completed by the physician who discharges the patient. Important process measures include time to complete the discharge of a COVID-positive patient (after discharge, physicians are requested to fill out a survey to determine the average time it takes to discharge a patient, as well as the average time it takes to fill out the standardized discharge checklist) and patient education (patients are contacted via telephone to determine if they understand their discharge instructions). The results of the discharge intervention will inform future PDSA cycles to ensure we are meeting the needs of discharged patients recovering from COVID-19.

Jalbert, Rochelle

The Role of the Immature Platelet Fraction in Predicting Response to Corticosteroids in Patients with Immune Thrombocytopenia: A Retrospective Study

Rochelle Jalbert Jason Arnold, Ben Hedley, Wendy Brown, Ian Chin-Yee, Cyrus Hsia

Immune thrombocytopenia (ITP) is an autoimmune disease mediated by destruction of platelets resulting in low platelet counts. The immature platelet fraction (IPF) is a measurement of immature platelets circulating in peripheral blood that is a non-invasive index of bone marrow megakaryocytic activity. In patients with consumptive causes of thrombocytopenia such as ITP, the IPF should be increased as the bone marrow is responding appropriately. ITP is a heterogenous disorder with variable response to corticosteroids. The role of this study is to determine if IPF could predict response to corticosteroid therapy. We retrospectively reviewed 30 ITP patients seen at LHSC and treated with corticosteroids from January to December 2019. 16 were included in final analysis. 15 had no previous therapy; 1 had two previous lines of therapy. 13 patients achieved response to corticosteroids. The average IPF was 22.4 in responders, whereas in non-responders, the IPF was 10.4 ($p = 0.05$). Of the responders, 7 had sustained response at 3 months, 3 relapsed, and 3 did not have the available data. The IPF in those with sustained response was 19.6, whereas the IPF in those who relapsed was slightly lower at 16.7 ($p = 0.72$). Our study demonstrates that a lower IPF may suggest poorer response to

corticosteroids, but it does not distinguish those with sustained remissions. The variation in IPF supports the clinical heterogeneity of chronic ITP. Different forms of therapy may be required to improve response in populations with low IPF values. Larger studies are needed to confirm our findings.

Jayawardena, Devika

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

Devika Jayawardena Sanjay Mehta, Lefeng Wang, Cynthia Pape,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 ?, interferon ?, and interleukin 1?)for 4 hours. 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.

Kassirian, Shayan

Delay in diagnosis of patients with head and neck cancer in Canada: impact of patient and provider delay

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Background: Head and neck cancers (HNC) often present at an advanced stage, leading to poorer outcomes. Late presentation may be attributable to patient delays (i.e., reluctance to seek treatment) or provider delays (i.e., misdiagnosis, prolonged wait time for consultation). The objective of this study

was to examine the length and cause of these delays in a Canadian universal health care setting.Methods: Patients presenting for the first time to the HNC Multidisciplinary Team (MDT) with a biopsy proven HNC were recruited to this study. Patients completed a survey querying initial symptom presentation, their previous medical appointments, and length of time between appointments. Clinical and demographic data on all patients were collected.Results: The average time for patients to have their first appointment at MDT Clinic was 15.1 months consisting of 3.9 month for patients to see a health care provider (HCP) for the first time since symptom onset and 10.7 months from first HCP appointment to MDT clinic. Patients saw an average of 3 HCPs before the MDT clinic visit (range 1-7). No significant differences in time to presentation were found for based on stage at presentation or anatomical site. Conclusions: At our tertiary care cancer centre, significant delays exist in a patient,'s clinical pathway to being seen by at the MDT clinic, particularly in time from first HCP visit to MDT referral. Possible methods to mitigate delay include education for both patients and providers on HNC and a more streamlined referral system.

Kelton, Danielle

Evaluating clinical and situational factors related to the likelihood of physician authorization for time-sensitive procedures during mandatory paramedic patches

Danielle Kelton Matthew Davis MD MSc, Kristine Van Aarsen MSc, Jovana Momic BSc, Sean Doran MD BEd BSc BA

Introduction: Delegation of medical acts by physicians to paramedics is an important component of prehospital care. Where directives require physician input, online medical control (a "patch") facilitates communication between a paramedic and a Base Hospital Physician. The aim of this study was to examine the impact of various clinical and situational factors on the likelihood of a patch request being granted. Methods: Prehospital paramedic calls that included a mandatory patch point point (excluding unavailable records and requests for termination of resuscitation) were identified through review of all records from January 1, 2014 to December 31, 2017 for Paramedic Services in our region. Written Ambulance Call Reports and audio recordings of paramedic patches were reviewed.Results: 214 patch records were screened for inclusion. 91 records were included in the analysis. 51 of 91 (56%) patch requests were granted by the physican. Of the 40 paramedic requests that were not granted, the most commonly cited reasons were close proximity to hospital (22/40; 55%) and low likelihood of the intervention making a clinical impact in the prehospital setting (11/40; 27.5%). All requests to perform needle thoracostomy for possible tension pneumothorax, administer atropine for symptomatic bradycardia and treat hemodynamically unstable hyperkalemia were granted (2/2, 3/3 and 7/7, respectively), while requests for synchronized cardioversion (7/19; 37%) and transcutaneous pacing (2/6; 33%) were approved less frequently.Conclusion: This retrospective review suggests that requests to perform certain critical interventions are more likely to be granted and calls into question the requirement for a patch for these procedures.

Kelton, Danielle

Evaluating factors related to effective interpersonal communication during mandatory paramedic patches

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Introduction: Delegation of controlled medical acts by physicians to paramedics is an important component of the prehospital framework. Where directives require physician input, online medical control (a “patch”) facilitates communication between a paramedic and a Base Hospital Physician. The aim of this study was to examine areas of potential improvement in this method of communication.Methods: Prehospital calls that included a mandatory patch point (excluding unavailable records and requests for termination of resuscitation) were identified through review of records from January 1, 2014 to December 31, 2017 for Paramedic Services in our region. Written Ambulance Call Reports and audio recordings of patches were reviewed. Pre-specified time intervals, clinical factors, specific patch requests and resulting orders were extracted. Differences between groups were compared using t-tests.Results: 214 records were identified and screened. 91 records were included in the analysis. 51/91 (56%) of patch order requests were granted by the physician. Clarification of information provided by the paramedic was required less often, but not statistically significant, in calls ultimately resulting in granted requests versus those that were not granted (mean 1.4 versus 1.7, ?-0.28; 95% CI -0.75-0.18 p=0.64). The mean time from first contact with the BHP to statement of the request was similar in patches where the request was granted and not granted (44.9 versus 46.3, ?-1.4; 95% CI -12.9-10.2, p=0.49).Conclusion: This retrospective review presents some novel targets for further research and potential education in patch communication to improve efficiency and quality of prehospital care for patients.

Kelton, Danielle

Evaluating factors related to quality of audio transmission during mandatory paramedic patches and technical barriers to efficient communication in the prehospital setting

Danielle Kelton Danielle Kelton MD BSc, Matthew Davis MD MSc, Kristine Van Aarsen MSc, Jovana Momic BSc, Sean Doran MD BEd BSc BA

Introduction: Delegation of medical acts by physicians to paramedics is an important component of prehospital care. Where directives require physician input, online medical control (a “patch”) facilitates communication between a paramedic and a Base Hospital Physician. The aim of this study was to examine the impact of transmission quality on the results of patch calls.Methods: Paramedic calls that included a mandatory patch point (excluding unavailable records and requests for termination of resuscitation) were identified through review of records from January 1, 2014 to December 31, 2017 for Paramedic Services in our region. Written Ambulance Call Reports and audio recordings of patches were reviewed. Pre-specified markers of transmission quality and comprehension as well as the resulting orders from the physician were extracted. Differences between groups was compared using chi-square analyses.Results: 214 records were screened. 91 records were included in the analysis. At least one reference to poor audio quality was made in 55/91 (60.4%) of calls and on average, 1.4 times per call. 48

of 91 (52.7%) patches experienced an interruption of the call. Order requests made by paramedics in calls with no interruptions were approved in 30 of 43 patches (70%) while those requests made in calls with one or more interruptions were approved in only 21 of 48 cases (44%) (?26.0%; 95%CI 5.6-43.5%, p=0.01).Conclusion: This retrospective review suggests that audio quality and interruptions of patch calls may impact a physician,'s ability to approve orders for interventions in the prehospital setting.

Khalil, Nadine

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

Nadine Khalil, 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 and mortality. Many studies have suggested that endocarditis in these patients is predominantly right sided while other studies suggest left sided disease. We hypothesized that the differences in results may be related to the type of drug most commonly injected. Stimulants can have marked impact on systemic hemodynamics and may predispose to left sided valvular damage. Injection of opiates is associated with poor solubility with large particles that may lead to tricuspid valvular damage and may predispose to right sided disease. Design: This case series studied PWID for a first episode of endocarditis between April 1, 2007 and March 30, 2016. Participants were adults (age >18) admitted to one of three hospitals in London, ON. Main outcomes that were measured were valvular site of endocarditis, survival among PWID, causative organisms, cardiac/non-cardiac complications, referral to addiction services, and medical vs. surgical management. Results: There were 370 cases of first episode endocarditis, 202 (54.6%) of which were in PWID. Among PWID, 105 (52%) were male, with the median age was 34 (28-32) years and most patients were positive for hepatitis C virus (69.8%). 92 patients injected only stimulants or only opiates. Pending statistical analysis. Conclusions: This study demonstrates an association between left sided or bilateral infection and stimulant injection. 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.

Khanna, Parul

Severe Hypercalcemia secondary to paraffin oil injections in a 31-year-old bodybuilder

Parul Khanna Dr. Amanda Berberich

Non-PTH mediated hypercalcemia in young patients is rare. It encompasses a broad differential including malignancy, granulomatous diseases, Addison,'s disease, and toxicity of Vitamin A or D. We report here a case of severe non-PTH mediated hypercalcemia secondary to paraffin oil injections for muscle augmentation in a previously healthy 31-year old bodybuilder.The patient presented to the Emergency department with hypertension, bilateral limb edema, acute renal failure (Cr 840 umol/L) and severe hypercalcemia (corrected Ca 3.1 mmol/L). Work up included suppressed PTH 1.0 pmol/L (1.6-

6.9), 1-25 Vitamin D 205 pmol/L (60-208), angiotensin converting enzyme (ACE) levels <8.0 U/L, and PTH-related peptide 23 pg/ml (14-27). On further history, he had been using anabolic steroids for bodybuilding for 8 years, with possible use of paraffin oil injections. CT imaging showed no evidence of sarcoidosis, tuberculosis or malignancy but did reveal multiple granulomas in the pectoralis muscles, suggesting granulomatous foreign body reaction as potential cause for his hypercalcemia. Subsequent testing showed repeat ACE level of 120 U/L and 1,25-vitamin D of 244 pmol/L. He was prescribed prednisone, but he discontinued it due to symptoms of acne. Unfortunately, due to poor adherence with medical direction, management of his hypercalcemia remains challenging.Granulomatous foreign-body reactions are a rare but important side effect of paraffin oil injections used for cosmetic muscle augmentation. They can lead to serious long-term side effects related to hypercalcemia, as seen in our patient. Prognosis is generally poor, with long-term moderate to high dose steroids as the most effective treatment.

Kulkarni, Nidhi

The Role of TIMP3 in Microvascular Endothelial Cell-Extracellular Matrix Interaction and Regulation of Microvascular Barrier Function

Nidhi Kulkarni Sanjay Mehta, Lefeng Wang, Cynthia Pape, and Sean E. Gill

Introduction: During sepsis, pulmonary microvascular endothelial cell (PMVEC) barrier dysfunction, caused by disruption of inter-PMVEC interactions, leads to leak, organ failure and death. PMVEC-extracellular matrix (ECM) binding facilitates these interactions, with data suggesting an association between decreased PMVEC-ECM interactions under pro-inflammatory conditions, indicated by altered focal adhesion kinase (FAK) phosphorylation, and leak. Tissue inhibitor of metalloproteinases 3 (TIMP3) also regulates barrier function through mechanisms currently unknown, as PMVEC from Timp3-/- mice show increased leak. Interestingly, studies in the developing lung showed TIMP3 also regulating PMVEC-ECM interactions. Ergo, I hypothesized that TIMP3 maintains PMVEC barrier function by promoting PMVEC-ECM interactions.Methods: Wild type (WT) and Timp3-/- murine PMVEC were cultured on various matrices and stimulated with PBS or pro-inflammatory cytokines. PMVEC-ECM interactions were assessed using adhesion assays, immunocytochemistry, and the XPERT-permeability assay.Results: Timp3-/- cells showed decreased ECM adhesion vs. WT PMVEC, though both cell types indicated preferential adhesion to fibronectin and lowest adhesion to collagen I. Assessment of phosphorylated FAK (pFAK) showed greater pFAK abundance in WT PMVEC vs. Timp3-/- PMVEC. Furthermore, pFAK distribution and abundance was altered in both cell types under cytomix-treatment. The XPERT assay indicated significant differences in total avidin fluorescence and avidin leak diffusion distance between PMVEC and the ECM in WT vs. Timp3-/- cells, particularly when treated with cytomix. Conclusions: These results indicate altered PMVEC interactions to the ECM under pro-inflammatory conditions, which may be mediated by TIMP3. This study could provide novel therapeutic targets to decrease PMVEC permeability and enhance barrier integrity in sepsis.

Kyle, Rachel

The 'Cognitive Vital Sign,' (CVS): A qualitative study into the feasibility of implementing a new delirium screening tool on the Acute Care of the Elderly unit in London, Ontario

Rachel Kyle Laura Diachun, Timothy Wong, Jenny Thain, Niamh O,'Regan

Delirium is common in inpatients and is independently associated with poor outcomes. Screening is recommended; however implementation is fraught with barriers. This study aimed to explore these in a clinical setting.CVS delirium screening protocol was introduced on the ACE unit at Victoria Hospital. Six-months post implementation, staff perceptions of the protocol were explored using semi-structured interviews until data saturation. Theoretical Domains Framework guided data analysis and recurrent theme identification.Analysis of ten interviews revealed routine delirium screening was perceived to have a positive impact on patient care. Facilitators included knowledge (delirium is a serious consequence of underlying pathology); skills (person-centred nursing care, emotional intelligence to read and respond appropriately to individual patient needs); environmental context/resources (ease and design of the screen, visual reminders for cuing) and social/professional role and identity (delirium screening, treatment and teaching became an important role). Barriers were also identified in these domains: knowledge (limited appreciation of varied delirium presentations); skills (differentiating comorbidities from delirium); environmental context/resources (timing of screen; rate of comorbid dementia); and social/professional role and identity (not valued as a team member). Emotional response was an additional barrier (patient/carer fear of abnormal mental status). Interestingly, all facilitator domains were also barriers, suggesting these would be high yield when implementing a new screen. The themes also reveal that a thorough understanding of the clinical context of those domains on each ward would aid successful implementation. The CVS was feasible and generally well accepted by front-line nursing staff. These insights may facilitate routine delirium screening.

Lakhani, Rajiv

Validation of the REALITY Hypertension Screening Questionnaire

Rajiv Lakhani George Dresser

Hypertension is one of the most common health conditions facing the public and complications from hypertension can have severe consequences for patients. Preventing these complications by optimizing control of blood pressure can not only reduce morbidity and mortality in patients, but also decrease strain on the healthcare system. Determining the underlying factors contributing to hypertension and control of hypertension is crucial in optimizing blood pressure control. Dr. George Dresser developed a questionnaire to screen patients for both medical and socioeconomic factors that may contribute to hypertension as well as potential complications from hypertension. The objective of this research project was to validate the questionnaire for future use. A literature review was done using PubMed and Google Scholar databases for each question to determine the amount and quality of evidence-based research supporting it. This information will be used to revise the questionnaire to improve the screening of key factors determining the control of blood pressure and complications from hypertension. In the future, the revised questionnaire can be used as a tool to increase the efficiency of hypertension clinic visits and to optimize control of hypertension in patients. The second part of this

research project is currently ongoing and involves collecting survey responses from voluntary participants in the Hypertension Clinic at Victoria Hospital. The responses will then be correlated with the participants,' actual blood pressure.

Lau, SiuYuZoe

Acute retinal necrosis secondary to varicella zoster with phenotypic resistance to acyclovir in an immunocompetent host: a case report.

Siu Yu Zoe Lau Megan Devlin

Acute retinal necrosis (ARN) is an inflammatory condition of the eye characterized by severe uveitis/vitritis, retinal vasculitis, and retinal necrosis. ARN is caused by infection from herpes simplex virus (HSV), varicella zoster virus (VZV), or cytomegalovirus (CMV). Here, we present the case of a 56-year-old woman with VZV ARN initially of the right eye. Aside from a three-year history of sub-optimally controlled type 2 diabetes, she had an unremarkable past medical history. Her disease progressed to the left eye while on treatment with oral valacyclovir and intravitreal ganciclovir injections. She was switched to intravitreal foscarnet and intravenous acyclovir, and her disease stabilized. While genetic testing for acyclovir resistance was negative, this report describes a case of phenotypic resistance to acyclovir. This is uncommon in viral infections causing ARN in immunocompetent hosts.

Le, Ryan

Long term outcomes of high dose fat soluble vitamins in disorders of lipoprotein metabolism.

Ryan Le Robert A. Hegele

Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder affecting the MTTP (microsomal triglyceride transfer protein) gene. MTTP is crucial in the assembly and secretion of normal apo-B containing lipoproteins such as LDL, VLDL, and chylomicrons. ABL patients have almost undetectable levels of these lipoproteins, and suffer from lipid malabsorption. As a result, fat-soluble vitamin deficiencies develop, subsequent complications including neuropathy, myopathy, coagulopathy, atypical retinitis pigmentosa, and osteopenia. In addition, patients also present with pathognomonic peripheral acanthocytosis. Homozygous familial hypobetalipoproteinemia (FHBL) is an autosomal codominant condition that involves the APOB gene, and phenotypically is indistinguishable from ABL. We describe a case series of 3 patients (2 with ABL, 1 with FHBL); each diagnosed and started on high dose vitamin supplementation at a young age, and report on their clinical status. On presentation, each of these patients similarly had undetectable levels of apo-B lipoproteins, neuropathy and peripheral acanthocytosis. Each of these patients on high dose vitamin therapy are now in their 5th to 6th decade of life, well beyond the previously well-established lifespan of 20-30 years before vitamin supplementation, and with the main complication being peripheral neuropathy that has remained remarkably stable despite barely detectable vitamin E levels on high dose supplementation.As minimal data exists in the current literature on long-term outcomes, we review the literature on ABL and FHBL, summarize clinical manifestations, diagnosis, treatment, and report on the outcomes of these patients

to further provide data on long-term management of this condition and further characterize disease trajectory.

Lee, Jooho

Reninoma Causing Resistant Hypokalemic Hypertension and VT Arrest

Jooho Lee George DresserMerrill EdmondsJonathan IzawaStan Van Uum

A 55 year old woman was brought to hospital after a witnessed cardiac arrest. She had a history of resistant hypertension and atrial fibrillation. She had a recent admission for recurrent symptomatic arrhythmias, hyponatremia that was diagnosed as psychogenic polydipsia, and hypokalemia. She was also under investigation for possible Cushing,'s syndrome and hyperreninemic hyperaldosteronism, with 24-hr urine free cortisol 2697 nmol/day (N<275) drawn during previous hospitalization, plasma renin concentration 38,350 ng/L (N<27.7), and plasma aldosterone 9850 pmol/L. ECG tracings post arrest showed torsades de pointes, and admission potassium was 2.2 mM. CT and MR showed a 2.4 x 2.4 cm right interpolar renal mass but no adrenal mass. Renal vein sampling lateralized to the right kidney but did not show increased renin levels post enalapril. She underwent right partial nephrectomy, with pathology confirming juxtaglomerular tumour. Plasma renin activity decreased to 170 ng/L within 4 days of surgery, her polydipsia resolved, and her blood pressure was well controlled with a single agent. Her urinary cortisol also normalized.We reviewed approximately 100 case reports of reninomas. They are rare tumours of the juxtaglomerular apparatus that cause headache, resistant hypertension, hypokalemia, and polydipsia. The mean age at diagnosis is 27 years, but the oldest patient was 69 at diagnosis. Diagnosis is often delayed due to nonspecific symptoms and masking from antihypertensive medications. Patients often have up to 100-fold elevations in plasma renin concentration and activity. Lateralization and stimulation post ACE inhibitor administration on vein sampling can support the diagnosis.

Li, Raymond

Effect of Implementation of a Standardized Hip Fracture Pathway on Osteoporosis Care on a Geriatric Rehabilitation Unit

Raymond Li Kristin Clemens, Jenny Thain

Fragility hip fractures are a significant source of patient morbidity and mortality. Once a patient has sustained a fragility fracture, they are at high risk of sustaining further osteoporotic fractures. As such, adequate investigation and treatment for osteoporosis is essential. However, there are significant care gaps that persist. Approximately 50% of admissions to the geriatric rehabilitation unit (GRU) at Parkwood Hospital are patients who have suffered a hip fracture. The GRU represents an ideal setting for addressing bone health to prevent further fractures. There were 3 quality improvement phases leading up to full implementation of a standardized hip fracture care pathway on the GRU which occurred in June 2017. Patients admitted to the GRU with a fragility hip fracture during the period of Jan 2016 to May 2018 were included in our quality improvement analysis. Primary outcomes assessed were

the proportions of patients who were identified as having osteoporosis, considered for bone protective therapy and started on new therapy when no contraindications were present. Run charts were used to compare the periods before and after the full implementation of the hip fracture care pathway. We found that the quality of osteoporosis care on the GRU in patients who have had a fragility hip fracture has improved significantly since 2016 and the implementation of a standardized hip fracture care pathway has helped to consolidate and sustain key areas of improvement.

Li, Katherine

Incidence, prevalence & mortality of giant cell arteritis over time: a meta-analysis

Katherine Li Daniel Semenov, Matthew Turk, Janet Pope

Introduction: Giant cell arteritis (GCA) is the most common large vessel vasculitis and exclusivelyaffects individuals over 50 years old. This meta-analysis examines the geographical and temporal distribution of the incidence, prevalence and mortality of GCA.Methods: A systematic review of the literature was conducted using EMBase, Scopus andPubMed databases. Cohort or cross-sectional studies were accepted with 50 or more patients with GCA and if population, location and time frame parameters were reported. Articles on mortality were included if standardized mortality ratio was mentioned. Two reviewers extracted data and a third verified inclusion. Results: Of the 3569 citations identified, 107 were included in analysis. The pooled incidence of GCA internationally was 10.00 [9.22,10.78] cases per 100 000 people over 50 years old. This incidence was highest in Scandinavia 21.57 [18.90,24.23], followed by North and South America 10.89 [8.78,13.00], Europe 7.26 [6.05,8.47], and Oceania 7.85 [1.48,17.19]. Mortality rate was standardized across cohorts to units of deaths per 1000 people per year. Only 9 studies reported prevalence. Pooled prevalence from these was 51.74 [42.04,61.43] cases per 100 000 people over 50 years old. Overall, pooled mortality was 20.44 [17.84,23.03] deaths/1000 per year. Mortality had a generally decreasing trend over the years of publication.Conclusions: The incidence of GCA varies nearly 3-fold between regions. The reasons for thisare likely genetic and possibly environmental. Incidence and prevalence are important forplanning costs of biologic treatment in GCA.

LimFat, Guillaume

Adverse events in Alternate-Level-of-Care patients awaiting long-term care in hospital

Guillaume Lim Fat Aquila Gopaul, Dr. Margaret Taabazuing

A rising number of elderly patients are awaiting long-term care (LTC) placement in hospital while designated Alternate-Level-of-Care (ALC). In addition to infrastructural strain created by occupying acute care beds, ALC patients often incur healthcare-associated adverse events during their prolonged hospitalization. Our retrospective cohort study describes rates of adverse events in ALC patients awaiting LTC in hospital, with the aim of comparing to rates in LTC. Our ongoing chart review includes a random sample of 156 patients of 2386 ALC-designated patients who were awaiting LTC at LHSC between 2015 and 2018. Incidence of adverse events was collected, including infections, falls, delirium, pressure ulcers, and venothrombotic events.Within our ALC cohort, 362 total adverse events occurred

over 8,668 ALC days. Patients waited an average of 55 days before LTC placement, with 7 deaths occurring prior to placement. The most common infectious adverse events were urinary tract infections (53.2%) and respiratory infections (27.6%). The most common non-infectious adverse events were delirium (28.3%) and falls (14.6%). Preliminary results indicate a positive correlation between length of stay and the incidence of adverse events, with an over fourfold increase in adverse events in the uppermost quartile compared to the lowermost (RR 4.41, p<0.01).This preliminary data suggests a large burden of adverse events in ALC patients. Once LTC data abstraction is complete, we will compare adverse events between the two groups. Our aim is to use this data to advocate for improved LTC infrastructure and access, with prospective strategies to reduce ALC stays.

Liu, Anna

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

Anna Liu Stan Van Uum, Kristin Clemens

Background: Pituitary carcinomas are rare, comprising only 0.2% of pituitary tumours. However, fewer than 50% of patients with pituitary carcinoma survive beyond one year of diagnosis. In this case, we highlight the signs and symptoms that should prompt a higher index of suspicion for this condition and review the efficacy of temozolomide chemotherapy for pituitary carcinoma.Case: A 56-year-old male presented with erectile dysfunction and binocular vertical diplopia. His prolactin level was 1517 mcg/L with central hypogonadism, secondary adrenal insufficiency and central hypothyroidism. He was diagnosed with a pituitary lactotroph macroadenoma measuring 2 x 2.2 x 3.1cm. Despite treatment with cabergoline, two transsphenoidal resections and one course of radiation, his prolactin level continued to rise. His Ki-67 proliferation index from surgical pathology was 20-25% and methylguanine-DNA methyltransferase (MGMT) was <10%. He was diagnosed with a prolactin-secreting carcinoma. Three years after diagnosis, he presented with lower extremity weakness and urinary incontinence with findings of metastases to the epidural space and thecal sac extending from the thoracic to sacral spine, and a new 5.5mm nodule inferior to the cerebellar tonsil. He is currently receiving temozolomide chemotherapy with resultant shrinkage of these lesions. Conclusion: Features that may help distinguish a benign prolactinoma from a carcinoma include its presence in males >50 years old, lack of response to dopamine agonists, visual symptoms and panhypopituitarism on presentation, and a high Ki-67 proliferation index. Pathology indicating low MGMT may predict a good response to temozolomide, and as such, pathologists might include this stain in their analysis.

Liu, Yideng(Eden)

A Systematic Review of Natural Supplements and Diets in the Treatment of Rheumatoid Arthritis

Yideng Liu Matthew Turk, Janet Pope

BACKGROUND: Despite excellent pharmacological therapies for Rheumatoid Arthritis (RA), 28-90% of patients with RA still utilize complementary and alternative medicine.OBJECTIVE: To determine the efficacy of non-pharmacological, orally-ingested interventions on clinically-relevant endpoints in

patients with rheumatoid arthritis.METHODS: We systematically reviewed EMBASE and MEDLINE electronical databases from inception until Feb 23, 2019. Only randomized-controlled trials (RCTs) which assessed oral, non-pharmacological interventions (e.g. diets, vitamins, oils, herbal remedies, fatty acids, supplements, etc.) in adult patients with RA, that presented clinically-relevant outcomes (defined as pain, fatigue, disability, joint counts, and/or disease indices) were included. RESULTS: A total of 4423 unique articles were assessed of which 72 articles met our inclusion criteria. Thirteen different interventions were studied more than once; however, only vitamin D and fatty acids met criteria for meta-analysis (minimum 3 RCTs presenting the same outcome). Pooled random effects models suggested vitamin D supplementation improved HAQ scores from baseline (mean difference = -0.10, 95% confidence interval (CI) = -0.17 to -0.02; p=0.01) but had no effect on DAS28 scores. Fatty acid supplementation improved total joint counts, pain, physician global assessment scores, HAQ, and DAS28 from baseline. There were significantly more patients who achieved ACR20 criteria (relative risk ratio = 2.73, 95% CI = 1.62 to 4.58; p<0.001).CONCLUSION: High-dose vitamin D and fatty acids supplementation in RA showed statistically significant improvement in some outcomes; however, the degree of improvement is unlikely to be clinically significant. Overall, many trials were of low quality and had high risks of bias including inadequate reporting of data.

Liu, Yideng(Eden)

Apixaban Levels in Class III/Extreme Obesity

Yideng Liu Ute Schwarz, George Dresser, Steven Gryn, Bradley Linton, Denise Keller, Richard Kim

BACKGROUND: There is very limited clinical data regarding safety and pharmacological levels of direct oral anticoagulants (DOAC) in patients with extreme obesity (defined here as BMI >40 kg/m2 or weight >120 kg). OBJECTIVE: To determine if apixaban levels in patients with extreme obesity are similar to matched controls. METHODS: We obtained apixaban levels from a single lab that services all of Southwestern Ontario. A total of 531 patients had apixaban levels drawn from February 2013 to August 2018. A total of 53 patients weighed >120kg or had a BMI >40 at the time pharmacological levels were obtained. These levels were then compared to controls that were matched for age, sex, apixaban dose, and concomitant use of CYP3A4 and/or P-gp inducers/inhibitors. A systematic literature search of MEDLINE and EMBASE from inception until December 1, 2019 was also completed looking at any study that provided clinical or pharmacological data in adult patients with extreme obesity on a DOAC. RESULTS: In this study, 57% (30/53) of the patients with extreme obesity had apixaban levels within the reference range, 11% (6/53) below the reference range, and 32% (17/53) above the reference range. This was not statistically different from the apixaban levels in 53 matched controls (p = 0.95). In this systematic review, a total of 52 patients from six different studies had apixaban levels measured. No patients had levels that were below the reference range. CONCLUSIONS: Apixaban levels in patients with extreme obesity were comparable to matched controls.

Liu, HsinYen

Risk factors of Antimalarial-induced Retinopathy in Systemic Lupus Erythematosus and other Autoimmune Conditions

Hsin Yen Liu Gemma CramarossaJanet Pope

Background: Hydroxychloroquine and chloroquine are effective antimalarial medications for systemic lupus erythematosus (SLE) and other autoimmune conditions, but long-term use can cause irreversible retinopathy. Few studies have compared the risks of antimalarial-induced retinopathy between rheumatologic conditions. Objectives: To describe the pattern of antimalarial-associated retinopathy, including diagnosis of SLE as a risk factor.Methods: We conducted a chart review for 680 patients at SJHC who had at least 3 months of antimalarial use. Antimalarial-induced retinopathy was determined based on characteristic visual field loss, abnormal retinal imaging, and eye specialists,' opinion. Logistic regressions were performed to determine risk factors for antimalarial-induced retinopathy. Results: Of the 680 patients, 282 patients had SLE and the remaining had rheumatoid arthritis (N=224), cutaneous lupus (N=41), or other connective tissue diseases (N=131). SLE patients tended to be younger and had more chloroquine and total antimalarial exposure. Antimalarial-induced retinopathy was observed in 12 patients, 11 of whom had SLE and 7 had chloroquine exposure. The earliest onset of retinopathy occurred at 5.4 years of antimalarial use, and the prevalence beyond 5 years was 2.7%. In univariate analysis, a diagnosis of SLE (P=0.0080) and cumulative chloroquine dose (P=0.011) were significantly associated with retinopathy. In multivariate analysis, SLE diagnosis was significantly associated with ocular toxicity (P=0.00149) after adjusting for antimalarial dosages, age, sex, weight, hypertension, and renal impairment.Conclusions: The risk of antimalarial-induced retinopathy increases after 5 years of use. SLE patients may be at increased risk due to longer treatment duration, AM choice, and underlying disease processes.

Lubchansky, Stephanie

Rapidly enlarging thyroid gland ,Äì a challenging case in diagnosis and management of suspected Riedel,'s thyroiditis.

Stephanie Lubchansky Anthony Nichols, Deric Morrison

A 50-year-old woman with hypothyroidism developed rapid thyroid growth, hoarseness, solid food dysphagia, 15-pound weight loss, night sweats and fevers. Thyroid was diffusely enlarged and firm without lymphadenopathy. Thyroid lymphoma was suspected and core biopsy with flow cytometry was performed, but demonstrated dense collagenous fibrosis, acute and chronic inflammation; negative for lymphoproliferative neoplasm or IgG4-associated sclerosing disease. CT Head/Neck/Thorax: Diffuse thyroid enlargement, extrathyroidal infiltration and mild tracheal narrowing; no abnormal lymphadenopathy or metastases. Ultrasound showed a diffusely large thyroid with presumed fibrosis causing shadow artifact.Investigations: Anti-thyroglobulin > 4000 kIU/L, anti-TPO 243 kIU/L, CRP 86.29 mg/L (<6), TSH 0.18 mIU/L (0.32,Äì4.00) and thyroxine 23 pmol/L (9,Äì19). IgG4 normal.She underwent isthmusectomy, lymph node, thymus and thyroid biopsies. Histology and flow cytometry were negative for malignancy. She was treated as suspected Riedel,'s thyroiditis (RT). Prednisone improved compressive symptoms, but they recurred with tapering. Tamoxifen initially improved compressive

symptoms and steroids were discontinued, but symptoms recurred eight months later, requiring high dose prednisone. Repeat MR Neck was consistent with RT; stable compared to previous CTs. RT is a rare inflammatory thyroid disorder that causes fibrosis and invades neighbouring structures. RT is thought to be an IgG4-related disease and must be distinguished from fibrosing Hashimoto,'s thyroiditis. Initial treatment includes glucocorticoids and tamoxifen. Case reports suggest Rituximab for steroid and tamoxifen failure. We present a case of a rapidly enlarging thyroid gland with pathology showing fibrosis and local invasion, suggestive of RT, which has been resistant to steroid and tamoxifen therapy.

Lubchansky, Stephanie

Reducing Hyperglycemia in Patients Post-Solid Organ Transplants: An Endocrinology Quality Improvement Initiative

Stephanie Lubchansky Parul Khanna, Jooho Lee, Kristin Clemens

Introduction: More than 80% of transplant patients have inpatient post-transplant hyperglycemia, and within one year, 20-40% will progress to New Onset Diabetes After Transplant (NODAT). Post-operative hyperglycemia is associated with graft rejection, delayed wound healing, infections, and increased length of stay (LOS). Inpatient diabetes management plays an important role in reducing LOS and 30-day readmission rates. In this project, we aimed to reduce mean number of days of hyperglycemia and mean number of days before endocrinology consultation in liver and kidney transplant recipients in the Multi-Organ Transplant Unit (MOTS). Methods: We reviewed charts of 23 patients who had an endocrinology consultation for hyperglycemia (?2 blood glucose [BG] >12 mmol/L) between March 1st and August 1st, 2019. Mean number of days of hyperglycemia before endocrinology consultation was 4.08, mean number of days in hospital before an endocrinology consultation was 10.56, mean LOS 18.86 days.We performed a root cause analysis and identified contributing factors, including lack of BG orders in post-operative powerplan and lack of a medical directive for managing hyperglycemia.As a first test of change, we created a standardized algorithm for identifying post-transplant hyperglycemia with parameters for automatic inpatient Endocrinology consultation. This protocol was reviewed by key stakeholders including endocrinologists, hepatology and nephrology transplant experts, transplant program coordinators and unit quality and safety specialists. Results: We created a standardized algorithm and decision-support tool to reduce hyperglycemia in the MOTS unit. Discussion: Implementation has been deferred due to the COVID-19 pandemic but will be rescheduled for the summer/fall of 2020.

Madrazo, Lorenzo

Azathioprine-Induced Severe Anemia Potentiated by the Concurrent Use of Allopurinol

Lorenzo Madrazo Emily Jones, Cyrus C. Hsia

BackgroundAzathioprine, a steroid-sparing immunosuppressant, is commonly used for various inflammatory disorders. Myelosuppression, usually in the form of leukopenia or rarely anemia, is a known side effect that may be potentiated by dysfunction of the genes coding for thiopurine

methyltransferase (TPMT) or inhibition of xanthine oxidase (XO). Case PresentationA 66-year-old man with a history of gout treated with allopurinol presented with confusion, hypotension, and severe anemia three months following initiation of azathioprine for IgG4-related disease. He presented with a hemoglobin of 56 g/L requiring packed red cell transfusions while in hospital. Investigations ruled out bleeding, hemolysis, nutritional deficiencies, and malignancy as causes for his anemia. Further, a bone marrow aspirate and biopsy reviewed megaloblastoid changes. His anemia gradually improved over several weeks upon discontinuation of azathioprine and allopurinol.DiscussionConcurrent use of azathioprine and allopurinol inhibits XO and potentiates the myelosuppressive effect of azathioprine. This combination has been used clinically with close monitoring and dose adjustments to optimize therapeutic benefit and minimize hepatotoxicity from azathioprine. While generally well tolerated, this combination can lead to significant myelosuppression without appropriate dose adjustments. On review of the literature, severe anemia remains to be a rare yet serious complication of this combination therapy.ConclusionThis case highlights severe anemia as a rare yet serious complication of azathioprine toxicity. The potentiated toxicity of azathioprine by allopurinol also highlights the importance of careful review of medications to avoid unintended drug-drug interactions and careful monitoring when this combination therapy is utilized.

Malik, Ali

Use of Indwelling Pleural Catheters for Patients with Hematological Malignancies in Canada

Ali Malik Emilie Deschner, Debarati Chakraborty, Sharan Kassirian, Curtis Addison, Kavyan Amjadi, Inderdeep Dhaliwal, Michael Mitchell

Malignant pleural effusions (MPEs) secondary to a hematological malignancy occur despite optimal medical therapy of underlying disease and require serial thoracentesis. An indwelling pleural catheter (IPC) may be inserted for symptomatic management. The objective of this study was to examine the proportion of Canadian patients with MPEs due to hematological malignancies who have their IPCs removed. Secondary outcomes include time to catheter removal, infection rate, additional pleural procedures required and survival after requiring an IPC.This was a retrospective study that analyzed data from the chronic ascites and recurrent effusions (CARE) database at The Ottawa Hospital, collected between 2006 and 2015. IPCs were inserted for patients who had symptomatic malignant pleural effusions with a life expectancy longer than 1 month. The total sample included 81 patients with a mean age of 67 years. The majority were males and 72.8% had lymphoma. Fifty-eight percent of patients had their catheter removed due to resolution of their pleural effusion. The mean time toremoval was 76.8 days and 5% of patients had an infectious complication. Thirty two percent of patients survived until the end of the study. Eighty-two percent of patients experienced an improvement in dyspnea following IPC insertion.This study provides valuable prognostic information on IPCs in patients with hematological malignancies for the Canadian population and allows patients to make an informed decision on opting for an IPC. This study was limited by a small sample size and lack of information on specific subtypes of hematological malignancies.

Manji, Aminmohamed

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 is defined as multiple organ dysfunction due to a dysregulated host response to infection. 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. Previous studies have demonstrated PMVEC barrier dysfunction occurring by disruption of inter-PMVEC junctions through modification of junctional proteins, including vascular endothelial (VE)-cadherin. Prior studies identified a potential role for caspases in inducing endothelial barrier dysfunction. Caspases are multi-functional proteases that regulate apoptosis. However, caspases have been shown to cleave non-apoptotic targets including ?-catenin, an adapter protein for VE-cadherin. Pilot data from our lab demonstrated caspase-dependent cleavage of ?-catenin in septic human PMVEC in vitro. Based on this, we hypothesize that endothelial barrier dysfunction, under septic conditions, is due to caspase-dependent cleavage of proteins associated with inter-PMVEC junctions. To address this hypothesis, control (receiving PBS) and septic (receiving pro-inflammatory cytokines) mouse PMVECs will be treated with or without a broad-spectrum caspase inhibitor, Q-VD. Western blots will be performed to assess abundance and cleavage of inter-PMVEC junctional proteins, including proteins within adherens and tight junctions (VE-cadherin and occludin, respectively) as well as associated adapter proteins (?-catenin, ?-catenin, ?-catenin, p120-catenin, and zona occludens 1-3). We anticipate septic PMVEC barrier dysfunction is associated with increased cleavage of junctional proteins, which will be abrogated in the presence of the caspase inhibitor. Our results may elucidate the intrinsic mechanisms of sepsis-induced endothelial barrier dysfunction and may provide a possible therapeutic target for treatment.

Mansory, Eman

Institutional Review of Reflex Factor Coagulation Testing In Patients With An Unexplained Prolonged aPTT

Eman Mansory Fadi Bahodi,Chai Phua

Background: We aim to determine the clinical utility of reflex coagulation investigations (RCI) for prolonged lupus insensitive activated partial thromboplastin time (aPTT) at LHSC. Methods: We retrospectively reviewed all potential RCI [lupus insensitive aPTT of ? 32s (normal range 20s-29s)] from April 2014 to June 2019. Our diagnostic algorithm requires completion of RCI only if samples had no interfering medications to explain a prolonged aPTT and were either from a pre-operative sample or patient presenting with unexplained bleeding. If so, reflex one-stage factor activities for Factor VIII(FVIII), IX(FIX) and XI(FXI) were completed. Data were obtained through electronic medical records to capture clinical characteristics, laboratory findings, prophylactic hemostatic replacement and bleeding outcomes.Results: 3317 samples from 2940 patients were identified as potential RCI during the study period. 263 patients had RCI completed. Of those, 55 (21%) had abnormal factor testing. 41/55 (75%) of RCIs were in the pre-operative patient. 5/41 (12%) were referred to hematology and had no post-operative bleeding despite only 3 received pre-operative hemostatic support, as suggested by hematology. 5 had post-operative bleeding, and 3 on retrospect were deemed to potentially benefit

from additional pre-operative hemostatic support. 5 patients had RCI triggered for unexplained bleeding, all identified with a clinically significant bleeding disorder. Conclusion: RCI benefited patients presenting with unexplained bleeding as this expedited the diagnosis of clinically significant bleeding disorders. RCI for pre-operative evaluation infrequently led to additional hemostatic support/referral to hematology. We suspect that lab alert fatigue could be the main contributory factor.

McDonald, Cassandra

A randomized double blind clinical trial of high volume simethicone to improve visualization during small intestinal capsule endoscopy

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BACKGROUND: The use of simethicone before capsule endoscopy is controversial as studies have reported inconsistent results, with some showing improved visualization only in the proximal small intestine. We hypothesized a higher volume of simethicone may produce more consistent cleansing, especially in the distal small bowel. METHODS: A phase III double-blind randomized controlled trial was conducted comparing high volume (1125 mg simethicone in 750 ml water) and control volume (300 mg simethicone in 200 ml water) solutions, both at 1.5 mg/ml. The primary outcome was adequate bowel preparation, defined as a KODA score >2.25, overall and stratified by the proximal and distal half of the small bowel, read in duplicate by blinded readers. Secondary outcomes included mean KODA score, diagnostic yield, cecal intubation rate, and adverse events. All analyses were intention-to-treat. RESULTS: A total of 159 patients were randomized (mean (SD) age 58.7 (15.7), 54% female) and the most common indication was obscure gastrointestinal bleeding (71.7%). Compared to the control volume, high volume was not more likely to achieve adequate bowel preparation (48% vs. 50%, p=0.82) overall, for the proximal half (64% vs. 71%, p=0.40), or the distal half of the small bowel (37% vs. 36%, p=0.88). There was no difference in the mean (SD) KODA score (2.18 (0.4) vs. 2.20 (0.4), p=0.73), diagnostic yield (56% vs. 53%, p=0.71), or cecal intubation (both 95%). There was one adverse event, nausea, reported in the control group. CONCLUSION: High volume simethicone does not improve visualization during capsule endoscopy.

Mikail, Maria

An unusual case of large, multifocal pyoderma gangrenosum in a patient with ulcerative colitis.

Maria Mikail Aze Wilson

Background: Pyoderma gangrenosum (PG) is an uncommon neutrophilic dermatosis which can be associated with pathergy in the setting of trauma or surgery, systemic disease (inflammatory bowel disease, rheumatoid arthritis, etc.) or idiopathic. A recently published cohort study of 356 PG cases illustrated that 66.9% of patients had an underlying medical co-morbidity and 41% had inflammatory bowel disease.Aims: To present the case of a patient with ulcerative colitis who underwent a subtotal colectomy with an end ileostomy secondarily to colonic perforation and presented post-operatively with large, multifocal PG at two abdominal sites treated with maintenance IV Infliximab. Case: A 67-year-old female underwent an emergency subtotal colectomy and end ileostomy secondarily to a perforated colon in the setting of newly diagnosed ulcerative colitis. Post-operatively she developed peristomal ulceration and a significant abdominal wound dehiscence of her midline laparotomy incision. The largest wound measured 10x20 cm and about 3-5 cm in depth. Biopsies were highly suggestive of PG. She was started on high-dose systemic steroids and transitioned to high-dose IV Infliximab empirically. She also received intralesional injections of Triamcinolone. She was managed with a multi-disciplinary approach by gastroenterology, dermatology, plastic surgery, infectious disease and wound care. As a result, her abdominal PG improved dramatically with maintenance IV Infliximab.Conclusion: This is an interesting case of a 67-year-old female with a diagnosis of ulcerative colitis with subtotal colectomy secondarily to a colonic perforation who presented with large, multifocal PG. This case-report illustrates the significant role high-dose Infliximab has in the treatment of PG.

Mouard, Omar

Development of Late-Onset CMV Disease in Patients Receiving Liver Transplants with Appropriate CMV Prophylaxis

Omar Mouard Dr. Seyed Hosseini

INTRO: CMV is a significant infectious entity liver transplant patients. Current practice is to provide high risk patients (D+/R-) 3-months of antiviral prophylaxis to prevent disease development. While this does reduce development of this disease in the first 3 months it is thought that a significant portion of patients will go on to develop CMV disease in the late period.METHODS: We analysed 212 liver transplant patients at University Hospital who received transplants between 2012-2016. These patients were followed for two-years to assess the results of their transplants. Primary endpoint was the development of late-onset CMV disease.RESULTS: Final results of the data collection are still pending. Early analysis suggests that CMV prophylaxis in high risk patients who receive liver transplants still develop a significant amount of CMV disease when compared to their low risk counterparts despite appropriate CMV prophylaxis.CONCLUSIONS: If the data collected so far continues to follow the trend of the preliminary results this would suggest that we should be re-approach how we view CMV in high risk patients with liver transplants. CMV prophylaxis may not be adequate therapy for prevention of development of CMV disease.

Moynahan, Alisha

Testing a Novel Peptide-Infused Cream for the Treatment of Rheumatoid Arthritis in a Humanized Mouse Model

Alisha Moynahan Garth Blackler, Eva Turley, David Bell, Ewa Cairns, and Lillian Barra

Current treatments for rheumatoid arthritis (RA) involve non-specific immunosuppressive drugs that have severe side effects. RA specifically expresses immune responses to proteins/peptides containing citrulline and homocitrulline amino acids. Studies have shown that application of proteins/peptides to the skin of mouse models reduces pro-inflammatory immune responses through immune tolerance. The objective of this study is to determine if transdermal delivery of synthetic citrullinated (CitJED) and homocitrullinated (HomoCitJED) peptides will induce immune tolerance and treat RA. To test this, we used a humanized mouse model containing the human HLA-DR4 allele, the strongest genetic risk factor for RA. When these mice, called DR4tg mice, are subcutaneously immunized with HomoCitJED, they develop RA-specific immune responses and arthritis after HomoCitJED is injected into their knees. To deliver the peptides, we used a patented Hyaluronan-Phosphatidylethanolamine cream that is able to penetrate into the dermal layer of the skin. CitJED and HomoCitJED (n=12) or PBS (n=10) infused cream was topically applied to arthritic DR4tg mice. Joint swelling was measured using calipers and was not different between groups (p=0.5636). Splenic T cell recall responses to HomoCitJED measured by 3H-thymidine incorporation assay were seen in 3/16 mice and were not different between groups (p=0.9796). HomoCitJED antibodies by ELISA were detectable in 16/17 mice with no significant difference seen in the levels between groups (peptides=1162 RU/mL; PBS=2114 RU/mL; p=0.5472). Here we describe a novel approach to peptide therapy in RA. Future work consists of assessing arthritis severity by histologic scoring and examining antibody and T cell responses at earlier timepoints.

Ni, Lianting

Pilot of Electronic Handover Tool on CTU

Lian Ting Ni Alan Gob

IntroductionCurrent practices require in general two handovers between medical staff daily. Critical information and outstanding tasks are sometimes lost in the process. In recent years there has been interest in structured handover tools and methods to improve information transfer. In our study we tested the usability of an electronic handover tool. MethodsAn IPASS based clinical handover tool was deployed into powerchart and piloted by two CTU teams for three weeks. Data was collected on user uptake of the tool and a focus group meeting was conducted to elicit feedback on the experience. ResultsDuring the study period, usage was low on both teams (3/21 days in Team 1 and 8/21 days in Team 2). The general consensus from the focus group was that while it is good for handover information to be in powerchart and be accessible to everyone using the tool adds to an already busy day and requires some duplication of work done. DiscussionDue to the low usage a planned chart review portion of the study was abandoned as no reliable conclusion can be drawn. In part some technical issues identified contributed to the low uptake; of particular concern is the printability of the data and

unnecessarily complicated data entry process. ConclusionA more accessible and standard handover system is likely beneficial and desired but the current tool requires some improvements and more consideration in order to fit into the current workflow.

Nicholl, Davd

Sex differences in bioimpedance in humans with obstructive sleep apnea with normal kidney function before and after CPAP therapy

David D. M. Nicholl Patrick J. Hanly, Ann A. Zalucky, Jennifer M. MacRae, George B. Handley, Darlene Y Sola, and Sofia B. Ahmed

BackgroundObstructive sleep apnea (OSA) is associated with chronic kidney disease (CKD) development, progression, and fluid retention. Sex-based differences in OSA and CKD exist and the consequences of OSA are more severe in women, though the pathophysiology remains unclear. Fluid retention contributes to comorbidity and complications of OSA. We evaluated whether sex differences exist in total body water (TBW) and bioimpedance parameters in otherwise healthy humans with OSA pre-/post-continuous positive airway pressure (CPAP) therapy.MethodsTwenty-nine (10F/19M) sodium-replete OSA participants (desaturation index >15h-1) were studied using bioimpedance technology pre- and post-CPAP (>4h/nightx4wks). Bioimpedance (TBW, extracellular {ECF] and intracellular [ICF] fluid) and anthropometric (fat-free mass [FFM], body mass index [BMI]) parameters were evaluated for sex differences.ResultsPre-CPAP, TBW (74.6¬±0.4 vs 74.3¬±0.2 %FFM, p=0.14; women vs men) and BMI (36¬±3 vs 35¬±1kg/m2, p=0.9) were similar between sexes, though FFM (56.3¬±1.7 vs 71.7¬±1.5 %weight, p<0.001) and absolute TBW (42.4¬±3.0 vs 57.1¬±1.6L, p<0.001) were lower in women. ECF:TBW (0.50¬±0.006 vs 0.44¬±0.009, p<0.001) and ECF:ICF (1.00¬±0.002 vs 0.80¬±0.004, p<0.001) were increased in women despite overall reduced absolute ECF (21.3¬±1.7 vs 25.2¬±0.8L, p=0.006) and ICF (21.1¬±1.2 vs 31.9¬±1.0L, p<0.001). While CPAP corrected OSA, there were no differences in bioimpedance parameters vs pre-CPAP.ConclusionsWomen with OSA had expanded ECF compared to men. Differences in TBW distribution may contribute to sex differences in OSA pathophysiology. CPAP for 1-month did not mitigate these differences.

Nicholl, Davd

SEX DOES NOT INFLUENCE THE ASSOCIATION BETWEEN NOCTURNAL HYPOXEMIA, RENAL HEMODYNAMICS, AND RENAL RENIN-ANGIOTENSIN SYSTEM ACTIVITY IN HUMANS WITH OBSTRUCTIVE SLEEP APNEA TREATED WITH CPAP THERAPY

David D. M. Nicholl Patrick J. Hanly, Ann A. Zalucky, George B. Handley, Darlene Y. Sola, and Sofia B. Ahmed

BackgroundNocturnal hypoxemia (NH) in obstructive sleep apnea (OSA) is associated with renal renin-angiotensin system (RRAS) up-regulation and loss of kidney function, though animal studies suggest female sex is protective against hypoxemia. We evaluated whether the association between NH severity and RRAS response to CPAP differs by sex in otherwise healthy humans with OSA.MethodsThirty

(10F/20M) sodium-replete OSA participants (desaturation index ?15h-1) with NH (SaO2<90%?12%/night) were stratified by NH severity (moderate[mean SaO2(MSaO2)?90%; N=4F/11M] or severe [MSaO2<90%; N=6F/9M]) and studied pre-/post-CPAP (>4h/nightx4wks). Glomerular filtration rate (GFR) and renal plasma flow (RPF) were measured at baseline and post-Angiotensin-II (3ng/kg/minx30min, 6ng/kg/minx30min; RRAS marker).ResultsNo sex differences were observed in baseline renal hemodynamics pre- or post-CPAP. Pre-CPAP, severely hypoxemic women demonstrated blunted GFR (?30min, 0¬±2 vs -16¬±5mL/min, p=0.019; ?60min, 1¬±4 vs -12¬±5mL/min, p=0.055) and RPF (?30min, -53¬±25 vs -170¬±30mL/min, p=0.033; ?60min, -89¬±16 vs -211¬±43mL/min, p=0.033) responses post-Angiotensin-II vs moderate women. Similarly, pre-CPAP, severely hypoxemic men demonstrated blunted RPF responses (?30min, -120¬±23 vs -163¬±14mL/min, p=0.050; -127¬±36 vs -207¬±20mL/min, ?60min, p=0.027) vs moderate men. RRAS responses did not differ by sex. Post-CPAP, both severely hypoxemic women and men demonstrated augmented RPF responses vs pre-CPAP. Post-CPAP, RRAS responses were similar irrespective of sex or hypoxemia status.ConclusionsNH severity is associated with greater baseline RRAS activity, irrespective of sex. NH correction with CPAP has similar beneficial effects on renal hemodynamics and RRAS activity in both sexes.

Papernick, Sam

Validation of 3D ultrasound segmentation reliability compared to MRI for assessing knee cartilage degradation in osteoarthritis

Sam Papernick Robert DimaDerek J GilliesTom AppletonAaron Fenster

Introduction: Arthritis is the most prevalent chronic health condition in Canada, with the most common form being osteoarthritis (OA). There is a tremendous clinical need for an objective/imaging-based point-of-care tool to assess OA status, progression, and response to treatment. We aim to validate a handheld mechanical 3D ultrasound (3DUS) device we have developed against MRI for assessing articular knee cartilage at the patient's bedside.Methods: Knee images of 25 healthy volunteers were acquired using our 3DUS scanner with accompanying 3.0T MRI scans. The trochlear articular cartilage was manually segmented by 2 raters, and 3DUS segmentations were registered to MRI using a semi-automated surface-based registration algorithm. Intra- and inter-rater reliabilities of manual 3DUS segmentations were assessed using intraclass correlation coefficients (ICC) calculated from segmentation volumes. Mean surface distances (MSD), Hausdorff distances (HD), and Dice similarity coefficients (DSC) were calculated between the registered segmentations.Results: Intra-rater ICC were 0.99 and 0.98 for 2 raters, and inter-rater ICC was 0.95. Segmentation comparisons between intra-rater, inter-rater, and 3DUS to MRI registration resulted in DSC of 0.93 and 0.88 (intra-rater 3DUS), 0.87 (inter-rater 3DUS), and 0.74 (registration). Global mean MSD and HD were 0.35 mm and 3.80 mm respectively for 3DUS to MRI segmentation registration.Conclusion: We have developed and validated a 3DUS device that enables accurate and precise volume measurements of knee tissues in healthy subjects. 3DUS is a reliable modality for assessing the trochlear cartilage in healthy knees at the bedside and may replace the need for MRI in OA clinical trials.

Parker, Brent

Comparison of Bone Marrow Blast Cell Percentage in Myelodysplastic Syndrome obtained using Flow Cytometry and Morphologic Evaluation

Brent Parker Ian Chin-Yee; Ben Hedley; Nikhil Sangle; Mike Keeney; Janice Popoma and Cyrus Hsia;

Introduction: Bone marrow (BM) blast percentage is an important factor in the management of myelodysplastic syndrome (MDS) and an essential component of the International Prognostic Scoring System (IPSS) score required for funding therapies in Ontario. As per the World Health Organization (WHO), morphologic evaluation of a BM aspirate is the gold standard in determining blast count. Flow cytometry (FCM), a potentially useful tool in blast enumeration has not been incorporated into standardized prognostic scores. We hypothesize that FCM would provide a more reliably reproducible blast count used in conjunction with morphology than morphology alone.Methods: BM aspirates from patients with MDS were independently assessed by three hematopathologists morphologically and three laboratory technologists with FCM. Interobserver differences were calculated by intraclass correlation coefficients (ICC) and differences between morphology and FCM results by Pearson,'s coefficient of correlation and Bland-Altman charts. Results: 25 BM aspirate samples were evaluated. Blast percentages differed between FCM and morphology in 19 of 25 (76%) samples, Pearson,'s coefficient -0.041. Both morphology and flow cytometry had reasonable ICC values of 0.870 and 0.993 respectively. Bland-Altman analysis showed a consistent large variation in differences between the blast count from FCM compared to morphology.Conclusion: Correlation between independent FCM and morphology blast counts were non-existent. Intraobserver FCM results agreed better than intraobserver morphologic results did suggesting FCM blast counts are more reproducible than morphologic counts. FCM used as an adjunct to morphology may provide more accurate diagnoses and prognoses of MDS and related conditions.

Patton, Petrease

A Single Center Randomized Control Trial of Intravenous Lidocaine for the Management of Traumatic Rib Fractures

Petrease H Patton Dr. Kelly Vogt, Dr Neil Parry, Dr. Arjun Kundra, Fran Priestap, Lynn Kelly and Dr Ian Ball (PI)

Background: Traumatic rib fractures (TRFs) are a common occurrence with a 10% incidence in all trauma patients and are associated with significant morbidity and mortality. Adequate analgesia is paramount for preventing pulmonary complications and death. There is evidence of intravenous (IV) lidocaine,'s effectiveness and safety in the post-operative thoracic and abdominal surgical patient and we hypothesize that it may be ideal in trauma patients with TRFs. We evaluated IV lidocaine,'s analgesic efficacy in this population.Methods: A single-centre, double-blind, randomized control trial comparing IV lidocaine plus usual analgesics to placebo infusion plus usual analgesics for 72-96 hours. A total of 36 participants, who were adult trauma patients diagnosed with two or more RFs requiring hospital admission, were enrolled. The study was powered to detect a 20% reduction in pain scores, which has been deemed as clinically meaningful.Results: The primary outcome was mean pain score at rest and with movement, as measured on the Visual Analog Scale (VAS). The results of mixed linear modeling on

the mean VAS pain scores demonstrated significant pain reduction with movement (p=0.015) and a trend toward reduced pain scores at rest (p=0.361) in the lidocaine group compared to placebo. Conclusions: These results demonstrate that lidocaine has a beneficial analgesic effect in patients with TRFs. The next phase of our research program will evaluate IV lidocaine,'s ability to reduce respiratory failure and other morbidities in older trauma patients with rib fractures.

Perrault-Sequeira, Laurent

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

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

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 the Clinical Teaching Unit (CTU) at University Hospital. 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 the CTU. 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. 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.Discussion: Our results have implications for transition planning in hospitalized multimorbid patients. Recognizing salient network features can help identify patients who would benefit from enhanced discharge support.

PHILIP, SHONA

Efficacy of Oral Ribavirin in Respiratory Syncytial Virus Infection in Hematopoietic Stem Cell Transplant Patients A Single-Centre Experience.

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Background: Respiratory Syncytial Virus (RSV) is a common respiratory viral pathogen that causes significant morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients with lower respiratory tract infection (LRTI). Mortality rates for hematologic and HSCT populations who progress to lower respiratory tract infection (LRTI) have been reported to range from 20-60%. The treatment of RSV

is challenging and ribavirin has been studied for this indication however, controversy exists surrounding the efficacy of this agent, its route of administration and the role of adjunctive immunoglobulin and corticosteroids. Results: From January to March 2012, there was an outbreak of RSV with 11 hematology patients including 5 HSCT patients (Allo-2, Auto-3) and 3/5 patients had nosocomially acquired infections. Patients were managed with supportive care alone. The mortality rate was 80% (4/5 patients). This led to the development of a protocol for the HSCT patients during the winter season focusing on prevention of nosocomial transmission, early PCR testing and treatment with oral ribavirin for those with RSV and signs of LRTI. After institution of this protocol, in 2013 there were 2 HSCT patients (Allo-1, Auto-1) with documented RSV LRTI, one being nosocomial. In 2017 another five HSCT patients had confirmed RSV (Allo-4, Auto-1), 4 had community acquired infection and one nosocomial transmission. All patients were treated with oral ribavirin and survived the infection. Conclusions: Oral ribavirin provides a potential option for the early treatment of HSCT patients with RSV associated LRTI and an ongoing review of our experience with this protocol is necessary.

PHILIP, SHONA

Excellent outcomes with the use of R-BuMelTt conditioning regimen for primary and secondary diffuse large B-cell lymphoma of the central nervous system.

SHONA A PHILIP Uday Deotare MD, Adrienne Fulford NP-PHC, MScN, Selay Lam MD FRCPC, Chai Phua MD FRCPC, Joy Mangel MD FRCPC, Kang Howson-Jan MD FRCPC, Brandon Dorland NP-PHC, MN, Karen Atkinson NP-PHC, MN and Anargyros Xenocostas, MD, FRCPCAdrienne Fulford, NP-PHC, MScN1, AnneMarie Bombassaro, BScPhm, PharmD2, Krista Biederman, BScPhm2, Brandon Dorland, NP-PHC, MN1, Anargyros Xenocostas, MD, FRCPC3.

Background: Primary central nervous system lymphoma (PCNSL) and Secondary central nervous system lymphoma (SCNSL) have a 2 year progression free survival (PFS) of 42%. Autologous Stem Cell Transplant (ASCT) with various conditioning regimens have been used as second line therapy for this patient population. We hypothesized that the use chemotherapeutic agents such as Thiotepa and Busulfan, by using the R-BuMelTt regimen regimen in this population will be effective to achieve higher remission and survival rates given CNS penetration. Methods: 5 patients, 2 with SCNSL and 3 with PCNSL (median age 62 years) were evaluated over a two year period from December 2017 till September 2019. The induction chemotherapy regimen used for SCNSL was CHOMP, and for PCNSL was MATRix. The median duration of chemotherapy cycles was 4, and all of them had achieved remission prior to transplant based on PET/CT scan. All patients were planned to undergo ASCT using the R-BuMelTt regimen of rituximab, thiotepa, busulfan, and melphalan. Results: Patients received a median cell dose of 4x106 CD34+cells/kg (range: 2.5-5.7), had neutrophil engraftment at 11 days (range:9-13), platelet recovery was achieved on days 11,15 and 16 for three patients but was delayed at 46 and 89 days for 2 patients. Infectious complications were common with documented bacteremia in 4 out of 5 patients. At a median follow up of 19 months (range: 10-21 months), all patients had complete metabolic response on radiological imaging with PET/CT in conjunction with MRI head and there was no deaths.

Philpott, Holly

Mechanobiological response in synovium: insights into the benefits of exercise and the role of inflammation in knee osteoarthritis

Holly T. Philpott Trevor Birmingham, Steven MacDonald, Brent Lanting, Benoit Fiset, Logan Walsh, Tom Appleton

Purpose: Synovium is critical for maintenance of joint health and undergoes marked changes in osteoarthritis (OA). Exercise is recommended to treat OA, but pain lowers exercise tolerance end-stage knee OA. Synovium is stretched during walking (flexion-extension) at predictable frequencies, but mechanobiology of synovium and the effects of OA-related inflammation on nociception-related mechanobiological responses during the gait cycle are unknown. Here, we assessed mechanobiological responses to mechanical stretch loading and whether these responses are modified by inflammation in patients with end-stage knee OA. Methods: Synovial tissue samples collected from 6 patients with end-stage knee OA knee arthroplasty (n=6) were split into three equal pieces. Each matched sample was mechanically loaded with 10% stretch for 30-minutes at 0.3 or 1 Hz, or remained static (control). Synovial infiltration by leukocytes was determined as high (n=3) or low (n=3) by tissue histology. Following mechanical stimulation, whole tissue RNA was collected for RNA sequencing. Findings: Mechanoresponsive genes (differentially expressed in stretch-loaded vs controls, $p<0.05$) included those involved in phagocytosis, and innate immune activation including Toll-like receptor, chemokine, and TGF-beta signaling. Suggesting that mechanical loading induces innate inflammatory mechanisms in end-stage OA synovium. In secondary analyses, we explored differences in mechanically-induced gene expression between tissues with high vs low burden of inflammation. Venn analyses showed that 1.8% (17) of genes were mechanoresponsive in both low and high inflammation groups, while 98.2% (945) of significantly mechanoresponsive genes were influenced by inflammation in the tissue. Thus, suggesting that inflammation strongly influences gene expression in response to stretch.

Philpott, Holly

Pain-related behaviour in a non-Invasive rat model of post-traumatic knee osteoarthritis

Holly T. Philpott Garth Blackler, Ahmed Al-Mohammed, Tristan Maerz, Tom Appleton

Purpose: Knee joint injuries are a major cause of post-traumatic osteoarthritis (PTOA). Pain is the most common symptom experienced by individuals with PTOA but is frequently not evaluated in animal models. Surgical joint destabilization is used to model PTOA; however, surgical models fail to replicate traumatic aspects of joint injury typically occurring in humans. Non-invasive joint impact models involving ligament rupture are proposed to model more clinically relevant features of PTOA, but pain-related behaviours have not been well-studied. Herein, we characterize pain and joint histopathology in a non-invasive joint impact model of PTOA.Methods: Compressive force was used to rupture the ACL in 14 male rats. Knee joint hyperalgesia and hind-paw mechanosensitivity were measured at 4-, 8-, and 12-weeks post-impact using pressure application measurement and electronic von Frey, respectively. Histopathology was used to assess changes in cartilage and synovial tissue. Findings: Non-invasive ACL rupture produced ipsilateral knee joint hyperalgesia and hind-paw mechanosensitivity post-PTOA induction. Pressure pain threshold decreased from 390.3 +/- 92.9g at baseline to 240.0+/-62.5g at 4-

weeks, remained decreased until 12-week endpoint (224.9 +/- 66.2g). Hind-paw withdrawal threshold decreased from 75.2 +/- 12.0g (baseline) to 54.1 +/- 9.6g (4-weeks) and recovered to baseline-threshold by 8-weeks (71.5 +/- 14.6g) and 12-weeks (88.9 +/- 13.1g). Histopathology is delayed because Covid-19. Non-invasive rupture of ACL induced decreases in pressure pain threshold and hind-paw withdrawal threshold, which are characteristic features of OA-related pain. To understand what model is better-suited to study pain-related outcomes in PTOA, future analyses will compare the non-invasive model with a surgical model of PTOA.

Qamar, Adnan

Mitochondrial Permeability Regulates Cardiac Graft Ischemia-Reperfusion Injury and Allograft Rejection

Adnan Qamar Jifu Jiang, Xuyan Huang, Patrick McLeod, Anthony Jevnikar, Zhu-Xu Zhang

The clinical relevance of ischemia-reperfusion injury (IRI) in the context of organtransplantation is well-established. IRI is associated with various forms of programmed cell death (PCD), of which necroptosis is particularly significant. Necroptosis is an inflammatory form of PCD that promotes alloimmunity and adversely affects allograft viability and function. We have recently shown the role of cyclophilin D (CypD), a critical mediator of mitochondrial permeability transition pore (mPTP) formation, in necroptosis. In this study, we investigated the downstream mechanism of hypoxia/reoxygenation-induced necroptosis and the effect of CypD inhibition in mitigating IRI-induced allograft injury and the subsequent alloimmune response in a clinically relevant model of cardiac transplantation. Our data indicate that inhibition of caspases during cold hypoxia-reoxygenation injury decreases apoptosis but increases necroptosis and that inhibition of CypD attenuates hypoxia/reoxygenation-induced necroptosis (n=3; p?0.001). Interestingly, we found that hypoxia/reoxygenation-induced necroptosis involves apoptosis-inducing factor (AIF) translocation to the nucleus and that AIF silencing also attenuates hypoxia/reoxygenation-induced necroptosis (n=3; p?0.001). Our in vivo studies confirm that CypD deficiency in ischemia-treated donor hearts mitigates IRI and allograft rejection (n=8; p=0.008). Our findings suggest that CypD inhibition following transplantation substantially attenuates necroptosis and mitigates allograft injury and the subsequent alloimmune response. Our data also indicate that AIF may be the downstreameffector molecule that executes IRI-induced DNA damage in necroptosis. As such, targetingmitochondrial permeability may be a plausible approach in formulating therapeutic strategies aimed at improving allograft viability and function

Rahman, Sadaf

The impact of first-line therapy with novel agents in multiple myeloma patients age 80 and above: a systematic review

Sadaf Rahman Cody Sider, Fadi Bahodi, Selay Lam, Martha Louzada, Chai Phua

BACKGROUND: Novel therapeutic agents in multiple myeloma (MM) have significantly improved treatment outcomes, however, data for patients aged ?80 is sparse. METHOD: MEDLINE and EMBASE search concluded March 4, 2019. We included studies assessing novel agents as first-line treatment in

transplant-ineligible MM patients aged ?80. Primary outcomes were overall survival (OS) and progression-free survival (PFS). A qualitative analysis was undertaken due to the small number of articles.RESULTS: 6 of 1683 retrieved articles were included [total 819 patients age ?80 (range 80-96)]. Median OS was significantly shorter in age ?80 (reported ranges: age ?80 = 19.5-31.9mo; age 66-79 = 46-54.8mo; age ?65 = 81-83.8mo or not reached). Shorter survival was associated with anemia, elevated LDH, and worse performance status, ISS stage and Charlson Comorbidity Index. In one study, patients attaining ?VGPR had improved median OS (30.4mo vs 18.8mo, p=0.001). A significantly lower median PFS by age occurred in 1 of 3 studies reporting PFS [age ?80 = 19.1mo, age 66-79 = 26.3mo (p=0.033), age ?65 = 54.3mo (p=0.0009)]. Early mortality was significantly greater in patients age ?80, primarily due to infection or renal failure. One study noted that despite reduced OS, the relative survival rate was higher in patients aged ?85 at 2 years than in younger age groups.CONCLUSION: While MM patients aged ?80 experience shorter OS and PFS, treatment with a novel agent may offer comparable survival outcomes to younger groups in those able to attain ?VGPR. Relative survival also favours active treatment in elderly patients, while balancing the risks of early mortality.

Rosa, Andrew

Patient and paramedic experiences with a direct electronic referral program for hypoglycemia (HG) education following Emergency Medical Services (EMS) assist-requiring HG: A qualitative study

Rosa, A. Spaic, T., Liu, S., Carter, D., Peddle, M., Mahon, J., & Sibbald, S. L.

Hypoglycemia requiring EMS assistance negatively impacts outcomes in people with diabetes. Prior studies have shown that a small proportion of those with EMS assist-requiring HG are brought to hospital; these episodes are “invisible” to the health care system. An innovative direct electronic referral program in which paramedics sent a referral for focused HG education to the Diabetes Education Centre (DEC) at the time of paramedic assessment was implemented for 18 months. Program uptake was lower than expected (133 referrals, 79 scheduled, and 50 attended). This qualitative study examines barriers and facilitators for DEC attendance for HG education after EMS assist-requiring HG. We conducted semi-structured interviews with patients who had EMS-assisted HG and surveyed paramedics about their experiences. Of 34 paramedics, 30 (88%) attended at least 1 HG call in the study period and 26 (76%) used the referral program. Fourteen patients (18% response rate) participated: Eight (57%) recalled the EMS referral, 6 (43%) did not, and 4 (29%) thought they were referred by their family doctor. Themes identified included: positive impact of diabetes education, importance of spousal support and in-person education. Barriers included prior DEC attendance, especially in those with long diabetes duration and embarrassment (failure to self-manage, memory loss around the HG event). While patients acknowledged HG education as an excellent strategy to reduce recurrent episodes, many had already attended similar sessions and did not feel further education was needed. Hence, an important gap in providing HG education to patients with severe HG may be both system-based and disease-related.

Sadeghi, Saghar

A novel BTK gene mutation, T354I, in a patient with X-linked agammaglobulinemia (XLA)

Saghar Sadeghi Amin Kanani

BackgroundXLA is a hereditary primary immunodeficiency that results from Bruton's tyrosine kinase (BTK) gene mutations leading to early-onset agammaglobulinemia and recurrent infections. There have been over 1000 mutations in BTK gene reported to be responsible for XLA. These mutations lead to defective B-cell development, profound deficiency of immunoglobulins and an increased susceptibility to infections.Case reportA 55 year old gentleman presented to our clinic with recurrent sinopulmonary infections. At age 4 he was found to have hypogammaglobulinemia and was diagnosed with common variable immunodeficiency (CVID) and was treated with IVIG; despite this he continued to have recurrent infections. Blood work from 2009 had revealed no mature B-cells and therefore the suspicion of X-linked agammaglobulinemia was raised. BTK gene analysis was done revealing a novel T354I missense mutation in the BTK gene, reported as highly likely to be associated with XLA. DiscussionBTK mutations in XLA consist of missense mutations, small insertion and deletions, Splice-site mutations, and nonsense mutations.The patient we describe was found to have a novel T354I missense mutation of BTK gene. T354I is a non-conservative amino acid substitution in that a polar Threonine residue is replaced with a non-polar Isoleucin at a position conserved across mammals in the SH2 domain of BTK. Early diagnosis, treatment, and genetic counseling are essential to reducing mortality and morbidity. This case emphasizes that suspicion for XLA and gene-study is essential for patients presenting with clinically overlapping disorders that would include XLA as a differential diagnosis.

Sadeghi, Saghar

A case of hereditary angioedema with possible de novo mutation in a patient with systemic lupus erythematous

Saghar Sadeghi Hannah Trainor Roberts

BackgroundHereditary angioedema (HAE) is a disease characterized by recurrent episodes of angioedema. Although the swelling is self-limited and resolves in two to five days without treatment, laryngeal involvement may cause fatal asphyxiation. The best characterized forms of HAE arise from deficiency or dysfunction of C1 inhibitor. HAE types 1 and 2 are autosomal dominant mutations in the SERPING1 gene with about 25% of mutations being de novo. HAE can have association with autoimmune conditions such as SLE. In the literature review, 38 cases of lupus combined with HAE were identified. Case report A 26 year old female presented to our clinic in January 2019 with 10 years history of recurrent angioedema involving the abdomen, genitourinary tract and face. She was also noted to have complaints of intermittent inflammatory arthritis along with recurrent aphthous ulcers with a positive ANA suggestive of lupus. Her workup of angioedema interestingly did reveal a high C1 esterase inhibitor function but low level, her C4 was also low normal but not done during an attack. Conclusion The association between lupus and HAE is rare. We have identified an interesting case of a patient with SLE and typical presentation for HAE most likely associated with a de novo mutation. The HAE symptom these patients most often present with is gastrointestinal in nature. This is consistent with our case. Our

case,'s presentation although not completely typical is suggestive of HAE with likely a de novo mutation and genetic testing is pending.

Safa, Samaunus

Age-Related Joint Histology in a Mouse Model of Rheumatoid Arthritis

Samaunus Safa Patti Kiser, David A. Bell, Ewa Cairns, Lillian Barra

Rheumatoid Arthritis (RA) is a debilitating autoimmune disease affecting the joints. We developed a novel RA-specific autoantigen-induced mouse model for RA, expressing the strongest genetic risk factor for RA, HLA-DR4. These mice, called DR4 transgenic (tg) mice, require up to 38 weeks to demonstrate pathological features of RA. Age-related cartilage degradation, chondrocyte disorganization, cyst-like formations and ossification of the meniscus occur in other mouse strains from 52 to 156 weeks. Therefore, an age-related baseline is needed to distinguish RA features from those that occur due to aging. In this study, we performed histopathological evaluation of DR4tg mouse knee joints at ages 5 to 38 weeks (N=16) stained using hematoxylin and eosin or toluidine blue, to observe changes in soft tissues and cartilage. We compared these changes to age-matched background C57Bl/6J (B6) mice (N=7). Irregular chondrocyte organization and meniscal ossification was seen in >65% of DR4tg and B6 mice 10 weeks or older. Cyst-like formations were seen at 38 weeks in >75% of DR4tg and B6 mice. Increased chondrocyte death was seen in 75% of DR4tg mice at 10 or 38 weeks, but not in age-matched B6 mice, suggesting that the HLA-DR4 transgene may mediate some of these differences. These cartilage changes, which are signs of osteoarthritis, appeared at earlier ages in our study than previously reported; the study mice may be prone to earlier degenerative joint disease. In future we will compare joint histopathology of autoantigen-induced arthritic to naive mice to determine the overlap of age-related features in disease presentation.

Sattin, Michael

Analysing the role of a COVID-19 questionnaire at LHSC: a quality improvement initiative.

Michael Sattin Neha Sharma. Marko Mrkobrada. Megan Devlin. Erin Spicer.

In early 2020, the spread of SARS-CoV-2 was declared a pandemic. Accurate screening of at-risk patients, and thus appropriate allocation of limited viral tests, became an important Public Health initiative worldwide. Ontario,'s Public Health screening questionnaire for COVID-19 consists of patient-reported symptoms and exposures. As the main mode of transmission has shifted from travelers to community spread, and the symptom profile of COVID-19 has expanded, there is increasingly concern that the questionnaire does not capture the most predictive data. This quality improvement initiative aimed to analyse the predictive capacity of the questionnaire for identifying COVID-19 positive cases and then study the effects of modifications to the questionnaire on its predictive capacity. The analysis included 248 patients admitted to London Health Sciences Centre(LHSC) under a medicine service between March 23rd to April 13th who completed a standard screening questionnaire, and for whom at least one PCR for SARS-CoV-2 was available. All three symptoms included on the questionnaire (fever, cough,

dyspnea) had poor individual positive predictive values (PPV) (0.202, 0.185, 0.133), but good negative predictive values (NPV) (0.926, 0.947, 0.888). The combined absence of fever and cough had a strong NPV (0.971). The combined presence of all three symptoms had only a PPV of 0.378. No other risk factors (e.g. travel within 14 days, exposure to probable/symptomatic cases) had a PPV > 0.500 or NPV < 0.910. Based on these early data, we have recommended changes to the questionnaire, which will be assessed for better predictive accuracy through ongoing PDSA cycles.

Semenov, Daniel

The association of latitude and the epidemiology of Giant Cell Arteritis

Daniel Semenov Katherine Li, Matthew Turk, Janet Pope

Introduction: Giant cell arteritis (GCA) is an immune-mediated disease of the large vessels, and occurs in adults over 50 years old. Other immune-mediated diseases including multiple sclerosis have evidence of an association between latitude and the prevalence, however, this association has not been studied in GCA. This meta-analysis examines the relationship of latitude and the incidence, prevalence and mortality of GCA.Methods: A systematic review of the English literature was conducted using the EMBase, Scopus and PubMed databases. Articles were included if they were cohort or cross-sectional studies with 50 or more patients with GCA and reported on population and location parameters. Review articles, case-control studies and case-series were excluded. Two reviewers extracted data and a third verified inclusion of studies. The website www.latlong.net was used to determine the latitude of the population location (city/region) examined in each included article. Regression analysis was performed on latitude and incidence, prevalence and mortality, respectively.Results: Of the 3569 citations identified by the literature search, 107 were included in analysis. Once values were graphed, there was a visual trend for increasing incidence with magnitude of latitude. The R squared values suggest there is no statistical significance of the association of magnitude of latitude with incidence, prevalence, or mortality.Conclusion: Latitude does not have a statistical significant association with incidence, prevalence or mortality. There may be other factors at play that result in increased incidence and prevalence of GCA in Scandinavian countries which may potentially include genetic factors unique to the population.

Sharma, Neha

The validity of ACSM calculation of VO2peak in a cardiac rehabilitation population

N. Sharma T. Hartley, D. Pananos, C. Faubert, R.S. McKelvie, N.G. Suskin

Cardiorespiratory fitness (CRF), expressed as peak oxygen consumption (VO2peak), is a strong predictor of mortality and morbidity. The gold standard for measuring CRF is through cardiopulmonary exercise testing (CPET), but it is more often estimated from treadmill speed and grade using the American College of Sports Medicine (ACSM) formula (METsTM). This study aims to compare METsTM to the CPET measured VO2peak METs (METsVO2) to determine if an equation specific to CR patients is warranted. Routinely collected CPET patient data were analyzed from 524 patients entering CR from Apr 1, 2017-

Sept 30, 2018 at St. Joseph,'s Health Care. SPSS v. 24.0 was used to compare METsTM to METsVO2 through t-test and Bland Altman plots, and develop a regression equation to calculate METsTM for a CR population. METsTM and METsVO2 were highly and significantly correlated (R=0.88, p<0.001). The mean difference between METsTM and METsVO2 was 2.6 METs (95% CI=6.68 ,Äì -1.49). A model to adjust the ACSM calculated METs was developed: METsVO2 = 1.98 + 0.45(METsTM). A simplified Rule of Thumb equation is METsVO2 = 2 + 0.5(METsTM). Using this model to predict METs on subject data found an expected error of 0.59 METs (95% CI=0.48,Äì0.71). The Rule of Thumb equation may be more accurate in calculating METs in the CR population. Future directions of this research are to include data from other sites in Canada that conduct CPET analyses to validate and increase the applicability of our findings.

Shin, Alice

Role of macrophages in the initiation of colitis-associated cancer

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

BACKGROUND: Colorectal cancer (CRC) is the second leading cause of cancer death, with a major risk factor being chronic inflammation. Despite the clear association between inflammation and cancer, the mechanism by which colitis leads to CRC is still unknown. Using our published murine model of colitis-associated cancer (CAC), we previously showed that the presence of colonic inflammation does not always correlate with tumorigenesis. Instead, it is specific to the colitis-inducing agent used. Therefore, we hypothesized that various forms of colitis contribute to tumorigenesis.METHODS: Following Tamoxifen induction, Dclk1-CreERT2;ROSA26-tdTomato;APCfl/fl mice were treated with the colitis-inducing agents DSS, trinitrobenzene sulfonic acid (TNBS), oxazolone, Citrobacter rodentium, or doxorubicin. The tumor studies were repeated using azoxymethane (AOM)-DSS induced CAC model.RESULTS: DSS, TNBS, oxazolone, C. rodentium, or doxorubicin induced colonic inflammation as detected by myeloperoxidase (MPO) activity and histology. Surprisingly, DSS administration led to colonic tumors, whereas TNBS, oxazolone, C. rodentium, or doxorubicin did not induce tumorigenesis. Upon flow cytometric analysis of immune cells in the colon, we detected increased levels of F4/80+ macrophages in the DSS-treated mice when compared to other models of colitis. As such, addition of macrophage-secreted cytokines induced lineage tracing of Dclk1+ tuft cells in intestinal organoids. Interestingly, depletion of macrophages in mice given DSS-colitis reduced tumor number.CONCLUSIONS: Our data suggest that infiltration of macrophages, unique to DSS-induced colitis, leads to colonic tumor formation. This demonstrates that specific immune cell type, rather than the presence of inflammation, plays a crucial role in the initiation of CAC.

Sirisegaram, Luxey

Holding Hip Fracture Care to a Higher Standard; A quality improvement initiative to improve hip fracture care at LHSC

Luxey Sirisegaram, BSc, MD. Aquila Gopal BSc, MB BCh BAO.Jenny Thain BM BS, BMed Sci, MRCP.

Background70-90% of fragility hip fractures (FHF) are due to osteoporosis. In 2013/2014, OOS* reported ~80% of Ontarian FHF did not receive investigations nor treatment for osteoporosis after 6 months. The Hip Fracture Intervention Program (HFIP), launched in 2018, is a multi-intervention program at Victoria Hospital aimed at improving FHF care as per HQO** quality standards (QS). This QI initiative focuses on QS 14 ‚Äì Osteoporosis Management. The aim is to improve osteoporosis management in patients with FHF, to 70% within one year.MethodsHFIP is standardized pre-operative powerplans with automatic geriatric consultation, bone health assessment and osteoporosis bloodwork (BW). Inclusion criteria were: age ?65 years, fragility intertrochanteric or subcapital hip fracture, admission to B9-200. Baseline (BL) and intervention (INT) data were analyzed with the variables of powerplan usage, BW, geriatric consultation, in-patient initiation of antiresorptive treatment and discharge bone-health plan. ResultsQI cycle 1: Intervention initiated in October 2018. 38 baseline patients, aged 82.6 +/- 7.5, 72 intervention patients, aged 82.7 +/- 8. Percentage of patients (Baseline/Intervention): 25-hydroxyVitamin D (21/68), Calcium (44/72), Albumin (28/56), TSH (18/46), geriatric consult(18/72), vitamin D supplementation (73/96), discharged on antiresorptive therapy (27/31) and discharge bone health plan (39/83).ConclusionHFIP achieved its aim of improving bone health assessments, vitamin D supplementation and discharge plans to over 70%. Rates of inpatient anti-resorptive initiation remained low but with high rates of follow-up arranged. Areas for improvement in cycle 2 include interventions to improve BW requests and inpatient initiation of therapy. *Ontario Osteoporosis Strategy**Health Quality Ontario

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Song, Yifeng

Preventing rheumatoid arthritis-associated autoimmunity using peptide-containing transdermal cream in DR4tg mice

Yifeng Song Garth Blackler, Sheri Saunders, Gagan Singh, Eva Turley, Ewa Cairns, Lillian Barra

Rheumatoid arthritis (RA) is a chronic inflammatory disorder preceded for years by a pre-clinical phase (pre-RA), which is associated with risk factors and asymptomatic autoimmunity. Circulating anti-citrullinated and anti-homocitrullinated peptide/protein autoantibodies (ACPAs and AHCPAs, respectively) detected during pre-RA are disease-specific predictive biomarkers. Pre-RA autoimmunity may be preventable by delivering RA-associated autoantigens into the skin to induce immune tolerance. We explore the efficacy of a transdermal cream treatment containing citrullinated and homocitrullinated peptides in preventing autoimmunity against citrullinated and homocitrullinated antigens in DR4tg mice. DR4tg mice express the strongest human RA genetic risk factor, which is linked with ACPA and AHCPA production. To model RA, DR4tg mice were immunized with homocitrullinated peptides to induce autoimmunity and arthritis. Mice were treated with the transdermal cream containing citrullinated and homocitrullinated peptides before immunization. ACPA and AHCPA levels were screened using ELISA bi-weekly up to and including the endpoint 137 days later. Mice treated with

peptide-containing cream (n=8) developed significantly lower AHCPA IgG levels over time than mice treated with peptide-absent control cream (n=8) ($p<0.0001$). No significant differences in ACPA IgG levels or changes in ratios of pro-inflammatory (IgG2b) vs. anti-inflammatory (IgG1) AHCPA IgG subclasses were observed. T cell responses were measured at the endpoint using 3H-Thymidine incorporation assay but were not detected in most mice. We effectively prevented an RA-specific autoimmune response (AHCPA production) using a novel skin-based treatment. Using transdermal cream to induce immune tolerance towards autoantigens holds the potential for innovative RA-specific prevention therapies.

Strum, Scott

CSNK2 in Cancer: Pathophysiology and Translational Applications

Scott W Strum Dr. Laszlo GyenisDr. David Litchfield

Background: CSNK2 is a pleiotropic serine/threonine kinase that holds prognostic and therapeutic significance in multiple cancer types. This systematic review summarizes the current knowledge from in vitro and in vivo studies on the biology of this kinase in cancer alongside preclinical/clinical investigations from 24 different human cancers. Methods: PRISMA methodology was used to generate a study protocol and building-block search strategy from which a total of 796 publications in PubMed were retrieved. 245 of these met both screening and inclusion criteria. Data was systematically extracted, including CSNK2 mRNA/protein/activity levels, phosphotargets, phenotypic changes, in vivo studies, and prognostic/therapeutic data. Data was then summarized and analyzed. Results: Five CSNK2 phosphotargets were identified in at least 4 cancers: AKT, STAT3, RELA, PTEN, and TP53. The most heavily cited was AKT, identified in 15 cancers. Phenotypically, behaviours influenced by CSNK2 that were found in 11 or more cancers included: evasion of apoptosis, proliferation, invasion/metastasis, and cell cycle control. These phenotypes correlated heavily with the most commonly cited CSNK2 targets. Clinically, CSNK2 held prognostic significance in 17 cancers. Furthermore, xenograft experiments were completed in 13 cancers where CSNK2 inhibition resulted in a positive response to treatment. Lastly, early studies have shown promising results with CSNK2-specific inhibitors, with several clinical trials now underway to further investigate. Conclusions: Our analysis supports CSNK2 as an attractive target for cancer therapy with promising pre-clinical results, and points to specific areas where additional investigation is critical to advance our understanding of CSNK2 pathophysiology and improve clinical outcomes.

Taha, Nada

Longitudinal functional changes with clinically significant radiographic progression in idiopathic pulmonary fibrosis: are we following the right parameters?

Nada Taha Dejanira D,'Amato2, Karishma Hosein1, Tiziana Ranalli2, Gianluigi Sergiacomi2, Maurizio Zompatori3, Marco Mura1

Background. Progression of the disease in idiopathic pulmonary fibrosis (IPF) is difficult to predict, due to its variable course. The relationship between radiographic progression and functional decline in IPF is unclear. We sought to confirm that a simple HRCT fibrosis visual score is a reliable predictor of mortality in IPF, when longitudinally followed; and to ascertain which pulmonary functional variables best reflect clinically significant radiographic progression.Methods. One-hundred-twenty-three consecutive patients with IPF from 2 centers were followed for an average of 3 years. Longitudinal changes of HRCT fibrosis scores, forced vital capacity (FVC), total lung capacity and diffusing lung capacity for carbon monoxide were considered. HRCTs were scored by 2 chest radiologists. The primary outcome was lung transplant (LTx)-free survival after the follow-up HRCT.Results. During the follow-up period, 43 deaths and 11 LTx occurred. On average, the HRCT fibrosis score increased significantly, and a longitudinal increase >7% predicted LTx-free survival significantly, with good specificity, but limited sensitivity. The correlation between radiographic and functional progression was significant, but only moderate. HRCT progression and FVC decline predicted LTx-free survival independently and significantly, with better sensitivity but worse specificity for a ?5% decline of FVC.Conclusions. The HRCT fibrosis visual core is a reliable and responsive tool to detect clinically meaningful disease progression. Although no individual pulmonary function test closely reflects radiographic progression, a longitudinal FVC decline integrates the prognostic information of radiographic progression. However, the accuracy of these methods remains limited, and better prognostication models need to be found.

Tan, Sonya

Guideline-directed online tool for prescribing antiplatelets and anticoagulants following cardiac procedures

Sonya Tan, BSc Patrick Teefy, MD, FRCPC

Prescribing an ideal antithrombotic regimen following cardiac procedures requires careful consideration of the delicate balance between the risk of hemorrhage and the risk of thrombosis. Further, with the addition of novel oral anticoagulants, it is becoming increasingly difficult for clinicians and patients to understand the exact combination of medications indicated in each clinical scenario. In fact, anticoagulants were found to cause the most serious adverse events1 with nearly half of them related to medication errors2. We aimed to create an online tool to clarify medication prescriptions for both clinicians and patients.We met with a variety of stakeholders to determine the individualized needs of cardiologists, pharmacists and family physicians in designing our tool. Priorities included recommendations based on updated guidelines, clarification of appropriate drug dose and duration, and effective patient education. Based on this information we created an algorithm that allows clinicians to input patient procedures and individual patient factors, and generates recommendations based on updated guidelines. In complex clinical scenarios, we ensured our algorithm prioritized absolute

indications for specific conditions over relative indications for other conditions.Finally, our tool generates a printable discharge form with a graph outlining the antiplatelet/anticoagulant agents, their indication and precise dose and duration, which can then be distributed to the patient and clinicians. We also created a patient education package that is tailored to include information relevant to each patient,'s condition. In future studies, we will aim to determine if the use of this tool decreases adverse events associated with inappropriate anticoagulant use.

Ting, Janine

Reducing Urinary Catheters at University Hospital: Current State Analysis

Janine Ting Joseph Carson, Alan Gob

BackgroundProlonged indwelling urinary catheter (UC) use is associated with longer hospital stays, accelerated functional decline, and urinary tract infections. We plan to implement Choosing Wisely Canada,'s Lose The Tube toolkit to reduce unnecessary UCs on general medicine units at University Hospital (UH). In this preliminary study, we aimed to measure baseline UC utilization and identify barriers to UC discontinuation. MethodsWe measured baseline prevalence on a process control chart of 25 convenience audits. We also measured baseline appropriateness through a physician audit of all UCs on one day. We used quality improvement tools to analyze the current state and root causes of catheter overuse with nursing staff. Our study included a leadership focus group, process mapping, an Ishikawa diagram, and a multi-voting survey with a Pareto chart to identify barriers for improvement.ResultsOn average, 24% of patients had UCs; performance was mostly stable with minor special-cause variation. The appropriateness audit found 35% of catheters (n=8/23) were non-indicated. In our root cause analysis, nursing staff ranked the greatest barriers to UC removal as patient immobility; no trigger for catheter reassessment; and unclear catheter indications. ConclusionOur current state analysis validated the need to address UC overuse. Since the Choosing Wisely toolkit recommended nurse-led catheter removals, our root cause analysis focussed on understanding nurse perspectives. We believe their participation and input is critical in designing sustainable change strategies. Our next study will use these findings to customize toolkit interventions for catheter reduction.

Tong, Justin

Vismodegib in advanced basal cell carcinoma: local experience at the London Regional Cancer Program

Justin Tong Brandon Mitchell, Diane Logan, Scott Ernst

Background: Vismodegib is a novel Hedgehog pathway inhibitor which has revolutionized the treatment of patients with advanced basal cell carcinoma (aBCC) who are poor candidates for surgery or radiation or have experienced recurrence. Few studies have explored the use of vismodegib to facilitate further surgery or radiation, and optimal treatment duration to balance outcomes with adverse effects has yet to be established.Objectives: To characterize the outcomes of BCC patients treated with vismodegib, as well as duration of treatment and occurrence of surgical or radiotherapeutic intervention.Methods: We performed a retrospective observational study of 46 adult patients with aBCC treated with vismodegib

at London Regional Cancer Program (LRCP) at any time between January 1, 2012 and July 1, 2019.Results: Twenty-three patients (50%) achieved complete response and 19 (41.3%) achieved partial response. Median time from vismodegib initiation to maximal response was 5.8 months in complete responders and 4.4 months in partial responders. Eleven patients (23.9%) received post-vismodegib resection. Eleven patients (23.9%) received post-vismodegib radiation. Thirty-two patients (69.6%) experienced progression after achieving maximal response, at a median of 17.9 months after vismodegib initiation. Twenty patients (43.4%) discontinued treatment at least once due to adverse effects.Conclusions: LRCP,'s experience with vismodegib supports its effectiveness in the treatment of aBCC. However, most patients eventually develop progressive disease after achievement of maximal response, so further investigation into optimal combination with other treatment modalities is warranted. Additionally, toxicity remains a significant factor limiting duration of therapy, motivating continued efforts into managing adverse effects.

Townsend, Cassandra

Improving Bowel Preparation Quality for Inpatient Colonoscopies at a Tertiary Care Hospital

C Townsend MD M Gandhi MD FRCPC MSc, M Cheah MD, M Almaghrabi MD, H Akhtar MD, A Alotaibi MD, N Khanna MD FRCPC, B Yan MD FRCPC and M Brahmania MD FRCPC MPH

INTRODUCTION: Optimal bowel preparation during inpatient colonoscopy is essential. AIM: Our goal was to reduce the absolute percentage of poor-quality bowel preparation for inpatient colonoscopies by 10% over a 12-month period.IMPROVEMENT CYCLES: This study was conducted at University Hospital from March 2018 ,Äì December 2019. In the first PDSA cycle, we modified an existing order-set on our electronic medical record so split-dose bowel preparation would more reliably be ordered. Our second PDSA cycle focused on providing junior residents written instructions of how to order bowel preparation. PDSA cycle three involved making bowel preparation quality assessment more objective by standardizing how poor-quality bowel preparation was defined in post-procedure documentation. Our fourth PDSA cycle further optimized our order-set to make sure bowel preparation orders were appearing at a specific time on the patient medical administration record. The fifth PDSA cycle added a verbal teaching session regarding inpatient bowel preparation for residents at the start of their Gastroenterology rotation. PDSA cycle six was aimed at improving patient education by providing patients with written instructions on the day prior to their scheduled colonoscopy. PROJECT IMPACT: Ten percent of patients (52/541) who had an inpatient colonoscopy between September 2018 and December 2019 had poor-quality bowel preparation, reduced from 14% (31/221) in the six months prior to our first intervention. Data demonstrates a shift, i.e., non-random variation, towards improvement in percentage of patients who had poor-quality bowel preparation. LESSONS LEARNED: Simple and sustainable PDSA cycles can be implemented to improve quality of bowel preparation.

Townsend, Cassandra

UNDERSTANDING THE IMPACT OF TNF-ALPHA ANTAGONISTS ON THE SEVERITY OF NON-MELANOMA SKIN CANCER IN INFLAMMATORY BOWEL DISEASE AND THE CONSEQUENCES FOR THERAPY

Cassandra M Townsend Reena Khanna, Aze Suzanne Wilson

Background: Minimal data exists highlighting the differences in clinical course of patients diagnosed with non-melanoma skin cancer (NMSC) who have inflammatory bowel disease (IBD) and are tumor necrosis factor-alpha (TNF-?) antagonist exposed. Aims: Our goal is to determine whether TNF-? antagonist exposure in IBD is associated with a high risk NMSC at diagnosis, as defined by the National Comprehensive Cancer Network stratification. Methods: We reviewed 471 IBD patients seen at London Health Sciences Centre and found 27 patients who had been diagnosed with NMSC. Seventeen patients had a pre-NMSC TNF-? antagonist exposure while 10 patients who developed an NMSC and had no TNF-? antagonist exposure prior to NMSC diagnosis.Results: Forty-seven percent (8/17) of patients who have been exposed to TNF-? antagonist therapy presented with a high risk NMSC lesion at diagnosis compared to 40% (4/10) who were not exposed (OR 2.76, 95%CI 0.42-18.02; p=0.290). Thirty-five percent (6/17) of patients exposed to TNF-? antagonist had positive margins compared with 0% (0/10) of patients who were not exposed. No patients in either group presented with metastatic disease. Twenty-nine percent (5/17) of patients in the exposed group received more advanced treatment compared with 0% (0/10) in the non-exposed group. Six percent (1/17) of patients in the TNF-? antagonist group had their IBD therapy changed to an alternate biologic class, and 29% of patients (5/17) in the TNF-? antagonist group had recurrent NMSC lesions.Conclusions: TNF-? antagonist exposure may be associated with higher risk NMSC lesion at presentation.

Tuomi, Jari

Dapagliflozin Reduces Atrial Remodelling and Atrial Fibrillation Susceptibility post Myocardial Infarction

Jari Tuomi Kaiyuan Wang, Sharon Lu, Qingping Feng

abstract unavailable

Valiaveettil, Christina

In Support of Meaningful Assessment and Feedback: A Study of Reasoning Tasks Used During Clinical Case Review in the Ambulatory Internal Medicine Clinic

Christina Valiaveettil MD Jacqueline Torti PhD, Mark Goldszmidt MD, PhD, FRCPC

Background: Most clinical teaching focuses on completing clinical tasks, such as history taking and physical exams. Less focus is placed on what we reason about (reasoning tasks) and how that helps us learn to be more effective clinicians. The purpose of this study is to explore how clinical reasoning tasks are used by learners versus attending physicians during case review in general internal medicine (GIM) clinics.¬†Methods: Data consists of 29 audio-recorded case review discussions, 21 new and 8 follow-up cases, between 7 attending internists and 13 trainees (medical students, residents, and fellows). A

framework of 27 clinical reasoning tasks was previously developed and validated in the setting of clinical teaching unit admissions. Transcripts were analyzed using constant comparison and template analysis. Results: Expertise effects were evident in the use of clinical reasoning tasks. Junior learners focussed on listing presenting complaints, whereas fellows and attending physicians would reprioritize complaints to identify the most salient issues for the encounter. Attending physicians and fellows were more likely to address how risk factors and comorbid conditions impact the presenting complaint, and reason around educational strategies for patients. Only attending physicians considered documentation and follow-up strategies. Interestingly, goals of care and patient decision-making capacity were only addressed in 2/29 and 0/29 cases, respectively. Discussion: Clinical reasoning tasks provide a standardized vocabulary to communicate case-based reasoning during case review discussions. This can be a valuable way of understanding seniority-dependent differences in clinical reasoning and identify opportunities for quality improvement and competency-based education.

Varghese, Timothy

Prevalence of Osteoporosis in Osteoarthritic Patients: A Systematic Review

Kim, Dongkeun Li, YueyangVarghese, TimothyPirshahid, Ali Ahmadi

There is controversy regarding relationships between osteoarthritis (OA) and osteoporosis(OP). While OA may be associated with increased bone mineral density (BMD) due to increased weight, incidence of OP may also be increased in patients with OA. In this study, we compared age and sex-matched populations to determine whether the prevalence of OP is increased in patients with OA. We conducted a systematic literature review using the databases PubMed, Embase, Scopus, and Web of Science, including articles that that analysed the frequency, rate, prevalence, incidence, risk, or excess risk of OP in patients with OA compared to age and sex-matched control groups. Articles with fewer than 200 participants, and those without controls were excluded. Two reviewers conducted title and abstract screening of 2772 unique articles, 49 articles were chosen for full article screening, and 4 articles met our inclusion criteria. Data from 2 and 4 studies used OP in men and women, respectively. Articles reporting on BMD, and not OP, were excluded. In women, 998 participants with OA were compared with 1903 controls. The pooled estimate of the odds ratio for prevalence of OP vs general matched population was not statistically different. In men, 136 participants with OA were compared with 682 controls. The results did not show a statistically significant different in the frequency of OP in OA in men. We concluded that the frequency of OP in participants with OA was the same in both men and women, compared to the matched controls.

Wang, Qian(Mary)

Investigating the Role of Novel NUDT15 Variant in Azathioprine-related Myelotoxicity

Qian (Mary) Wang Dr. Aze Suzanne Wilson, Dr. Ute Schwarz

Azathioprine (AZA), an immunosuppressant, has classically been used to treat patients with inflammatory bowel disease (IBD). AZA acts through inhibiting purine synthesis, and its metabolism occurs via a pathway involving thiopurine methyltransferase (TPMT). While standard TPMT genetic screening is conducted for IBD patients initiating AZA treatment to minimize adverse drug effects (ADE), a majority of patients experiencing ADE do not have TPMT variants. Another gene, NUDT15, has been found to have variations in patient populations that experience AZA-related myelotoxicity. In order to further our understanding regarding the role of NUDT15 in AZA-related myelotoxicity, we have genotyped patients with wild-type TPMT who experience AZA-related ADEs. A novel NUDT15 variant has been discovered as a result. After sequencing the novel NUDT15 variant, we have found a point mutation in its start codon. As of such, this study aims to characterize this variant,'s gene expression and explore the relevant genetic mechanisms behind AZA-related ADEs. RT-PCR results show that the mutation found in variant gene does not appear to be detrimental to its gene expression. The variant,'s protein expression will be characterized through the use of western blot. Further, the study hopes to elucidate the function of the variant protein in relation to that of the wild type.

Weiler, Madina

Real-world predictors of starting different advanced DMARD treatments in rheumatoid arthritis: A prospective investigation from the Canadian Early Arthritis Cohort (CATCH) group.

Madina Weiler Orit Schieir, Marie-France Valois, Susan J. Bartlett, Louis Bessette, Gilles Boire, Glen Hazlewood, Carol Hitchon, Edward Keystone, Diane Tin, Carter Thorne, Vivian Bykerk, Janet Pope

Background: RA patients with inadequate DMARD response may be treated with a TNF inhibitor (TNFi), non-TNFi or janus kinase inhibitor (JAKi).Objectives: Compare characteristics of real-world early RA (ERA) patients starting TNFi, non-TNFi, and JAKi post DMARD failure. Methods: Analyzed data from ERA patients (symptoms <1 year) enrolled in CATCH who started TNF, non-TNF or JAKi as first-line advanced therapy from 2014-2019. Descriptive statistics, t-tests and chi-square summarized and compared secular trends and patient characteristics initiating each class of therapy. Multinomial logistic regression analyses were used.Results: 246 participants started advanced therapy during the study period; 75% female, mean(SD) age 50(14) years. First-line prescriptions for JAKi increased (0%-33% 2014-2019) and TNFi decreased (87%-61%). Patients starting JAKi had longer disease duration 50.8(39.3) months, fewer tender joints 2(6), lower DAS28 3.6(1.4), CDAI 16.5(3.7), ESR 3.6(1.4) (all p <0.05). Strongest predictor of starting JAKi vs TNF was province (Ontario where access is preferential for JAKi and TNFi, versus Quebec); OR 0.44(0.20, 0.94), adjusted for age, sex, education, RDCI, province, RF positive, private insurance, CDAI. Patients starting TNF had shorter disease duration 32.5(29.1) months. Those prescribed non-TNF had higher DAS28 4.8(1.5), and compared to non-TNF, had greater comorbidities OR 1.35(1.01, 1.81), higher education 2.92(1.28, 6.63), trended towards older age 1.01(0.97, 1.05) (adjusted for age, sex, education and comorbidity). Conclusions: Patient- and physician-related factors (practice location)

determined which advanced therapeutic was prescribed. JAKi usage is increasing as first advanced therapy.

Wu, Yutong

Single-cell RNA Sequencing

Yutong (Leen) Wu Abdalla Abdlelhady, Jenn Biltcliffe, David E. Carter, John Robinson, Robert A. Hegele.

Bulk RNA sequencing (RNA-Seq) is one application of Next Generation Sequencing (NGS) which revolutionized genomic research with its sequencing depth, high throughput data, and ability to measure gene expression of complex transcriptomes. Single-cell RNA sequencing (scRN-seq), as the name implies, enables RNA sequencing of induvial cells and allows visualization of various cell types within a tissue or cell mixture. The 10X Genomics Chromium Next GEM Single Cell 3,' assay measures all eukaryotic poly-A-tailed RNA at the single-cell level. Starting with single cells in suspension, the 10X Chromium Controller combines single cells, Gel beads EMulsion (GEM) beads with Unique Molecular Identifiers (UMI) and reagents into oil droplets. Cell lysis and reverse transcription then occur in each of the droplets, resulting in barcoded cDNA. Partitioning oil is then removed to break the droplets, allowing barcoded cDNA to be amplified, indexed and sequencing on Illumina platforms. Resulting data is analyzed by a set of pipelines, starting with demultiplexing and FASTQ generation, reference genome alignment, UMI deduplication, normalization, statistics and filtering to only include informative genes. Next, Principal Component Analysis (PCA) is performed to reduce data dimensionality. Visualization is then achieved using t-SNE and UMAP algorithms, in which the latter provides meaningful insight on inter-cluster relations. Filtered gene lists are subjected to hierarchical clustering, which generates heatmaps to present differential gene expression and reveal cellular heterozygosity of the tissue. The London Genomic Regional Center (LRGC) now provides this leading-edge technology and single cell data analysis to the local scientific community.

Yotis, Demitra

Elucidating a novel immune evasion mechanism in renal cell carcinoma

Demitra Yotis Brad Shrum, Marie Sarabusky, and Lakshman Gunaratnam

Renal cell carcinoma (RCC) is the most common and lethal form of kidney cancer. Cancer immune evasion is a major obstacle for effective immunotherapy in RCC. Mechanisms of immune evasion are characterized by three phenotypes: Immune Inflamed; tumour contains infiltrating T cells rendered inactive within the tumour microenvironment due to localized inhibition. Immune Desert; tumour is devoid of activate T cells due to defective antigen presentation, and/or T cell activation. Lastly, Immune Excluded; tumour is surrounded by T cells unable to penetrate the parenchyma, caused by inhibiting factors in the tumour stroma. Kidney Injury Molecule-1 (KIM-1) is a cell-surface glycoprotein aberrantly expressed in >90% of RCC tumours. The significance of KIM-1 in RCC pathogenesis is unknown. Using a murine model of RCC (Renca), we have found that KIM-1 expression on RCC cells promotes tumour growth in syngeneic immunocompetent BALB/c mice, but not in RAG1-/- immunodeficient BALB/c mice

suggesting that KIM-1 mediates immune evasion.Using flow cytometry we found fewer T cells within KIM-1pos vs. KIM-1neg tumours. Furthermore, microscopy showed fewer CD3+ cells within the KIM-1pos vs. KIM-1neg tumour parenchyma, with CD3+ cells of the KIM-1pos tumours localized to the tumour stroma. We also observed significantly more myeloid derived suppressor cells (MDSCs) within KIM-1pos vs. KIM-1neg tumours. Transcriptomic and histological profiling revealed KIM-1pos cell lines and tumours increase biosynthesis of extracellular matrix, causing a thicker stromal capsule (which may contribute to immune evasion). Our data suggests that KIM-1 expression in RCC specifically promotes Immune Exclusion, by altering the tumour microenvironment.

Zhao, PeiJun

Genetic Determinants of Myocardial Infarction Risk in Familial Hypercholesterolemia.

Pei Jun Zhao Matthew R. Ban, Michael A. Iacocca, Adam D. McIntyre, Jian Wang, Robert A. Hegele

Background: Familial hypercholesterolemia (FH) is an inherited condition of elevated serum low-density lipoprotein (LDL) cholesterol leading to premature coronary heart disease. We evaluated whether FH mutations are independently associated with the development of myocardial infarction (MI), after adjusting for LDL cholesterol level and clinical risk factors.Methods: In 182 unrelated patients from different families referred with clinically suspected FH, targeted next-generation DNA sequencing was performed on 73 lipid-related genes and 178 single nucleotide polymorphisms, at 300-times mean read depth, to identify monogenic mutations and high-risk single nucleotide polymorphisms.Results: Pathogenic FH mutations were identified in 27% of patients. Patients with mutations, compared with those without, were 12 years younger when referred to the lipid clinic ($P < 0.001$) and had higher baseline and post-treatment LDL cholesterol by 1.11 mmol/L ($P < 0.001$) and 0.62 mmol/L ($P = 0.01$), respectively. The hazard ratio for premature MI with respect to having an FH mutation, controlling for sex, hypertension, body mass index, diabetes, LDL cholesterol, and smoking, was 4.51 ($P = 0.002$).Conclusion: FH is a genetically diverse condition. FH mutations are independently associated with higher risk of premature MI in patients referred for hypercholesterolemia. Therefore, genotyping could guide cardiovascular risk stratification in the personalized treatment of FH.https://www.ncbi.nlm.nih.gov/pubmed/32159113