Schulich School of Medicine & Dentistry
Western University

Department of Medicine

RESEARCH DAY

Friday, May 10, 2019
Best Western Lamplighter Inn
591 Wellington Road South
London, Ontario

This program has no commercial support.

CME INFORMATION

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

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

Learning Objectives:

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

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

Department of Medicine
Resident Research Day 2019

Friday May 10, 2019
Best Western Lamplighter Inn
591 Wellington Road South

Schedule of Events

Start	End		
8:00	8:30	**Breakfast**	**Poster Setup** (Crystal Ballroom South)
8:30	8:40	**Welcome & Opening Remarks** (Crystal Ballroom North)	
8:40	9:40	**Trainee Oral Presentations – (4)** (Crystal Ballroom North) *10 min presentation 5 min Q&A*	
9:40	10:00	Answering clinically important questions using the mixed methods available to quality improvement scientists **Dr. Erin Spicer** (Crystal Ballroom North) *15 min presentation 5 min Q&A*	
10:00	11:00	**BREAK**	**Poster Presentation and Judging** (Crystal Ballroom South)
11:00	11:45	So you want to do research? Finding that question and getting it done **Keynote - Dr. Christopher McIntyre** (Crystal Ballroom North) *40 min presentation 5 min Q&A*	
11:45	13:45	**LUNCH**	**Poster Presentation and Judging** (Crystal Ballroom South)
14:00	15:15	**Trainee Oral Presentations – (5)** (Crystal Ballroom North) *10 min presentation 5 min Q&A*	
15:15	15:30	**Presentation of Awards & Final Remarks** (Crystal Ballroom North)	
		*Please ensure that you complete the **Program Evaluation form** before you leave for the day. To access the online version use the QR code. Hard copies can be found at the Registration Desk.*	

Oral Presentations

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8:40am	**Parker, Brent**	PGY-1	CEP Chemotherapy in Relapsed or Refractory Aggressive Lymphomas: A Retrospective Review	47
8:55am	**Tan, Charlie**	PGY-2	Bloodstream Infections in Persons Who Inject Drugs on Treatment for Infective Endocarditis	56
9:10am	**Burrell, Alishya**	PGY-5	Factors Associated With a Diagnosis of Failure to Cope in Older Medical Inpatients: a case-control study	20
9:25am	**Cullen, Stephanie**	MSc Student	Association Between Cognitive Impairment Subtypes and Dual-Task Gait Performance in a Clinical Setting.	25

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2:15pm	**Kelly, Sara**	PGY-5	A Comparative Study of Hip Geometry in Older Patients with Acetabular versus Hip Fractures	40
2:30pm	**Thulasie Manokaran** *presenting for* Lipkus, Marc	PGY-5	Awareness and Barriers to Access of a Ministry of Health Mandated 'Do Not Resuscitate' Confirmation Form: An Interim Analysis	43
2:45pm	**Dionne, Alexander**	MSc Student	Cell-free DNA release during programmed cell death in kidney ischemia reperfusion injury	26
3:00pm	**Good, Hayley**	PhD Student	Aspirin inhibits the initiation of tuft cell-derived colitis-associated cancer	30

Poster Presentations

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A Case of Thyroid Hormone Resistance in Pregnancy

Minan Abbas, Dr Ruth McManus.

CASE PRESENTATION A 19 year-old woman presented with panic attacks, palpitations, tremor, heat intolerance and enlarged thyroid X 6 months. Examination confirmed a diffusely goitre and mild tremour. Initial lab tests: TSH 1.73 miu/l; Free T3 7.6 pmol/l; Free T4 33.5 pmol/l. She started methimazole. One month later: TSH 3.04 miu/l; FT4 30.1 pmol/l; FT3 8.6 pmol/l. Assay interferences were ruled out; MR pituitary was negative for a mass. Genetic testing confirmed a heterozygous mutation at location 3p24.2 (c.938T>C (p.Met313Thr)) in the THRB gene. Methimazole was stopped, atenolol was started for symptom control. She returned a year later at 26 weeks' gestation: TSH 0.74 miu/l; FT3 6.2 pmol/l; FT4 23 pmol/l. PTU 50mg BID was added, aiming for FT4 <20% over the ULN. Thyroid balance was assessed monthly; maternal-fetal medicine was consulted. Delivery of a normal-weight infant daughter was uneventful; child tested negative for the THRB mutation. DISCUSSION Thyroid hormone resistance (RTH) is an autosomal dominant syndrome characterized by variably reduced end-organ responsiveness to thyroid hormone (TH), caused by loss-of-function mutations in the THRB gene, and associated with an increased risk for miscarriage. High RTH maternal TH levels may suppress fetal TSH, increase fetal goitre risk and result in low birth weight even for gene-negative offspring so that maternal PTU therapy may be considered. Conversely, mothers carrying RTH-mutation positive fetus may not require treatment. Fetal genotyping is therefore recommended, but was unavailable so maternal suppression with PTU was offered along with frequent maternal and fetal monitoring.

Reducing Unnecessary Pituitary Hormone Testing for Patients with Nonfunctional Pituitary Adenomas: A Quality Improvement Project

Minan Abbas, C. Foster, M. Lu, S. Sadat, S. Van Uum, and K. Clemens.

INTRODUCTION: Patients with pituitary adenomas are at risk of anterior and/or posterior pituitary hormonal deficiency following transsphenoidal resection. Although postoperative pituitary hormone testing is important, testing can be completed inappropriately. In this project we sought to reduce the number of unnecessary pituitary hormone tests completed at postoperative week 1 by 90%.METHODS: A retrospective chart review of pituitary surgeries from November 2017 to 2018 performed at LHSC identified 27 pituitary surgeries, 15 for non-functional adenomas. Postoperative bloodwork at week 1 for these patients included pituitary hormone tests not clinically relevant at that time point: TSH/free T3/freeT4, ACTH, LH/FSH, testosterone, estradiol, prolactin and IGF-1. We conducted a root cause analysis and found that the existing postoperative protocol contributed to the inappropriate bloodwork requested for patients. Our Division and colleagues from Neurosurgery then revised this protocol to include only clinically important laboratory investigations to complete at postoperative week 1. The revised protocol was made available to all staff and residents taking part in postoperative pituitary patient care and discharge. The impact of this intervention was assessed using PDSA cycles and auditing postoperative week 1 bloodwork to identify inappropriately requested bloodwork. RESULTS: To date, the revised testing protocol has reduced unnecessary pituitary hormone testing by 100% during the 3 months since its implementation.CONCLUSION: This quality improvement project has reduced clinically non-relevant and expensive postoperative pituitary testing at the one week time point at LHSC.

RNA-seq: From A to U/You at the LRGC

Abdalla Abdlelhady, David E. Carter, Jenn Biltcliffe, John Robinson, Robert A. Hegele.

Next Generation Sequencing (NGS) refers to powerful genomic technologies which permit massively parallel, high throughput nucleic acid sequencing. RNA Sequencing (RNA-Seq) is an

NGS application used to study cellular transcriptomes, providing biological insights into post-transcriptional modifications, alternative gene splicing and differential gene expression between tissues and treatments. The starting material for RNA-Seq experiments is total RNA. After the RNA is isolated and quality tested, the ribosomal RNA is depleted to enrich for the RNA species of interest. The resulting material is used to create a sequence library, typically using a commercially available kit. Typical library creation steps include fragmentation, cDNA synthesis and amplification with indexed primers, which permits multiplexing. The library is then sequenced on an NGS platform such as the Illumina Next-Seq, which can produce up to 500 million reads from one High Output flow cell. The resulting reads are aligned against an annotated reference genome, quantified and normalized. Normalized data then undergoes statistical analysis to produce p-vales and fold changes for detected genes. Filtered gene lists are then subjected to enrichment algorithms to determine biologically significant Gene Ontology and Pathway terms. Data visualization tools such as hierarchical clustering, principal component analysis and genome browsers provide relative and genomic context to the data. Here, we describe a user friendly, cloud based RNA-seq data analysis work flow able to deliver biological insights from raw sequence reads in fastq format. To date, the London Regional Genomics Centre (LRGC) has processed over 55 RNA-seq experiments for over 20 scientists.

Obesity documentation for patients admitted to clinical teaching unit (CTU) at University Hospital

Rasha Abdul-Karim, Erin Spicer.

Background: Obesity is a chronic disease associated with increased morbidity and mortality, and with decreased quality of life. Documentation of obesity can improve the rates of referral for medical and surgical interventions. While obesity is common amongst CTU patients, documentation is poor. Our aim is to improve documentation of obesity and overweight status by 50% by July 2019. Methods: Baseline BMIs and rates of documenting obesity or overweight status among medicine patients were collected by examining admission and discharge notes over 12 weeks (November 2018 to February 2019). Change ideas (plan-do-study-act cycles) were planned based on root cause analyses (RCA) including Fishbone/Ishikawa and Five-Whys tool.Results: The total number of charts reviewed were 118 (ten deceased patients were excluded). A total of 28 patients were overweight; a total of 35 were obese (53.39% of patients admitted to medicine were either overweight and obese). Only 7.9% of those had obesity documented on their admission or discharge notes. Those were discharged without outpatient plans to address obesity. The number of patients with obesity may also be underestimated as there were 19 patients with insufficient data to calculate a BMI. RCA identified the commonest reasons for the lack of obesity and BMI documentation were technical difficulties in obtaining weight and junior residents feeling helpless regarding treatment options.Conclusion: Chart review found approximately half of patients admitted to inpatient medicine service are overweight or obese, but only 7.9% have documentation of this. Interventions targeting obtaining weights and educating residents can help improve documentation.

Reducing Length of Stay in Patients Following a Liver Transplant

Abdulrhman Alamr, Corinne Weernink BScPT MScPT, Peggy Kittmer BScN, Melanie Dodds BScN, Sandy Williams RN(EC) MScN NP, Kelly Thomas MSW RSW, Lynne Sinclair RD, Joanne Plugfelder BPT, Sanjay Patel FRCSC, Anton Skaro FRCSC PhD, Mayur Brahmania FRCPC MPH.

There are seven transplant centers in Canada, however, data on length of stay (LOS) has not been analyzed in any center. Some United States transplant centers have suggested a target of ten days. Prolonged LOS in hospital can result in increased rates of infection, malnutrition, and increased healthcare resource utilization thus a multidisciplinary effort to reduce LOS may improve patient outcomes and reduce costs. London health Sciences Centre had a median LOS of 18 days from January 2015- August 2017.

The aim of the current project was to reduce the median LOS by 3 days over a 16-month period.We used the model for continuous improvement and instituted four Plan-Do-Study-Act (PDSA) cycles to achieve our aim. The first PDSA cycle (n=23) included educational sessions among liver transplant team members. The second PDSA cycle (n=9) included development of a liver transplant clinical pathway. The third PDSA cycle included institution of a clinical order set (n=14). The fourth PDSA cycle (n=19) involved a patient oriented clinical pathway instrument. Over a 16-month period we had 49 liver transplants discharged from hospital with a median LOS of 9 days. We also analyzed balancing measures and found 30 day and 90 readmission rates to be 18.4% and 22.4%, respectively, which was not significantly different from the 2015-2017 rates of 15.4% and 22.7%. In conclusion, development of a multidisciplinary care pathway with patient engagement led to improved discharge rates within a target of ten days with no clinically significant differences in readmission rates.

The impact of gastrointestinal follow up care on healthcare utilization in patients with eosinophilic esophagitis (EoE).

Alazemi K, Alkhattabi M, Caruana J, Gregor J. Department of Medicine, Western University.

Background: EoE is an increasingly recognized condition that causes significant morbidity. There are variety treatments methods available that are practically guided by a subspecialist familiar and experienced with the condition. There is a perception among some physicians that follow up is sporadic and may be related at least in part to patient compliance. **Methods:** We used a retrospective cohort of patients diagnosed with EoE between July 2011 and June 2014 who met the traditional diagnostic criteria. The impact of follow up on subsequent healthcare utilization was analyzed. **Results:** 123 patients with biopsy confirmed EoE were analyzed. Follow up appointments were made for 114/123 patients. 55/123 had repeat elective endoscopy. No complications attributable to any of the procedures. 10/114 of initial appointments went unattended but 15/55 of patients offered follow up failed to attend 5/123 patients required repeat emergency room endoscopy for food impaction. Two patients required this on multiple occasions. 4/5 patients requiring repeat emergency room endoscopy for food impaction had received follow up, although 4/5had at least one missed appointment. 2/5 patients having emergency room endoscopy required overnight admission. No perforations noticed in the cohort. **Conclusion:** Patients with a confirmed diagnosis of EoE do have a risk of requiring subsequent emergency endoscopy for food impaction although it is not clear that scheduled follow up significantly reduces that risk. Contrary to the perception of some physicians, patients with EoE are very likely to attend their first follow up visit although the attrition rate for subsequent scheduled visits is not insignificant.

Immunosuppression Reduction after Diagnosis of Sustained BK Viremia and The Risk of Allograft Rejection, Allograft Loss and Mortality

Fahad Al dhufairi, Fahad Al dhufairi, Mostafa Shokoohi, Anthony M Jevnikar, Andrew A House, Deepali Kumar, Seyed M Hosseini-Moghaddam.

Management of post-transplant BK viremia requires immunosuppression reduction (IsR). We demonstrated the risk of graft rejection, graft loss, and death after IsR considering baseline immunologic risk.BKV screening included plasma BKV-PCR (RealStar® BKV PCR, Altona Diagnostics, Kit 1.2 assay) every 1-3 months in the first 2 years after transplantation. In case of sustained BK viremia (i.e., 2 consecutive BKV positive plasma samples spanning 3 weeks), we regularly reduced the dose of mycophenolate mofetil while targeting tacrolimus trough level <6 ng/ml. We monitored viral load and allograft function for 2 years. 37 recipients (16.7%) developed sustained BK viremia (median 66, IQR: 48-121 days after transplantation). Median viral load at the time of IsR was 19,600 (IQR: 1,200-3,380,000) copies/ml. 94.6% of patients achieved BKV nadir (viral load <500 copies/ml) after IsR. Recipients with sustained viremia requiring IsR were 2.44 (1.71, 3.48) times more

likely to develop acute rejection. In multivariable regression model, IsR significantly increased the risk of rejection (ARR: 2.43; CI95%:1.72-3.45). However, this complication was frequently mild and borderline according to Banff criteria (74%). Allograft function improved in 47% of patients with borderline rejection without treatment. 2-year risk of allograft failure (5.6% vs 4.9%, p=0.867) and death (0 vs 0.5%, p=0.657) did not considerably increase after IsR. IsR following the diagnosis of sustained BK viremia significantly increases the risk of allograft rejection however rejection is frequently borderline and may not require treatment. IsR does not seem to be associated with allograft loss or mortality.

Safety Of Combination Biologic And Immunosuppressive Therapy Post-Orthotopic Livertransplantation In Patients With Inflammatory Bowel Disease: A Systematic Reivew

Saleh Al Draiweesh1,3, Christopher Ma2, Maan Alkhattabi1, Tran Nguyen2, Cassandra McDonald1,Mayur Brahmania1, Vipul Jairath11Gastroenterology, Western University, London, ON, Canada, 2Robart Clinical Trials Inc, London, ON, Canada,3 Department of Medicine, Division of Gastroenterology, King Fahad Specialist Hospital, Dammam, Saudi Arabia.

BackgroundInflammatory Bowel Disease (IBD) patients post orthotopic liver transplantation (OLT) often have ongoing mucosal inflammation necessitating biologic therapy. The safety of combined biologic and immunosuppressive therapy post-OLT in this population is unclearAim:To systematically review the evidence for safety of combination biologic and immunosuppressive therapy in patients with IBD after OLTMethods:EMBASE, Medline, Cochrane CENTRAL, clinialtrials.gov, and the International Clinical Trials Registry Platform were searched without language restriction using keywords identifying OLT and IBD up to March 1, 2018 All studies evaluating the safety of combined biologic and anti-rejection therapy were included in addition to our recent case series. All eligible studies were reviewed for safety outcomes. ResultsA total of 2713 citations were identified: 2314 articles were screened after removal of duplicates (n=399) and we identified 20 articles (12 case series and 8 case reports) that were eligible. From these studies, in addition to our case series (n=19), a total of 122 IBD patients were treated with combination biologic and immunosuppressive therapy. PSC was the primary indication for OLT. UC was the most common IBD type. The most commonly used biologic therapy was TNF antagonists. The most commonly used anti-rejection therapy was tacrolimus. 32 patients experienced an infectious complication, most commonly gastrointestinal infections. Malignancy was reported in 6 patients. There were two deaths reported.ConclusionsPost-OLT IBD patients receiving anti-TNF therapy are at an increased risk of enteric and postoperative infectious complications. Enteric infections should be actively screened for in patients experiencing worsening IBD symptoms.

Safety of Combination Biologic and Anti-Rejection Therapy Post-Liver Transplantation in Patients with Inflammatory Bowel Disease: London Ontario Experience

Saleh Al Draiweesh1,3, Christopher Ma1, Maan Alkhattabi1, Cassandra McDonald1, Tran Nguyen2 , Nilesh Chande1, Brian G. Feagan1, Jamie C. Gregor1, Reena Khanna1, Paul Marotta1, Amindeep S. Sandhu1, Karim Qumosani1, Anouar Teriaky1, Mayur Brahmania1, Vipul Jairath11Gastroenterology, Western University, London, ON, Canada, 2Robart Clinical Trials Inc, London, ON, Canada,3 Department of Medicine, Division of Gastroenterology, King Fahad Specialist Hospital, Dammam, Saudi Arabia.

Background:Despite anti-rejection immunosuppressive therapies post-liver transplantation (LT), patients with concurrent inflammatory bowel disease (IBD) may have persistent bowel inflammation that requires addition of biologic therapyAim:To evaluate the safety of combination biologic and anti-rejection therapy in IBD patients after LTMethods:The LT Registry at London Health Sciences Centre

(LHSC) was searched to identify all patients undergoing LT from 1985-2018. IBD patients initiated on biologic treatment post-LT, in addition to anti-rejection therapy, were included. Medical chart was reviewed to extract safety outcomesResult:19 patients were included (UC=8, PSC=14), followed for a median duration of 19 months. Post-LT, six patients were treated with only TNF antagonists, eight patients with only anti-integrin therapies and five patients with sequential biologic therapyThe most commonly used anti-rejection therapies were tacrolimus and mycophenolate mofetil. Six patients required long-term prednisone. Infections developed in nine patients, most commonly Clostridium difficile colitis. Other infections included cytomegalovirus colitis and viremia, cholangitis, perianal abscess, JC virus seroconversion but without progressive multifocal leukoencephalopathy and hospital-acquired pneumonia. Two patients required colectomy for refractory colitis. One patient required re-transplantation due to PSC recurrence. No deaths or malignancies were reported although one patient developed low grade colonic dysplasiaConclusion:While there appeared to be an increased risk of enteric infections, especially C. Difficile, in IBD patients after LT who received combination biologic and anti-rejection therapy, there were no life-threatening infections reported. Active screening for enteric infections should be pursued in these patients presenting with increased IBD symptoms

Teduglutide In Patients With Active Crohn's Disease And Short Bowel Syndrome

Saleh Al Draiweesh, Christopher Ma1,3,4, Cassandra McDonald1, James C Gregor1, Adam Rahman1, and Vipul Jairath1,41Department of Medicine, Division of Gastroenterology, Western University, London, Ontario, Canada2Department of Medicine, Division of Gastroenterology, King Fahad Specialist Hospital, Dammam, Saudi Arabia3Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Alberta, Canada4Department of Epidemiology and Biostatistics, Western University, London, Ontario, Canada.

Background:Teduglutide is a GLP2 analogue that has been approved for the treatment of short bowel syndrome (SBS). There is a limited evidence for its use in Crohn's disease (CD) patients. There is a theoretical risk of exacerbating mucosal inflammation with teduglutide due to intestinotrophic effects of GLP2.Case Report:We present two cases of CD patients with active inflammation and SBS treated with biologic therapy and teduglutide. The first case is a 38-year-old male with ileocolic stricturing CD, who previously failed immunomodulators, infliximab and adalimumab. He underwent multiple small bowel and ileocolic resections resulting in SBS and was initiated on home PN in 2011. Teduglutide was commenced in January 2017 and he was able to wean completely off PN. Ileocolic anastomotic inflammation was treated with ustekinumab, and both treatments have been maintained for 14 months without any adverse events. The second case is a 39-year-old male with stricturing small bowel CD, who previously failed immunomodulators, infliximab, and adalimumab, and was steroid-dependent. After multiple small bowel resections, he had SBS. Daily PN was initiated in 2003. He was initiated on vedolizumab and 6-mercaptopurine in 2016 due to pancolonic ulcerations. Teduglutide was added in August 2017 with significant clinical improvement, and reduction in PN requirements. Conclusion:These cases suggest that teduglutide may be safe, effective and can be used with concomitant biologic agents and immunosuppressants in patients with active CD and SBS. However, longer term follow-up and more reports are needed to evaluate the safety of teduglutide in this setting.

A Rare Case of Obscure GI Bleeding Secondary to Ectopic Small Intestinal Varices Post Roux-en-Y Gastric Bypass

Almaghrabi, M, Qumosani, K, Mujoomdar, A, Parfitt, J, Leslie,K, Sey, M.

Background: Ectopic varices are considered a rare cause of gastrointestinal bleeding (GIB) as they only account for 5% of all variceal bleedingCase: 39 year old female was referred for a five year history of obscure GIB requiring

over 300 units of blood in total. Her only medical history was Roux-en-Y gastric bypass for weight loss in 2009. Starting in 2012, she presented with recurrent episodes of melena and underwent extensive investigations. She was found to have esophageal varices that were banded. Work up for liver diseases including liver biopsy was unremarkable. Her bleeding persisted, culminating with a TIPS procedure that thrombosed within 24 hours. Unfortunately, her bleeding did not stop so we repeated antegrade double balloon enteroscopy. At the biliopancreatic limb proximal to the jejunojejunostomy, multiple ectopic varices were seen. Prior imaging was reviewed and chronic SMV thrombosis was identified and deemed to be present since at least 2012. She underwent embolization of the ectopic varices by intervention radiology and her hemoglobin stabilized and she did not require blood transfusions for the first time in 5 years. Unfortunately, her melena recurred after 2 months. Overall, it was felt that resection of the jejunojejunostomy was the best management option for her and that was pursued. Post operatively, her melena resolved and her hemoglobin normalized. One year after surgery, her melena has recurred. Conclusion: Ectopic varices should be considered in the differential diagnosis of obscure GIB and it might be challenging to treat depending on its location.

An Unusual Case Of Blow-Out Perforation Of A Defunctioned Stomach Post Roux-En-Y Gastric Bypass Due To Crohn's Disease

Dr.Alotaib, Ammari, Dr. McIntosh,Keith, Dr.Sandhu,Amindeep, Dr.Jairath,Vipul, Dr.Sey,Michael.

Background: Inflammatory bowel disease has been reported after bariatric surgery. Three previous cases were reported with stricturing at the gastrojejunostomy but there has been no prior case with stricturing causing gastric obstruction and blow-out perforation of the defunctioned stomachAims: To present a rare case of Crohn's disease presenting as recurrent stricturing post Roux-en-Y gastric bypass resulting in a blow-out perforationCase: A 55 year-old female who underwent gastric bypass surgery 20 years ago presented with recurrent stricturing of the gastrojejunostomy and ulceration of the Roux limb felt to be secondary to local ischemia, eventually requiring surgical reconstruction. Shortly after, she presented with acute abdominal pain and was diagnosed with a blow-out perforation of the defunctioned stomach, requiring surgical repair and insertion of a venting G tube. Antegrade double balloon enteroscopy revealed recurrent ulceration and stricturing of the gastrojejunostomy, a normal Roux limb, and stricturing at the duodenal side of the pylorus. Endoscopy through the gastrostomy showed normal stomach. Biopsies revealed a chronic inflammatory infiltrate in the laminal propria, pseudo-pyloric metaplasia, branched crypts, and mild villous blunting. CT showed patent Celiac and superior mesenteric arteries. Crohn's disease was suspected and the patient was treated with a course of prednisone. Repeat EGD showed complete resolution of ulceration at the gastrojejunostomy. Prednisone was restarted and she was started on ustekinumabConclusion: Recurrent stricturing and ulceration after Roux-en- Y gastric-bypass should raise the suspicion for Crohn's disease. Early recognition and treatment of inflammation will minimize the morbidity of the disease

Efficacy of Trimethoprim-sulfamethoxazole in Prevention of Urinary Tract Infection in Renal Allograft Recipients

Enad Alsolami, Anthony M Jevnikar, Patrick Luke, Andrew A House, A. Sener, Seyed M Hosseini-Moghaddam.

Introduction: Urinary tract infection (UTI) commonly occurs after renal transplantation. Post-transplant prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) has been shown to reduce the risk of UTI. The prophylactic effect of TMP-SMX against UTI is not clear while growing number of patients receive this antibiotic to prevent pneumocystis pneumonia (PCP). Method: In this retrospective cohort, all renal transplant patients who received allografts at a single institution from Jan 2011 to December 2013 were included. We determined all episodes

of UTI in the first year after transplantation.Results: 33/182 recipients (18.13%) developed 57 episodes of UTI (cumulative incidence: 31.3%). Of these, 24.6% were associated with bacteremia (n=14) and 61.4% (n=35) required hospital admission. E. Coli (33.3%) and Klebsiella pneumoniae complex (26.3%) were the most frequent isolates. UTI did not significantly increase the risk of graft loss (6.1% vs 1.3%, p=0.15) or death (6.1% vs0.7%, p=0.085). Median interval between the first episode of UTI and transplantation was 92 days. 16 out of 61 females (26.2%) vs 17 out of 121 males (14%) developed UTI (p=0.037). 168/182 recipients (92.3%) were on TMP-SMX. 35/57 UTI episodes (61.4%) were with microorganisms resistant to TMP-SMX and half of these (18 episodes, 31.6%) were MDR pathogens. 40 episodes occurred while patients were on TMP-SMX (70.17%). Conclusion: Current guidelines recommend UTI prophylaxis with TMP-SMX at least 6 months after renal transplantation. However, recipients frequently develop UTI with TMP-SMX resistant uropathogens. TMP-SMX (160 /800mg) 3 times/week is not a reliable regimen to prevent UTI even when the causative microorganism is susceptible.

The Outcome of Expanded Criteria Donor Kidney Transplant

Enad Alsolami, Khaled Lotfy, Andrew House.

Introduction: Expanded criteria donor (ECD) kidneys are known to have poor outcomes when compared to standard criteria donor (SCD) kidneys. However, They are widely used to increase the pool of organs offered. Methods: In this quality improvement study, We included all ECD renal transplant recipients in our institution between January 2008 and December 2017. We compared a 3-year patient and graft survival between donation after circulatory death (DCD) and neurological determination of death (NDD).Results: 169 ECD renal transplant recipients, 49 (29%) were DCD and 120 (71%) were NDD. Mean age was 62 years for DCD recipients and 62.5 years for NDD recipients. Mean cold ischemia time was 705 minutes for DCD and 790 minutes for NDD. Mean donor age was 60 years for DCD and 62.5 years for NDD. 5 (10.2%) DCD recipients and 26 (21.7%) NDD recipients received a dual kidney transplant. 30 (61.2%) DCD recipients & 54 (32%) NDD recipients had delayed graft function. The rest of the results will follow. Conclusion: It seems that DCD/ECD kidneys have inferior outcome when compared to NDD/ECD kidneys. Time on dialysis, waiting time and panel reactive antibody should be taken into account when offering these organs to patients.

The incidence of outpatient bowel preparation related complications and “no show” for colonoscopy: a single tertiary care centre review

Alzahrani, May, Gregor, Jamie.

Background: Colonoscopy remains the preferred screening and diagnostic test in gasteroenterology and excellent bowel preparation is needed to get the best result. Recently, many cases were released reporting the development of sever symptomatic hyponatremia with seizure and encephalopathy as a complications of bowel preparation formulas. Other studies showed development of dysnatremia with unknown significance. Aims: To detect the incidence of missing elective colonoscopy secondary to seven complications like significant hyponatremia resulting from bowel preparation prior to colonoscopy leading to admissionsMethods: We are reviewing all endoscopy outpatient lists and the electronic medical records of all patient who were booked for elective colonoscopy but did not show up to have it in a single large tertiary care hospital over a period of one year (2017) to correlate that with development of sever hyponatremia that required hospital admission to manage it.Results: Out of 2430 procedure booked, 111 patients did not show for their procedures. Only 2 patients missed it because of hospital admissions and both of them were not related to the bowel preparation. Another 2 patients did not show up as they did not tolerate the preparation.Conclusions: The risk of developing severe complications secondary to any form of bowel preparation is still very low. We think they are safe with consideration of co-morbidities and risk factors that may contribute to

the electrolytes shift and their life threatening complications.

Inhibitory Effects of Soluble Clr Proteins in NK Cell Mediated Tubular Epithelial Cell Death

Shilpa Balaji, Benjamin Fuhrmann, Dameng Lian, Hong Diao, Shengwu Ma, Zhuxu Zhang, Anthony M. Jevnikar.

Purpose: We have previously shown that NK cells can mediate kidney tubular epithelial cell (TEC) death, kidney ischemia reperfusion injury (IRI), and chronic transplant rejection. MHC-independent mechanisms, such as binding of NKRP1 receptors to C-type lectin receptor (Clr) family proteins, may regulate NK cell function. TEC may negatively regulate NK cell activation and cytotoxicity by kidney-specific expression of a novel class of Clrs which may be exploited to prevent kidney IRI and chronic transplant injury. Methods: IRI was induced by renal artery clamping (30-45m) in uni-nephrectomized B6 mice, and changes in Clr-b/-f mRNA expression were determined. Wildtype (WT) and Clr-b-/- TEC were treated in vitro with Clr-f siRNA; silencing was confirmed by RT-PCR and flow cytometry. Cell death was measured in NK-TEC co-cultures by Chromium-51 release assay. Results: Clr-b and f expression increased in B6 kidneys following IRI. Elimination of either Clr-b or Clr-f in TEC did not increase NK-mediated killing. Simultaneous silencing of both Clr-b and Clr-f expression resulted in increased NK killing of TEC compared to silenced Clr-b or Clr-f alone in TEC ($n=3$, $p<0.01$), or WT control TEC ($p<0.001$). Treatment with soluble recombinant Clr-b/Clr-f proteins significantly decreased NK-mediated TEC death ($n=3$, $p<0.05$). Conclusion: Our data support that NKRP1-Clr binding is an important inhibitory pathway in NK-mediated kidney injury. As no current drugs target NK cells effectively, Clr-b/Clr-f soluble proteins may represent a novel strategy to protect organs from diverse forms of NK-mediated inflammation, cytotoxicity, and injury.

Sharing of Injection Drug Preparation Equipment is Associated with HIV Infection: A Cross Sectional Study

Laura Ball, Klajdi Puka, Mark Speechley, Ryan Wong, Brian Hallam, Joshua Wiener, Sharon Koivu, Michael S. Silverman.

Background. Sharing needles/syringes is an important means of HIV transmission amongst persons who inject drugs (PWIDs). London, Canada is experiencing an outbreak of HIV amongst PWIDs, despite a large needle/syringe distribution program and low rates of needle/syringe sharing.Objective. To determine whether sharing of injection drug preparation equipment (IDPE) is associated with HIV infection. Methods. Between August 2016 and June 2017, individuals with a history of injection drug use and residence in London were recruited to complete a comprehensive questionnaire and HIV testing. We conducted a cross sectional study to examine the risk factors associated with the HIV outbreak. Results. A total of 127 participants were recruited; 8 were excluded due to failure to complete HIV testing. The remaining 35 HIV infected (cases) and 84 HIV uninfected (controls) participants were assessed. Regression analysis found that sharing IDPE, without sharing needles/syringes, was strongly associated with HIV infection (Adjusted Odds Ratio: 22.1, 95% Confidence Interval: 4.51-108.6, $p<0.001$).Conclusions. Sharing of IDPE is a risk factor for HIV infection among PWIDs, even in the absence of needle/syringe sharing. Harm reduction interventions to reduce HIV transmission associated with this practice are urgently needed.

How appropriate is Non-Invasive Ventilation use on medicine floors at London Health Science Centre?

Saira Zafar, **Lara Banissmaeel.**

Background: Acute respiratory Failure has been a major cause for morbidity and mortality in the acute care setting. Many studies had showed significant positive outcomes with using Non

invasive Ventilation (NIV) machines in decreasing both mortality and morbidity of acute respiratory distress in specific circumstances. Aim of study: The purpose of this study is to assess if NIV use at LHSC follows the published guideline of NIV use by American thoracic society/ European Respirology Society in 2017 that had specifically outlined the circumstances when to use it in acute settings. In the future this project should help implement changes in this area to improve patient care . The main two indications outlined in the guidelines that are studies in this project are: 1) Hypercapnic respiratory acidosis secondary to COPD exacerbation. 2)Pulmonary edema secondary to congestive heart failure.Methods: We reviewed 100 charts between 2017-2018 retrospectively for patients admitted to medicine at LHSC and required bipap during their stay. We gathered information from blood work, images and clinical notes before BiPAP initiation to assess its appropriate use . Conclusion: To be followed

Hyoscine Butylbromide (Buscopan) for Abdominal Pain in Children: a Randomized Controlled Trial

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Abdominal pain is one of the most frequent reasons for an emergency department (ED) visit. Most cases are functional and no therapy has proven effective. We sought to determine if hyoscine butylbromide (HBB) (BuscopanTM) is effective for children who present to the ED with functional abdominal pain.We conducted a randomized, blinded, superiority trial comparing HBB 10mg plus placebo to oral acetaminophen (APAP) 15mg/kg (max 975mg) plus placebo. Children 8-17 years presenting to the ED at LHSC with colicky abdominal pain who rated > 40mm on a 100mm visual analog scale (VAS) were included. The primary outcome was VAS pain score at 80-minutes post-administration. Secondary outcomes included adverse effects; caregiver satisfaction; recidivism and missed surgical diagnoses.236 participants were randomized (116 APAP; 120 HBB). Mean age was 12.4 years and 64.8% were female. The mean (SD) pre-intervention pain scores in the APAP and HBB groups were 62.3mm (16.5) and 60.3mm (17.9). At 80 minutes, mean (SD) pain scores in the APAP and HBB groups were 30.1mm (28.8) and 29.4mm (26.4) and there were no significant differences adjusting for pre-intervention scores (p=0.96). In APAP and HBB groups, 4/6 and 6/8 returned with abdominal pain. There were no missed surgical diagnoses. The most common adverse effect was nausea (9% per group) and there were no significant differences in adverse effects (p=0.57). For children with functional abdominal pain presenting to the ED, both APAP and HBB produce a clinically important (VAS < 30mm) reduction in pain and should be routinely considered in this clinical setting.

Durability of Tumor necrosis factor inhibitors compared to Janus kinase inhibitors in the treatment of Rheumatoid arthritis.

Malcolm Blagrove, Janet Pope.

The development of biologic agents over the past two decades has dramatically improved the management of rheumatoid arthritis (RA). Tumor necrosis factor inhibitor (TNFi) therapies were the first biotherapies to be developed for rheumatologic diseases and are among the most commonly prescribed class of biologic drugs for the treatment of RA patients who failed traditional synthetic disease?modifying antirheumatic drugs (sDMARDs). However, this class of medications comes with limitations, namely, primary or secondary lack of efficacy. More recently, the addition of Janus kinase inhibitors (JAKi) as a treatment of RA has been promising. The most widely available medications, tofacitinib and baricitinib, show fast onset of response and acceptable safety in RA patients. Some studies suggest that JAKi have better effectiveness compared to TNFi in patients with RA. The aim of the review is to examine the long?term effectiveness in a population?based cohort of RA patients who received a TNFi or a JAKi

comparing the discontinuation rates between these two groups. This retrospective cohort study will review medical records of patients from St Joseph Health Centre (SJHC) diagnosed with RA who have been treated with either TNFi or JAKi. Results to follow.

Writing as thinking: Trainee documentation practices and their implications for learning in clinical settings

Dillon Bowker, MD candidate 2021, Dr. Mark Goldszmidt (MD, PhD, FRCPC)Dr. Jacqueline Torti (PhD, MA, BPHED).

Clinical documentation has been described by some educators and trainees as a low-value activity. Moreover, research often examines its value in communication and information storage but neglects its function in shaping learning and reasoning. The purpose of this study was to explore these latter functions. A better understanding of how documentation supports learning can guide curriculum and future electronic documentation development.This was a constructivist grounded theory study with iterative data collection and analysis. Data included field notes and field interviews from over 50 hours of observing senior medical students and first-year residents during admission and follow-up on an internal medicine ward at an academic centre. Analysis was supported by sensitizing concepts from Pare and Smart's framework for studying workplace-based communications.From a learning and reasoning perspective, clinical documentation has two critical periods, with different tasks: (1) Before patient encounters- tasks relate to past medical history, medications and available investigation results in which documentation practices are used to organize what is known, flag gaps in knowledge and develop a preliminary understanding of the patient's problem(s); (2) After patient encounters - tasks relate to results of investigations and development of assessment and plan in which documentation practice are used for sensemaking, identifying omissions and knowledge gaps.Clinical documentation is a time consuming but essential task during which trainees make sense of their patients' issues and how to manage them. While documenting, trainees must be able to easily move between existing sources of patient information within the electronic health record.

Treatment of Infectious Endocarditis in PWID: Is IV Therapy Necessary. A Systematic Review

Dr. Michael Silverman, **Ira Brown**, Celine Lecce.

BackgroundInfectious Endocarditis (IE) in PWID is rapidly increasing in incidence in Canada (Weir et al CMAJ 2019). This condition is associated with a very high mortality (33%) (Rodger et al JAMA Net Open 2018). In non-PWID patients partial oral regimens have been found to give equal outcomes with full IV therapy (Iversen et al NEJM 2019). Partial oral regimens may help to mitigate the high rates of IV-line abuse and secondary bacteremia associated with PICC line use in PWIDs (Tam et al. Manuscript in preparation). However, PWID patients also have an increased risk of non-adherence to oral therapy and thus may have better or worse outcomes with a partial oral regimen.Objective To review the literature of treatment of IE in PWID and determine the need for a Randomized Clinical Trial.MethodA computerized systematic literature search using the search terms Endocarditis AND Injection AND Treatment was carried out in PubMed. Included studies were published studies in English that assessed short- and long-term mortality for adult PWID IE patients using oral or IV therapy.Results458 results were obtained using the indicated search criteria. Title and abstract screening were completed by two reviewers and 118 results remained for full-text screening. Data extraction and study quality will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE). ConclusionsAt present no high quality prospective or RCT data exist to guide management of this increasingly prevalent condition. A proper prospective and ideally randomized trial would be necessary to inform practice.

Factors Associated With a Diagnosis of Failure to Cope in Older Medical Inpatients: a case-control study

Alishya Burrell, Saad Chahine, Laura Diachun.

Background The diagnosis of “failure to cope” (FTC) is commonly used when older adults present to hospital. This term provides no clinical diagnosis, and implies the patient is at fault. The purpose of this study was to identify factors associated with a diagnosis of FTC.MethodsAn age matched case-control study of patients 70 years of age or older admitted to medicine at LHSC. Univariate and multivariable logistic regression were used to identify factors associated with a diagnosis of FTC.ResultsThe charts of 185 patients were reviewed, 99 patients with FTC, and 86 controls. Patient characteristics associated with a diagnosis of FTC included a history of falls (aOR 4.33, 95% CI 2.11-8.90), readmission 30 days after discharge (aOR 3.70, 95% CI 1.73-7.89), living alone (aOR 3.58, 95% CI 1.7-7.52), living in an independent dwelling (aOR 2.61, 95% CI 1.11-6.11) and using a walker (aOR 2.20, 95% CI 1.04-4.62). A higher number of comorbidities was associated with a lower likelihood of being diagnosed with FTC (aOR 0.84, 95% CI 0.71-0.98).DiscussionA number of factors were found to be associated with a diagnosis of FTC including mobility, falls and living conditions. Patients who were “bounce backs” or had fewer comorbidities were more likely to be diagnosed with FTC, suggesting a judgemental use of the term.ConclusionThis study has identified patient factors associated with a diagnosis of FTC. Further study is required to understand the consequences of this diagnosis on patient care and outcomes.

A Case of Undiagnosed Secondary Hypertension in Pregnancy

Dayna Butler MD FRCPC, Dongmei Sun MD MSc FRCPC.

Background: Fibromuscular dysplasia (FMD) is a noninflammatory, nonatherosclerotic vascular disease which may manifest as arterial stenosis, occlusion, aneurysm or dissection. FMD most commonly affects the renal arteries, resulting in renal artery stenosis which may manifest as hypertension.1,4 Case description: A 40 year old G7T3P2A2L5 was seen postpartum regarding hypertension and peripartum ischemic stroke. She was diagnosed with chronic hypertension at age of 19 without a family history. All her deliveries were complicated by preeclampsia. During her sixth pregnancy she had a left MCA ischemic stroke at 4 weeks gestation and during her seventh pregnancy she had a right occipital ischemic stroke 3 weeks postpartum. Between pregnancies she was lost to follow up.At 8 weeks postpartum, her blood pressure was 148/89mmHg, despite being treated with nifedipine 30mg BID and labetalol 300mg TID. BMI was 41 kg/m2. She had residual blurring of the left visual field in keeping with prior infarction.Evaluation for secondary hypertension included a CT abdomen which revealed beading of bilateral renal arteries in keeping with fibromuscular dysplasia. Her blood pressure improved with stenting of right renal artery. Discussion: Hypertension in pregnancy is a leading cause of maternal and fetal morbidity.2 The current case demonstrates numerous complications of secondary hypertension in pregnancy. Pregnancy is an important opportunity to address chronic medical issues. As per the Hypertension Canada guidelines, patients presenting at <30 years of age with hypertension should be investigated for fibromuscular dysplasia- related renal artery stenosis.3

Correlation of Initial Echocardiographic Parameters and Emergency Room Admission Rates in Heart Failure Clinic Patients

X. Cai, S. Jia, S. J. Smith, S. De, R. McKelvie, R. A. Davey.

Purpose: Heart failure (HF) has increased demand on the healthcare system. Echocardiography is a non-invasive test with many clinical prognostic implications. We aim to identify echocardiographic parameters that would act as predictors for relative health care resource utilization in HF patients, by correlating with their annual emergency room visits (AERV).Methods:

A total of 263 patients' charts at SJHC HF clinic were reviewed including their initial baseline echocardiogram results. Specific predictors included ejection fraction (EF), left atrial volume index (LAVI), and tricuspid regurgitation peak gradient (TRPG). Each patient's number of AERV was recorded. Each predictor was divided into subgroups based on clinical guideline cutoff ranges. Patients were divided by EF into HFpEF (EF>50%) and HFrEF (EF<40%). Pulmonary hypertension was defined as TRPG>31.6 mmHg. Left atrial enlargement was defined by LAVI>34 mL/m2. We then compared the average AERV between each subgroup.Results: There were no significant differences in AERV when using LAVI (p=0.317) or TRPG (p=0.392) alone as a predictor. There was a significant difference in AERV when using EF alone as a predictor, where patients with EF>50% had significantly more AERV compared to patients with EF<40% (p<0.05). However, a major confounder for this difference was age, where HF patients with EF>50% were generally older (p<0.05).Conclusion: Neither LAVI nor TRPG were found to be a predictor of health care utilization through AERV. Patients with HFpEF had significantly more AERV compared to patients with HFrEF while the major counfounder was age.

Preliminary Outcomes of an Atrial Fibrillation Patient Navigator Demonstration Project

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Background: Atrial fibrillation (AF) is growing in prevalence and is associated with substantial health care utilization. Cardiac Rehabilitation (CR) interventions such as exercise and weight loss are proven to decrease AF symptoms and recurrence. Methods: A 2015 review of patients presenting to the emergency department (ED) with a primary diagnosis of AF showed prolonged follow up times and limited uptake of appropriate anticoagulation (OAC) likely secondary to concerns from ER physicians regarding lack of follow up. In March 2018, an atrial fibrillation demonstration project was initiated to improve process of care (through expedited telephone counseling, review of care by the navigator and cardiologist, best practice recommendations sent to family physicians and referral to specialty care and CR as needed). Here, the demonstration project results are compared to the 2015 review of 60 consecutive patients. Results: To date, 129 patients have been referred. Wait times (in days) to 1st in person follow up have dropped from 28 Â± 39 in 2018 to 10 Â± 15 now (p = 0.0034). ED starts of OAC have occurred in 22% of eligible patients versus 0% in 2015 (3% were started on warfarin). 84% of navigation patients were properly anticoagulated after follow up. 48% have accepted a referral to CR.Conclusion: A dedicated AF navigator reduces wait time to first follow up for patients with AF, improves rates of anticoagulation and offers uptake into a secondary prevention program. Further analysis and comparison of ED representations, time to first follow up and anticoagulation rates is ongoing.

Myeloma relapsing as an Angio-immunoblastic T Cell Lymphoma.

Rania Chehade, Joy Mangel, Martha Louzada, Jessica Sheppard, Uday Deotare.

Angioimmunoblastic T cell lymphoma (AITL) is a clinically aggressive type of Peripheral T cell Lymphoma derived from T follicular helper cells. A rare malignancy with poor overall survival, AITL is often accompanied by polyclonal or monoclonal proliferation of B lymphocytes, however, AITL is rarely associated with plasma cell proliferation. Here we describe a new diagnosis of AITL developing in a patient previously treated for multiple myloma. This highlights the role of circulating plasma cells, as well as, the interaction between T follicular helper cells and plasma cells in AITL tumorigenesis. To the best of our knowledge, this is the first report of newly diagnosed AITL in a patient with a previous history of multiple myeloma.

Demographics of women with Gestational Diabetes attending a Diabetes and Pregnancy Clinic: 2000-2002, 2010-2012 and 2014-2016

Lindsey Chow, Parul Khanna, Kingsley Anukam, Evan Brydges, Selina L. Liu, Jeffrey Mahon, Tisha R. Joy, Ruth M. McManus.

BACKGROUNDNumbers of women attending Diabetes and Pregnancy Clinics (DPC) are increasing. Potential reasons include: obesity; fertility intervention access; diagnostic changes for gestational diabetes (GDM). The DPC in London, Ontario sees all pregnant women with diabetes within the catchment area with stable clinic structure and procedures. Longitudinal characteristics of GDM women were documented for demographic insights. METHODSDPC pregnancy charts were assessed from 2000-2002, 2010-2012 and 2014-2016. Data were abstracted for: age; weight, infertility interventions; GDM diagnostic method. Continuous results were analyzed by one-way analysis of variance (ANOVA), non-parametric results by Chi-square testing; p? 0.05 signifying significance.RESULTSOver the study timeline, the number of women with GDM and proportion of deliveries with GDM increased significantly by 240%. Weight at first visit and the number of GDM diagnoses made with only the fasting 75 g OGTT increased significantly. Age at first clinic visit, week of GDM diagnosis, weight change at last visit and pregnancy via fertility intervention were all not significantly different over the study interval.CONCLUSIONSOver the study interval, women with a GDM diagnosis increased 240%. The change may be related to obesity and changes to GDM diagnostic criteria; but not late pregnancy weight gain, or use of fertility interventions.

Demographics of Women with Type 1 Diabetes Attending a Diabetes and Pregnancy Clinic 2000-2002, 2010-2012 and 2014-2016

Lindsey Chow, Parul Khanna, Kingsley Anukam, Evan Brydges, Selina L. Liu, Jeffrey Mahon, Tisha R. Joy, Ruth M. McManus.

BACKGROUNDThe numbers of women attending Diabetes and Pregnancy Clinics (DPC) are increasing. Some of the increase may reflect obesity effects on GDM prevalence, but changes in numbers and characteristics of women with Type 1 diabetes (T1DM) are unknown. The DPC in London, Ontario sees all pregnant women with diabetes within the catchment area with stable clinic structures and procedures. Longitudinal characteristics of women with T1DM were documented for demographic insights. METHODSDPC pregnancy charts were assessed from 2000-2002, 2010-2012 and 2014-2016. Data were abstracted for: age; weight, A1C and medication use. Continuous results were analyzed by one-way analysis of variance (ANOVA); non-parametric results by Chi-square testing; p? 0.05 signifying significance.RESULTSOver the study interval, pump use at first visit, pump use at last visit, A1c at first visit and A1c at last visit all increased significantly, although A1c values fell 0.5% from first to last visit in all time periods. Age at first visit was significantly different. Number of pregnant women with T1DM and proportion of deliveries with T1DM increased non-significantly. Weight at first visit, weight gain by last visit and gestational week at first visit were non-significantly different.CONCLUSIONSClinic numbers of pregnant women with T1DM increased non-significantly over the study timeline while pump usage rose concurrent with access to government funding. A1C values fell 0.5% from first to last visit in all time periods. A1C values at first visit rose over the time periods suggesting women with less optimal glucose control were conceiving pregnancies.

Demographics of Women with Type 2 diabetes attending a Diabetes and Pregnancy clinic 2000-2002, 2010-2012 and 2014-2016

Lindsey Chow, Kingsley Anukam, Parul Khanna, Evan Brydges, Selina L. Liu, Jeffrey Mahon, Tisha R. Joy, Ruth M. McManus.

BACKGROUNDThe numbers of women attending Diabetes and Pregnancy Clinics (DPC) are increasing. Some of the increase may reflect obesity effects on GDM prevalence, but numbers and characteristics of women with Type 2 (T2DM) diabetes are unknown. The DPC in London, Ontario sees all pregnant women with diabetes within the catchment area with stable clinic structures and procedures. Longitudinal characteristics of women with T2DM were documented for demographic insights. METHODSDPC pregnancy charts were assessed from 2000-2002, 2010-2012 and 2014-2016. Data were abstracted for: age; weight, A1C and medication use. Continuous results were analyzed by one-way analysis of variance (ANOVA); non-parametric results by Chi-square testing; p? 0.05 signifying significance. RESULTSOver the study interval, the proportion of deliveries with T2DM, number of women taking oral agents at last visit and A1c at last visit increased significantly, although A1c values decreased from first to last visit in all time periods. The number of pregnant women with T2DM increased significantly by 40%. Weight at first visit decreased significantly. Age at first visit, gestational week at first visit, number of women taking oral agents at first visit, A1c at first visit and weight change at last visit were all not significantly different.CONCLUSIONSNumbers of pregnant women with T2DM increased significantly by 40% with time. Mean weights were lower in the second and third time interval. A1c values were lower by final visit in all time periods. Oral agent use increased in the final time period coincident with increased clinical comfort using metformin.

Pharmacokinetics of Felodipine Disposition in Celiac Disease

ML Chretien, Dr GK Dresser, Dr DG Bailey.

Introduction - Celiac disease is a hypersensitivity reaction to gluten foods in genetically susceptible individuals. It is characterized by damage to the small intestinal mucosa ranging from inflammation to villous atrophy. CYP3A4 is constitutively expressed in human small intestinal villi and accounts for first-pass prehepatic metabolism of drugs. Celiac patients with severe disease have low duodenal CYP3A4 expression.Hypothesis - Oral absorption (bioavailability) of the drug probe felodipine will be increased dependent upon celiac disease severity.Materials and methods - Celiac patients were histologically stratified into three categories: Group A (n=15, normal), B+C (n=16, intraepithelial cell invasion with/without mild villous blunting) and D (n=16, moderate/severe villous blunting). Single dose oral pharmacokinetics of felodipine 10 mg were assessed. Healthy volunteers (n = 68) undergoing similar testing in prior felodipine-grapefruit juice interaction crossover studies were negative and positive controls. Results - Groups A, B+C and D had linear trends of increasing felodipine AUC0-8 (mean +/- SEM, 14.4+/-2.1, 17.6+/-2.8, 25.7+/-5.0; p<0.05) and Cmax (3.5+/-0.5, 4.0+/-0.6, 6.4+/-1.1; p<0.02), respectively. Healthy subjects receiving water had lower felodipine AUC0-8 (11.9+/-0.9 vs 26.9+/-0.9, p=0.0001) and Cmax (2.9+0.2 vs 7.7+0.2, p=0.0001) versus those receiving grapefruit juice. Group A and D had similar felodipine pharmacokinetics for healthy subjects with water and grapefruit juice, respectively.Discussion and Conclusions - Patients with severe celiac disease had increased oral felodipine bioavailability like grapefruit juice from low small intestinal CYP3A4 protein expression. They could be at risk of serious overdose toxicities with numerous grapefruit-affected drugs.

Guidelines on Prescribing and Monitoring Antimalarials in Rheumatic Diseases: A Systematic Review

Gemma Cramarossa, Janet Pope.

Objective: The purpose of this review was to identify existing guidelines for antimalarial prescribing and monitoring and how they compare and have evolved over time.Methods: A search was conducted using Embase and

Medline to identify guidelines published from 1946-2018. The following MeSH terms were employed: â€˜hydroxychloroquine' AND â€˜retinal diseases' AND â€˜practice guideline or gold standard or consensus or consensus development or professional standard'. Results: 243 results were reviewed obtaining 11 recommendations. The American Academy of Ophthalmology, Royal College of Ophthalmologists and American College of Rheumatology have published guidelines. Canadian recommendations include a Canadian Rheumatology Association consensus conference and ophthalmology editorials. American and British recommendations changed from suggesting hydroxychloroquine doses ?6.5 mg/kg/day to recently, ?5 mg/kg/day. American guidelines recommend baseline visual field (VF) testing and annual screening after five years. Field testing evolved from the Amsler grid to current recommendations of 10-2 automated VF and spectral-domain optical coherence tomography (SD-OCT). The 2012 Canadian recommendations suggest initial VF testing every two years, with SD-OCT after 10 years. Older British guidelines suggested baseline and annual assessment of VF with an Amsler grid during rheumatology clinic visits. The 2018 British guidelines support baseline and annual screening after five years with 10-2 VF, SD-OCT and fundus autofluorescence. Conclusion: The newest recommendations are heterogeneous suggesting lower hydroxychloroquine dosing. Retinal toxicity is irreversible and the risk increases over time. Annual screening after five years with automated VF and SD-OCT may be warranted to detect early changes and discontinue therapy if necessary.

Fecal microbiota transplantation in patients with non-alcoholic fatty liver disease has the potential to improve small intestinal permeability

Laura Craven, Rahman A, Parvathy S, Beaton M, Silverman J, Gloor G, Qumosani K, Hramiak I, Hegele R, Joy T, Meddings J, Urqhart B, Harvie R, McKenzie C, Summers K, Reid G, Burton J, and Silverman M.

Background and Hypothesis: Non-alcoholic fatty liver disease (NAFLD) is an obesity related disorder that is rapidly increasing in incidence and is considered the hepatic manifestation of the metabolic syndrome. The gut microbiome plays a role in metabolism and maintaining gut barrier integrity. Studies have found differences in the microbiota between NAFLD and healthy patients as well as increased intestinal permeability in NAFLD patients. Fecal microbiota transplant (FMT) can be used to alter the gut microbiome. It was hypothesized that an FMT from a thin and healthy donor given to NAFLD patients would improve insulin resistance, hepatic proton density fat fraction (PDFF), and intestinal permeability.Methods: Twenty-one NAFLD patients were recruited and randomized 3:1 to either an allogenic (n=15) or an autologous (n=6) FMT delivered by endoscope to the jejunum (2 g of stool in 125 mL of saline). Insulin resistance was calculated by HOMA-IR, hepatic PDFF was measured by MRI and intestinal permeability was tested using the lactulose:mannitol urine test. Additional markers of metabolic syndrome and the gut microbiota were examined. Patient visits occurred at baseline, 2 weeks, 6 weeks, and 6 months post-FMT. Results: There were no significant changes in insulin resistance or hepatic PDFF in patients who received the allogenic or autologous FMT. Patients with elevated small intestinal permeability (>0.03 lactulose:mannitol) at baseline had a significant reduction 6 weeks' post-allogenic FMT. Conclusion: FMT did not improve insulin resistance or hepatic PDFF but did have the potential to improve small intestinal permeability in patients with NAFLD.

Cardiovascular Disease Risk Factors May Negatively Impact Rheumatoid Arthritis Disease Outcomes: Findings from the Ontario Best Practices Research Initiative

Kangping Cui, M.Movahedi, C.Bombardier and B.Kuriya.

Background:Rheumatoid arthritis (RA) increases the risk of cardiovascular disease (CVD). The impact of CVD risk factors (RFs) on RA disease

activity and disability is unknown. We investigated the association between CVD RFs and RA outcomes. Methods:Data were extracted from the Ontario Best Practices Research Initiative, a clinical registry of RA patients followed in routine care. Disease activity was assessed by the Disease Activity Score-28 (DAS28), Clinical Disease Activity Index (CDAI) and disability by Health Assessment Questionnaire Disability Index (HAQ-DI). Patients were divided into mutually exclusive groups by baseline CVD status as: (1) no CVD/no RFs; (2) CVD; (3) CVD RFs (hypertension, diabetes, dyslipidemia, and smoking). Adjusted linear regression analyses were performed to determine the independent effect of CVD status on disease outcomes at baseline and 12-month follow-up. Results:Of 2033 patients examined, 45.1% had CVD RFs at baseline. Having a CVD RF was associated with worse disease activity by DAS28 (? 0.13, 95%CI 0.002-0.26, p 0.04) and disability (? 0.16, 95%CI 0.10-0.23, p<0.0001). At one year, CVD RFs was associated with worse disease activity (DAS28; ? 0.17, 95%CI 0.05-0.30, p 0.01) (CDAI; ? 0.96, 95%CI 0.05-1.87, p 0.04) but not disability (? 0.03, 95%CI -0.002-0.08, p 0.17). Conclusions:Traditional CVD RFs are associated with worse RA outcomes both at baseline and one year. Self-perceived impact of comorbidity and treatment-resistance may be driving this relationship. Management of CVD RFs in RA patients may be beneficial for both CVD and RA prognosis.

Association Between Cognitive Impairment Subtypes and Dual-Task Gait Performance in a Clinical Setting.

Stephanie Cullen, Michael Borrie, Susan Carroll, Manuel Montero-Odasso.

BACKGROUND: Decline in gait performance has been shown to be directly correlated with increased cognitive impairment. Recently, poor dual-task gait (walking while performing a cognitively demanding task) has been linked to progression to dementia in older adults with mild cognitive impairment (MCI). However, gait performance across the cognitive spectrum has not previously been studied in a clinical setting. PURPOSE: To examine whether patients from a memory clinic show differences in usual and dual-task gait speed and dual-task cost (DTC) based on cognitive diagnosis. METHODS: Patients in the Aging Brain Memory clinic (London, ON) were timed over a six-meter path marked on the floor with a stopwatch. All patients were asked to perform a usual gait walk and three dual-task gait walks: counting backwards by ones, naming animals and counting backwards by seven (serial sevens) out loud. One-way ANOVA was performed to evaluate associations between gait speed and DTC (%) across groups. RESULTS: Two hundred four patients with subjective cognitive impairment (SCI; n=47), MCI (n=81), or dementia (n=76) were assessed. Performance in usual ($p<0.001$) and dual-task gait speed (counting gait $p<0.001$; naming animals $p<0.001$; serial sevens $p=0.012$) decreased across the cognitive spectrum. Dementia patients had significantly higher DTC in both counting ($p=0.004$) and naming animals ($p=0.009$) conditions compared with SCI and MCI patients, who had statistically similar DTC in all conditions.CONCLUSION: Dual-task gait performance significantly declined across the cognitive spectrum. These results support, in a clinical setting, the previously described relationship between gait performance and cognitive impairments.

The association of APOE E4 in neurodegenerative disorders and cognitive function.

Allison Dilliott, Emily C Evans, Sali MK Farhan, Donna Kwan, Brian Tan, Paula McLaughlin, Angela Troyer, Mahdi Ghani, Christine Sato, Ming Zhang, Adam D McIntyre, John F Robinson, Morris Freedman, Sandra E Black, Corinne E Fischer, Lorne Zinman, John Turnbull, Elizabeth Finger, Carmela Tartaglia, Mario Masellis, Anthony Lang, Connie Marras, Rick Swartz, Leanne Casaubon, Dennis E Bulman, Ekaterina Rogaeva, Robert A Hegele, and the ONDRI Investigators.

ApolipoproteinE (APOE) E4 is the most commonly accepted genetic risk factor for Alzheimer's disease (AD); however, its associations with other neurodegenerative diseases and features of neurodegeneration

have yet to be fully elucidated. The Ontario Neurodegenerative Disease Research Initiative (ONDRI) is a multi-platform observational cohort study characterizing five neurodegenerative diseases: 1) AD and mild cognitive impairment (AD/MCI); 2) amyotrophic lateral sclerosis; 3) frontotemporal dementia; 4) Parkinson's disease; and 5) vascular cognitive impairment. We aim to investigate the association between APOE E4 and the five diseases, as well as with domains of cognitive function within disease presentation.In total, 519 individuals enrolled in ONDRI and 196 neurologically normal controls, were sequenced with a next-generation sequencing panel, ONDRISeq. Genotypes for the two defining polymorphisms within APOE were obtained from these data and mapped to their respective APOE genotypes. The APOE E4 allele and E4/4 genotype were significantly associated with AD/MCI presentation when compared to controls (OR=2.76, P<1.0x10-4 and OR=4.13, P=2.5x10-3, respectively). The other four ONDRI diseases were not associated with the E4 allele. Further, the neuropsychology platform assessed participants across five cognitive functioning domains using 26 tests. Current analyses are investigating the associations between APOE E4 carrier status and the neuropsychology measures.To our knowledge, this is the first study to analyze APOE across the five neurodegenerative diseases using harmonized enrollment criteria and rich phenotypic assessment. Based on the results, APOE may become a useful predictive genetic biomarker correlated to disease presentation and could serve as a future therapeutic target.

Cell-free DNA release during programmed cell death in kidney ischemia reperfusion injury

Alexander Dionne, Patrick McLeod, Zhu-xu Zhang, Anthony Jevninkar.

Transplantation is invariably associated with acute allograft injury caused by ischemia reperfusion injury (IRI). This injury causes cells of the allograft to undergo various forms of programmed cell death including apoptosis and necroptosis. During programmed cell death, immunogenic molecules are released from cells, one of which is cell-free DNA (cfDNA). We hypothesize that cfDNA is released by microvascular endothelial cells (MVECs) during programmed cell death of IRI and that cfDNA acts as both a biomarker for cellular injury as well as a biologically active molecule capable of amplifying inflammation and organ injury. Our results indicate that cfDNA is released by MVECs under both apoptotic and necroptotic conditions in vitro, as well as during IRI in an in vivo mouse model. We have also shown that cfDNA release is ameliorated by blocking necroptosis in vivo with the use of RIPK3-/- mice that are incapable of undergoing necroptosis. Lastly, we have shown that cfDNA is capable of activating immune cells, showing that NK cell activation markers are upregulated when purified NK cells are subjected to cfDNA in vitro. Our results indicate that cfDNA is a potential biomarker of allograft injury in a renal transplant setting. Donor-derived cfDNA from blood or urine may give rise to novel non-invasive tests to diagnose graft damage. cfDNA also appears to exacerbate inflammation by activating immune cells to produce pro-inflammatory cytokines which further escalates inflammation. It may be prudent to inhibit the release of cfDNA in a transplant scenario, a goal our lab is currently working towards.

Characterizing the genetic profile of hypertriglyceridemia (HTG)

Jacqueline S. Dron, Jian Wang, Henian Cao, Adam D. McIntyre, Michael A. Iacocca, Jyler R. Menard, Irina Movsesyan, Mary J. Malloy, Clive R. Pullinger, John P. Kane, and Robert A. Hegele.

Introduction: Hypertriglyceridemia (HTG) is a common dyslipidemia defined by elevated circulating blood triglyceride (TG) levels. Genetic factors can influence TG levels, including rare variants disrupting genes involved in TG metabolism and common variants with known associations to TG levels. We aimed to characterize the genetic profiles of individuals with HTG. **Methods:** We concurrently assessed rare variants and the accumulation of common variants in 134 and 563 patients with mild (TG ≥1.8 mmol/L and <10 mmol/L) and severe (TG ≥10 mmol/L) HTG, respectively. We studied 503

healthy individuals as controls. After sequencing each study subject, we screened genes involved in TG metabolism for rare variants, and we assessed the accumulation of 16 known common variants using a polygenic risk score. Comparisons between groups were done using odds ratios from 2x2 contingency tables. Significance was calculated using Fisher's exact tests. **Results:** After screening TG metabolism genes, 9.0% and 15.5% of mild and severe HTG patients, respectively, carried rare variants; only 4.0% of controls carried rare variants. After calculating polygenic risk scores for each study subject, we were interested in those with extremely high scores, defined as >90th percentile of scores from the control group. From the mild and severe HTG patients, 24.6% and 32.0% had high risk scores, reflecting an extreme common variant accumulation; only 9.5% of controls had high scores. **Conclusions:** We thus report the most in-depth, systematic evaluation of the genetic factors of individuals with HTG to date. We demonstrate a direct correlation between the prevalence of genetic factors and the severity of the HTG phenotype.

Characterizing Palindromic Symptoms in Early Rheumatoid Arthritis: Results from the Canadian Early Arthritis Cohort Study

Leah Ellingwood, Orit Schieir, Marie-France Valois, Susan J. Bartlett, Louis Bessette, Carol A Hitchon, Gilles Boire, Glen Hazlewood, Edward C Keystone, Diane Tin, Carter Thorne, Vivian P. Bykerk, Janet E. Pope, and CATCH Investigators.

Background: The frequency and characteristics of patients with Palindromic Rheumatism (PR) (transient acute attacks of articular inflammation) prior to early rheumatoid arthritis (ERA) are unknown. Objective: To compare ERA patients who did versus did not report a history of transient episodes of joint inflammation preceding RA diagnosis. Methods: Study participants were patients with ERA/suspected RA (symptoms <1 year; 83% met 2010 ACR/EULAR criteria) enrolled in the Canadian Early ArThritis CoHort (CATCH) April 2017 to March 2018 who completed a questionnaire on prior inflammatory joint symptoms that come and go. Chi-square and t-tests compared characteristics in patients with versus without a reported history of prior palindromic symptoms. Simple, and multivariable logistic regression with backward selection ($p<0.2$) were used to determine crude and adjusted predictors of palindromic symptoms.Results: 154 ERA patients were included; 66% were female and mean (sd) age was 54 (15) years. 54% had previous joint pain and swelling prior to their current episode; 42% endorsed prior episodic joint pain and swelling, approximately half of whom (20% of total, N=31) reported transient joint symptoms for over six months. Patients reporting previous palindromic symptoms were more often female, seropositive, had more comorbidities, and lower swollen joints and baseline CDAI ($p<0.05$). In multivariable regression, female sex, higher income, seropositivity, back/spine issues, and lower CDAI were associated with history of palindromic symptoms.Conclusion: Half of ERA patients self-reported transient episodes of inflammatory arthritis prior to RA diagnosis. They are more likely female, seropositive, with higher income and lower disease activity.

Frailty Impairs Obstacle Negotiation While Walking: Results from The Gait and Brain Study.

Frederico Faria, Nick Walter Bray and Manuel Montero-Odasso.

In this study we aim to determine the impact of frailty status on obstacle negotiation performance in older adults while walking. We hypothesize that frail individuals will have gait stability significantly more disturbed while approaching and crossing an obstacle compared with unobstructed walking, and compared with pre-frail and non-frail individuals. A total of 196 older adults (72.1 Â±5.4 years of age; 62.8% women) from the Gait and brain Study participated in this cross-sectional study. Participants were assessed and stratified as non-frail (n=65), pre-frail (n=108) and frail (n=23). Gait variables were measured using a 6-meter electronic walkway adapted with unobstructed and obstructed conditions using an ad-hoc obstacle (15% participant's height). Gait variables were measured during unobstructed

condition, prior to obstacle crossing (pre-crossing phase), and while crossing (crossing phase) the obstacle. Five gait variables from each obstacle negotiation phase were compared with the unobstructed condition using mixed repeated measures ANOVA, to detect interactions between frailty status and walking conditions on gait performance, adjusted for relevant covariates. An interaction revealed that only during the pre-crossing phase, frail individuals increased their stride width more than non-frail (p=.002). Another interaction revealed that only during the crossing phase, frail individuals increased stride width (p<.001) and single support time (p=.001) more than pre-frail and non-frail. Statistical adjustments for lower limbs function attenuated p-values from all interactions. Frailty status in older adults impairs walking stability during obstacle negotiation, potentially contributing to their increased falls risk. Muscle weakness in lower limbs may explain these associations.

Acromegaly - A Matter of the Heart

Chris Foster, Ali Kara, Pantelis Diamantouros, Neil Duggal, Brian Rotenberg, Stan Van Uum.

Background: Heart failure is a known complication of acromegaly. Though diastolic dysfunction is common, overt systolic dysfunction is rare. The pathophysiology of acromegalic heart failure differs from that of chronic heart failure. An initial hyperkinetic syndrome leads to biventricular hypertrophy with diastolic dysfunction and eventually to chamber dilatation with systolic dysfunction. Previous case series have described poor recovery despite appropriate cardiovascular and endocrine therapies.Case presentation: A 34-year-old man presented to hospital with hypertensive crisis and a one-month history of exertional dyspnea and anasarca. Echocardiogram showed left ventricular ejection fraction (LVEF) of 16%. Serum IGF-1 was 883 ug/L (normal 82-242) and pituitary MRI revealed a 12 x 12 x 9 mm adenoma. He was started on standard CHF therapy, and aggressive diuresis led to a 25 kg weight loss over his 11-day hospitalization. An echocardiogram after 6 weeks of therapy showed a LVEF of 35-40% and heavy left ventricular trabeculation. After a GH suppression test confirmed the diagnosis, he underwent an anatomically difficult transsphenoidal resection. Post-operative biochemistry showed persistent acromegaly despite no residual mass on MRI. He has recently started on somatostatin analogue therapy.Discussion: The unique aspects of our patient's case include overt CHF as the presenting symptom of acromegaly, the severe systolic dysfunction at such a young age, and great recovery of cardiac function with treatment. Clinical observation of his presentation and across several modalities of endocrine and non-endocrine therapy offer prognostic insights. Such information may be helpful when treating similar patients in the future.

Clinical predictors for sessile serrated adenoma detection: An analysis of 17,524 colonoscopies

Mandark Gandhi, Stephanie Cocco, Cassandra McDonald, Zaid Hindi, Debarati Chakraborty, Karissa French, Omar Siddiqi, Marc-Andre Blier, Bharat Markandey, Victoria Siebring, Mayur Brahmania, Nitin Khanna, Vipul Jairath, Brian Yan & Michael Sey.

BACKGROUND: Adenoma detection and removal is crucial for colon cancer prevention. Adenoma detection rate is the current colonoscopy quality benchmark. Sessile serrated adenoma detection rate (SSADR) is gaining interest as a supplementary metric as sessile serrated adenomas (SSAs) are more difficult to identify endoscopically. Our aim was to determine predictors of SSA detection.METHODS: We performed a prospective observational study using colonoscopy quality metrics collected by Cancer Care Ontario. All colonoscopies performed for any indication across 20 hospitals in Southwestern Ontario between April 2017 and February 2018 were identified. Cases without histology records were excluded. A multi-variable analysis was conducted.RESULTS: Of 17,524 colonoscopies (mean (SD) age = 59.6 (14.4), 53.9% female), 910 procedures had an SSA present (SSADR of 5.2%). Variables independently associated with higher SSADRs included patient age (OR 1.02, 95% CI 1.02-1.03, p<0.001), cecal intubation (OR 3.80, 95% CI

1.87-7.71, p<0.001), use of split-dose bowel preparation (OR 1.33, 95% CI 1.00-1.77, p=0.047), and very good bowel preparation quality (OR 2.48, 95% CI 1.38-4.44, p=0.002). Factors associated with lower SSADRs included non-screening colonoscopies (OR 0.55, 95% CI 0.48-0.63, p<0.001) and non-gastroenterologist endoscopist (general surgery OR 0.50, 95% CI 0.41-0.60, p<0.001; internal medicine OR 0.70, 95% CI 0.51-0.96, p=0.027; general practice OR 0.20, 95% CI 0.06-0.68, p=0.010). CONCLUSIONS: Modifiable factors associated with higher SSADRs include use of split-dose bowel preparation, better bowel preparation quality, cecal intubation, and endoscopist specialty. Ongoing initiatives emphasizing these variables should be encouraged.

Improving Bowel Preparation Quality for Inpatient Colonoscopies at a Tertiary Hospital

Mandark Gandhi, Cassandra Townsend, Majed Almaghrabi, Ammar Alotaibi, Nitin Khanna, Brian Yan and Mayur Brahmania.

INTRODUCTION: Adequate bowel preparation quality is required for appropriate mucosal visualization during colonoscopy. Several factors impede quality including patient, environmental and process factors. When colonoscopies demonstrate poor-quality preparation, it often delays further management and discharge for patients as they often need to return for a second procedure in order to get adequate visualization. This also results in increased costs to the healthcare system. AIM: Our aim was to identify the rate of poor-quality bowel preparation at our tertiary care hospital for inpatient colonoscopies and implement interventions to decrease this rate. IMPROVEMENT: The study was conducted at University Hospital in London, Ontario from March 2018 - March 2019. In the first PDSA cycle we improved an existing order-set such that split-dose bowel preparation would more reliably be ordered and administered. Our second PDSA cycle focused on teaching junior residents how to order bowel preparation for inpatient colonoscopies. PDSA cycle three involved making bowel preparation quality assessment more objective. Lastly, PDSA cycle four was aimed at improving patient education surrounding the importance of completing bowel preparation. PROJECT IMPACT: Poor-quality bowel preparation in the six months prior to intervention was 14.0%. After intervention this came down to 8.0%. Similarly our process measure of patients receiving split-dose bowel preparation administration increased from 81.2% to 94.6% during this period. LESSONS LEARNED: Several factors are involved with poor-quality bowel preparation for inpatient colonoscopies. Simple and sustainable interventions can be implemented to improve quality. We are continuing to identify new factors and interventions to further improve this metric.

Targeting the IL-5 Pathway in Eosinophilic Asthma: A comparison of mepolizumab to benralizumab in the reduction of peripheral eosinophil counts

Arian Ghassemian, Dr.H.Kim.

Asthma is a heterogenous disease with phenotypic differences and subsequent endotypes. The current study is interested in the type 2 asthma endotype which is characterized by a more allergic and inflammatory clinical picture including elevated IgE levels, serum eosinophils, and other markers of inflammation. Escalation of therapy for these patients includes biologics targeted against IgE and the IL-5 pathway with no inter-biologic comparison between these agents in the literature. As such, we conducted a retrospective chart review to compare two of the IL-5 agents, which have different molecular targets, in their efficacy in peripheral eosinophil reduction. These agents are mepolizumab (an anti-IL-5 monoclonal antibody which targets the IL-5 molecule) and benralizumab (an anti-IL-5 receptor α-antibody) whose target resides on the eosinophil. Omalizumab was also included as a non-placebo control. We hypothesized benralizumab to be a better IL-5 agent in reducing peripheral eosinophil counts. Both IL-5 agents were expected to be significantly better than omalizumab. However, given IgE's role in eosinophil proliferation, we expected omalizumab to have some effect in

peripheral eosinophil reduction. Complete data was available from 51, 36, and 18 patients in the omalizumab, mepolizumab, and benralizumab groups respectively, from which the relative reduction in eosinophils by the biologic was calculated as a percentage. Preliminary statistics done on this percentage revealed no statistically significant difference between the IL-5 agents mepolizumab and benralizumab, p=0.109. Both mepolizumab and benralizumab did significantly reduce peripheral eosinophil counts, p <0.001 (for both agents). Omalizumab however did not offer a significant change in eosinophil counts p=0.139.

Aspirin inhibits the initiation of tuft cell-derived colitis-associated cancer

Hayley J. Good, Alice E. Shin, Liyue Zhang, Elena N. Fazio, David Meriwether, Srinivasa Reddy, Timothy C. Wang, Samuel Asfaha.

Introduction: Inflammatory bowel disease is a major risk factor for colorectal cancer (CRC). However, the mechanism by which colitis leads to cancer is unknown. We previously showed that Dclk1+ tuft cells are long-lived and quiescent even upon mutation of the tumor suppressor APC, yet become cancer-initiating cells upon inflammation. Interestingly, Dclk1+ cells highly express cyclooxygenase (COX)-1 and -2, the direct target of non-steroidal anti-inflammatory drugs (NSAIDs) that are chemopreventative in CRC. Thus, we aimed to determine the effects of NSAIDs on colitis-associated cancer.Methods: Dclk1CreERT2/APCfl/fl mice were administered tamoxifen and the colitis-inducing agent DSS, followed by daily treatment with Aspirin (non-selective), celecoxib, rofecoxib (COX-2 inhibitors), or SC-560 (COX-1 inhibitor). Additionally, the effects of NSAIDs were tested in the AOM/DSS model of CAC, where azoxymethane (AOM) and DSS were administered to induce tumorigenesis. Sixteen weeks post-tamoxifen/AOM, colonic tumors were analyzed. Following colitis, prostaglandin levels were measured by LC-MS and colitis severity was assessed by myeloperoxidase activity and histology.Results: Treatment with Aspirin, but not COX-2 inhibitors, significantly reduced tumor number in both CAC models. SC-560 also reduced tumor number. We detected no difference in tumor size or colitis severity. Aspirin and SC-560, but not celecoxib, significantly reduced prostaglandin levels in colitis. Interestingly, Aspirin was also associated with a reduction in Dclk1+ cells.Conclusions: These findings show an important role for COX in initiation of CAC. Our results suggest that Aspirin is effective in chemoprevention of CAC, potentially through the reduction of prostaglandins that may be critical for Dclk1+ cell survival.

Breast cancer resistance protein (BCRP, ABCG2) genotype and amiodarone contribute to variation in apixaban concentration in Caucasian patients with atrial fibrillation

M Gulilat, D Keller, B Linton, DA Pananos, D Lizotte, GK Dresser, J Alfonsi, RG Tirona, RB Kim, and UI Schwarz.

Background: Apixaban, a Factor Xa inhibitor, belongs to an increasingly prescribed class of direct-acting oral anticoagulants used for stroke prevention in patients with atrial fibrillation (AF). Its pharmacokinetic profile is known to be influenced by cytochrome P450 (CYP)3A metabolism, while it is also a substrate of the efflux transporters ATP-binding cassette (ABC)B1 (P-glycoprotein) and ABCG2 (breast cancer resistance protein, BCRP). Objective: In this study, we assessed the impact of pharmacogenetic variation and interacting medication to better explain variation in drug exposure among 358 Caucasian AF patients. Methods: Venous blood samples were collected at steady state during regular apixaban dosing intervals. Genotyping (ABCG2, ABCB1, CYP3A4*22, CYP3A5*3) was performed by TaqMan assays, and apixaban quantified by liquid chromatography-mass spectrometry. The relative contribution of demographic, clinical and genetic factors to apixaban concentration was assessed by multiple regression analysis using samples obtained between 3 to 12 hours post-dose.Results: Patients were 46% female, 79 years, 82 kg, and had a serum creatinine of 91 Âµmol/L (median values). There was a 41-fold

variation (min-max) in apixaban concentration. The impaired-function variant ABCG2 c.421C>A and concomitant amiodarone use, an antiarrhythmic agent and moderate CYP3A/ABCB1 inhibitor, were associated with higher apixaban concentration, together with female sex, increased age, and elevated serum creatinine, explaining 35% of the observed variation. Conclusion: Our findings suggest that ABCG2 c.421C>A genotype and amiodarone use contribute to interpatient apixaban variability beyond known clinical factors.

Ethnicity and Breast Cancer Outcomes in Windsor-Essex County

Sanam Gurm, Richard Low, Dr. Abdulkadir Hussein, Dr. Caroline Hamm.

Objectives: To determine whether the ethnicity of a patient diagnosed with breast cancer in the Windsor-Essex County region influences baseline cancer characteristics or clinical outcome. If a relationship was found, this would provide an opportunity to explore improvements in management. Methods: A retrospective chart review was conducted with patients diagnosed with breast cancer at the Windsor Regional Cancer Centre (WRCC) between 2000-2010. To identify patient ethnicity, we used patient surnames as a proxy. Statistical analysis was performed (COX regression model and Kaplan Meier survival curves) to determine if there was any ethnic disparities in cancer outcomes or baseline cancer characteristics.Results: Baseline characteristics investigated included breast cancer stage, receptor status (ER, PR, HER2), and age. Clinical outcome was defined by survival in months. There were no statistically significant findings that tied ethnicity to differences in either baseline characteristics or clinical outcomes in patients diagnosed with breast cancer. Conclusion: There was no statistically significant relationship found between ethnicity and cancer outcomes or baseline characteristics. However, further studies are recommended to examine the reason for lack of ethnic disparities, which have been described in previous papers.

A reproducible design for myelin water imaging using 5 volunteers

Jeffrey Hamilton, Jonathan Thiessen, Susan Huang.

Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare and life-threatening blood disease characterized by insufficient activity in ADAMTS13 (A Disintegrin-like and Metalloprotease with Thrombospondin type 1 repeats 13), an important enzyme in hemostasis. Predominant symptoms include thrombosis, fever, anemia, kidney failure, and chronic neurological impairment (including confusion and seizures). Little is known about the chronic impact of this neurological pathology. Quantitative magnetic resonance imaging (MRI) will be used to investigate structural changes in brain white matter and the technique will first be validated in volunteers. Methods: MRI on five healthy volunteers will be acquired on the Simens 3T mMR Biograph at St. Joseph's Hospital. The 60-minute brain scan will specifically focus on quantitative sequences for myelin water imaging (mcDESPOT - multi-component Driven Equilibrium Single Pulse Observation of T1/T1). Results: The primary result to be reported from the analysis of the MRI scans is called the myelin water fraction (MWF). Histological evidence in previous studies confirms the strong correlation between MWF and white matter content. We expect to reproduce such whole brain MWF values across each of the 5 volunteer scans. Discussion: By comparing our MWF values to literature values, we will validate the myelin water imaging from MRI which will be applied to patients with TTP. To our knowledge, this work would be the first of its kind to investigate chronic neurological impairment in individuals who experience TTP.

Fatigue up to 5 years is affected by achieving a Low Disease State Within First 3 Months in Early Rheumatoid Arthritis: Results from a Canadian incident cohort

Dr. Melissa Holdren, Orit Schieir, Susan J. Bartlett, Louis Bessette, Gilles Boire, Glen

Hazlewood, Carol A, Hitchon, Edward Keystone, Diane Tin, Carter Thorne, Vivian P. Bykerk, Janet E. Pope and on behalf of Canadian Early Arthritis Cohort (CATCH) investigators.

Background: Fatigue is a complex multi-factorial process with adverse affects on patients' physical and emotional well-being. Objectives: To examine the relationship between disease activity and fatigue in early rheumatoid arthritis (ERA).Methods: Data were from patients with ERA enrolled in the Canadian Early Arthritis Cohort (CATCH). Bivariate relationships between disease activity and fatigue were estimated using the Pearson correlation coefficient. Repeated measures ANOVA were used to compare differences in fatigue in patient who did vs. did not achieve a low disease state within 3-months of cohort entry.Results: Of the 1864 patients included, 88% met criteria for RA, 72% were women and most had moderate-high baseline disease with a mean (SD) DAS28 of 4.9 (1.5). Fatigue was common with 19% reporting moderate and 59% severe fatigue at baseline. Fatigue was strongly correlated with pain and patient global ratings (r 0.56-0.67, p<0.001) and moderately correlated with disease activity score (DAS) (r 0.35-0.49, p<0.001) throughout the first year. Patients who reported low fatigue by three months continued to have significantly lower fatigue throughout follow-up compared to those with moderate or high fatigue (p<0.001). Patients who achieved remission or low disease activity within 3-months of cohort entry had significantly lower mean fatigue compared to those with more active disease persistent throughout 5-years of follow-up (p<0.001).Conclusion: Fatigue is common in ERA and is most strongly correlated with pain and disease activity. Early treatment response within 3-months was associated with short and long-term improvements in fatigue over time.

Clinical phenotype of familial atrial fibrillation due to MYL4 myosin light chain gene mutation: A case series

Lorne J Gula, **Bingyu Hou MD**, Michael H. Gollob MD.

A recently identified genetic variant in the atrial-specific myosin light chain gene MYL4 was shown to cause early onset atrial fibrillation, conduction disease and atrial myopathy. Here we present a clinical overview of a family of 5 members, in two generations, affected by this mutation. All symptomatic members of this family are heterozygous for the p.Glu11Lys mutation. MethodsThe medical records of the family members with early onset AF were reviewed. Affected family members underwent genome sequencing to identify the culprit mutation. Demographics, details of clinical presentation and progression, electrocardiography and echocardiogram images were collected. Details of left atrial electro-anatomic mapping were collected in patients who had undergone attempts at catheter ablation. ResultsSix patients were identified over two generations. All patients were found to exhibit early onset paroxysmal atrial fibrillation with the average age of onset of 28.4 years old. All individuals had normal ejection fraction and structural anatomy on echo at the time of presentation. Several members presented with low voltage P waves with at least 1 individual presenting with first degree AV block and Wenckebach on EKG. Two individuals underwent ablation with PVI for symptomatic atrial fibrillation that demonstrated low voltage on electro-anatomic mapping of the left atrium. Conclusion: A heterozygous p.Glu11Lys mutation in the MYL4 gene has been shown to cause an inherited form of early onset atrial fibrillation characterized by normal cardiac anatomy, low voltage P waves, first degree AV block. Low voltage was seen on electro-anatomic mapping of individuals who underwent PVI.

Endoscopic Removal Of Migrated Intrauterine Device: Case Report And Review Of Literature

Vadim Iablokov, Yang Lei, Riaz Karmali, Nauzer Forbes.

Intrauterine devices (IUDs) are an increasingly common and proven effective contraceptive method. Uterine perforation and IUD migration occurs at a rate of 0.3-2.6 per 1000 and is largely

dependent on the experience of the inserter. Ectopic IUDs have been reported in the peritoneum, bladder, adnexa and bowel. Migration of the perforated IUD into the bowel is rare and requires removal. Surgical removal of IUDs by laparotomy has been widely described; however, reports of endoscopic removal are few and may offer a safer alternative.A previously healthy 37-year-old female presented to her family doctor with a 6-month history of left lower quadrant abdominal pain. She had a history of IUD placement 2.5 years prior. She had become pregnant 6 months after insertion, when it was assumed the IUD had fallen out. Subsequent abdominal ultrasound revealed an echogenic focus at the uterine fundus. A computed tomography scan localized the IUD to the outside of the uterine cavity with the vertical arm in the myometrium or serosa. After the patient was admitted to hospital, the IUD was removed by flexible sigmoidoscope. Extraction of the IUD was uncomplicated, well-tolerated, and the patient was discharged later on the same day. No prophylactic hemostasis or antimicrobial coverage was required. Review of the literature identified 25 cases of ectopic IUDs removed through the anus. Antimicrobial coverage peri-procedurally was variable. Endoscopy is a safe and cost-effective technique for extraction of IUDs in the bowel lumen when compared to removal by laparotomy.

Investigation and management of secondary erythrocytosis: Canadian national survey

James Jae, Sangyang Jia, Dr. Chai Phua.

Introduction:The workup of patients with undifferentiated erythrocytosis is complex due to a wide variety of etiologies. Thus far, there are no specific evidence-based guidelines to establish an algorithm for the investigation and management of patients with secondary erythrocytosis. The current approach to investigation and management of these patients is poorly understood. We performed a survey on practicing Hematology and Internal Medicine specialists in Canada who are deemed to encounter these patient populations to better evaluate current local practices in the hope of identifying care gaps and unmet needs. This will hopefully create insights that may guide future research goals.Methods:This is a cross-sectional survey. All Hematology and Internal Medicine specialists in Canada will be invited to partake in a 10-minute online survey that includes 18 items on demographics of treaters, the extent of investigations (including assessment of first, second and third line of investigations - see below), and current treatment approaches. Hematologists from LHSC endorsed the survey materials.- CBC including HCT- Serum Erythropoietin, EPO- JAK2 V617F Mutation- JAK2 Exon12 Mutation- CALR Mutations- MPL Mutations- Bone Marrow Biopsy- Bone Marrow Karyotype- Lactate Dehydrogenase (LDH)- Tumor Lysis Screen (uric acid, potassium, calcium, phosphate)- Serum Ferritin- Serum Testosterone- Oxygen Saturation- Chest X-Ray- Echocardiogram- Abdominal Ultrasound- CT/MRI Head- CT/MRI Chest, Abdomen & Pelvis- Pulmonary Function Tests- P50 Oxygen Dissociation- Sleep Study- Hemoglobin Electrophoresis- Gene Mutations in Hypoxia Signaling Pathways (HIF-2a, VHL, PHD2)- Erythropoietin Receptor (EPO-R) Mutation- Methemoglobin- Globin Gene Sequencing- Endogenous Erythroid Colony- Red Cell MassResults:(Survey ongoing, pending results)

Ruxolitinib as effective treatment of refractory pruritus in polycythemia vera

James Jae, Sangyang Jia, Dr. Cyrus Hsia.

Introduction: Polycythemia vera (PV) is a myeloproliferative neoplasm involving proliferation of the erythroid lineage. Pruritus is a feature of PV with an incompletely known mechanism. Ruxolitinib is a Janus kinase 1/2 inhibitor that inhibits the deregulated signaling present in myeloproliferative neoplasms and has shown efficacy via the RESPONSE trials. However, these trials do not address management of pruritus specifically. We present a case of a patient with PV with refractory pruritus managed effectively with ruxolitinib.Case Description: A 65-year-old woman with PV placed on hydroxyurea had distressing pruritus. She was trialled on multiple antihistamines, multiple antidepressants, increases in aspirin, and

multiple topical creams to no effect. Interestingly, our patient had persistent pruritus despite achieving target hematocrit (<0.45) for PV in contrast to the RESPONSE trials. Finally, she was trialed on ruxolitinib, which led to full resolution of pruritus.Discussion: Unfortunately, cost and ease of access are barriers for patients who are in serious need with no alternatives. For ruxolitinib, the criteria for approval includes demonstrated resistance to hydroxyurea and adequate performance status. Based on our review of the literature and this case, we believe it is prudent to expand the criteria to cover more patients in need.Conclusion: Pruritus is a symptom of PV that may be present even with adequate hematocrit control. It may be refractory to anti-histamines and anti-depressants. We demonstrate a case of resolution of refractory pruritus with ruxolitinib and believe it should warrant further consideration as a first-line agent for distressing pruritus in context of PV.

Inhibition of Metalloproteinase Activity Promotes PMVEC Barrier Function Under Septic Conditions

Devika Jayawardena, Sean Gill.

Sepsis, a systemic inflammatory response to infection, is a major cause of death in the elderly. During sepsis, pulmonary microvascular endothelial cells (PMVEC) become injured, leading to loss of barrier function and accumulation of protein-rich edema fluid. Metalloproteinases, including matrix metalloproteinases (MMP) and a disintegrin and metalloproteinases (ADAM), are capable of cleaving cell surface proteins, such as cell-cell junctional proteins, suggesting a role in septic PMVEC barrier dysfunction. Our lab found PMVEC lacking tissue inhibitor of metalloproteinases (TIMP) 3, a critical regulator of MMP and ADAM, had increased permeability compared to wild type (WT) PMVEC. We hypothesize PMVEC-derived metalloproteinase activity will increase under septic conditions and vascular permeability will reduce with application of synthetic metalloproteinase inhibitors. PMVEC isolated from WT and Timp3-/- mice were stimulated with PBS or cytomix+LPS. Metalloproteinase activity was assessed in conditioned media and cell lysate, and trans-PMVEC macromolecular flux was assessed using Evans blue-labelled albumin. PMVEC surface localization of VE-cadherin (adherens junction) and claudin-5 (tight junction) was assessed by immunofluorescence. To confirm the role of metalloproteinases, WT and Timp3-/- PMVEC were treated with synthetic metalloproteinase inhibitors. Analysis of metalloproteinase activity revealed increased MMP13 and ADAM17 activity in septic PMVEC and Timp3-/- PMVEC, leading to loss of inter-PMVEC junctional proteins and subsequent barrier dysfunction. The application of synthetic metalloproteinase inhibitors reduced permeability and disruption of VE-cadherin and claudin 5 under septic conditions. These studies suggest inhibition of metalloproteinase activity may promote PMVEC barrier function by reducing inter-junctional protein degradation during sepsis, thereby reducing septic vascular permeability.

Comparison of JAK inhibitors in the treatment of rheumatoid arthritis: A systemic literature review

Jehanya Jegatheeswaran, Janet E Pope.

Several Janus kinase (JAK) inhibitors, oral targeted disease modifying drugs, will be approved for the treatment of RA and other diseases. This review compares and contrasts the efficacy of JAK inhibitors (Tofacitinib, Baricitinib, Upadacitinib, Filgotinib, Peficitinib, and Decernotinib) in RA including: early RA methotrexate-naïve patients, post-methotrexate failure and post-biologics. Trials in monotherapy, combination with disease modifying drugs such as methotrexate, and comparing to adalimumab in biologic-naïve patients were studied. The efficacy is superior to methotrexate in naïve patients and equal or superior to adalimumab depending on the drug and dose. Similar efficacy and safety are seen overall within the class for most of the JAK inhibitors, with proven efficacy across various RA. There is a class effect of adverse events. Serious infections occur at a rate similar to other advanced therapies in RA, although more reactivation of herpes zoster occurs.

Heart Transplant Induction Therapy National Canadian Survey

Sangyang Jia, Drs. Stuart Smith, Dave Nagpal, Ryan Davey, Sabe De, Robert McKelvie, Livia Goldraich.

Purpose: Indications and usage of induction therapy in heart transplantation is controversial. We aimed to capture a point-prevalence view of opinions and utilization of induction therapy among adult Canadian heart transplant programs.Methods: An electronic survey questionnaire was distributed to all heart transplant centers in Canada in August 2018. The survey consisted of questions on site-specific induction therapy protocols, induction agent selection, dosing, and complications.Results: All nine heart transplant centers in Canada completed the survey. Five centers (56%) use induction therapy on all patients and all centers use induction therapy on more than 50% of patients. Antithymocyte globulin (ATG) is the preferred drug in five centers (56%) whilst basiliximab (BAS) is the preferred drug in three centers (33%). One center used a single agent (ATG) exclusively. For patients who were at higher risk of infection, BAS was preferred in eight (89%) centers. For patients who were at higher risk of kidney failure, ATG was preferred in 5 (56%) centers. Four centers (44%) used a reduced dose protocol more than 50% of the time when using ATG. Centers perceived the relative increased risk of complications from induction therapy in descending order were: infection (21.4%), dehiscence (7.7%), acute respiratory distress syndrome (2.4%), and delirium (1.8%).Conclusion: Induction therapy use is inconsistent across Canadian centers and may be more dependent on local practice patterns rather than on true efficacy or utility. Despite potential benefits, there were specific perceived concerns regarding the therapy. This clinical equipoise presents an opportunity for further prospective study.

Survival Analysis of 513 Patients Receiving Immunosuppressive Therapy Post Heart Transplantation

Sangyang Jia, Drs. Stuart Smith, Dave Nagpal, Livia Goldraich, Ryan Davey, Robert McKelvie.

Purpose: The use of induction therapy for heart transplant remains in debate. Additionally, agent choice is a major consideration for centers and may influence survival outcomes. It is important to have evidence-based justification for the usage of induction therapy agents due to costs and risks.Methods: A retrospective analysis of heart transplant patients who received anti-thymocyte globulin (ATG), anti-lymphocyte globulin (ALG), and muromonab-CD3 (OKT3) at a tertiary academic center was conducted. Patients who received cyclosporine (CyA) alone served as control. Baseline characteristics were collected for each group. Survival at 3 months, 1 year, and 10-year post transplant were compared.Results: A total of 513 patients receiving induction therapy or CyA between April 1981 and September 2007 were included. Mean baseline characteristics of the three groups are detailed in Table 1. At 3-months post transplant ATG, ALG, OKT3, and CyA had survival rates of 78.7, 81.6, 85.1, and 61.9 percent, respectively. The survival 1-year post transplant for ATG, ALG, OKT3, and CyA were 74.5, 76.4, 81.1, and 61.9 percent, respectively. After 10-years post transplant 56.4, 53.6, 47.3, and 33.3 percent of ATG, ALG, OKT3, and CyA receiving patients survived, respectively. P>0.05 for all intervals.Conclusions: Anti-thymocyte globulin is not significantly associated with short and long-term survival differences in heart transplant patients compared to no induction and off-market induction agents. Further controlled trials are needed to provide additional evidence for current use.

Impact of Procurement Distance and Ischemic Time on Long Term Survival Post Heart Transplant - 3 Decade Experience

Sangyang Jia, Drs. Stuart Smith, Dave Nagpal, Livia Goldraich, Peter Pflugfelder, Ryan Davey, Robert McKelvie, Sabe De, Eadric Cai.

Purpose: Determining the boundaries of the catchment area for receiving donor hearts has important consequences in the balance between transplant ischemic times and increasing the supply of hearts. Methods: A retrospective analysis of all patients since the initiation of the heart transplant program at a tertiary academic center were included. Results: 513 patients between 1981 and 2009 were included. Patients that survived 3 months post transplant had a mean ischemic time of 211 minutes whilst those that did not had a mean ischemic time of 202 minutes. After 1-year post transplant, the mean ischemic time was 211 minutes for the survivors and 201 minutes for those that did not survive. And after 10-year post transplant, the mean ischemic time was 216 minutes for the survivors and 201 minutes for those that did not survive. Chi square analysis for the difference in survival at 3 months, 1 year, and 10 years for mean ischemic time categories of <2 hours, 2-4 hours, and >4 hours did not show significance. Chi square analysis for the difference in survival at 3 months, 1 year, and 10 years for mean procurement distance categories of <500 km, 500-1000 km, and >1000 km also did not show significance.Conclusions: There were no significant difference in short, medium, and long-term survival outcomes with regards to ischemic time and transport distance. Further multi-centered and multi-geographical studies are needed to determine if there is a benefit to restricting donor catchment area to improve transport time.

Literature Review and Case Report of Granular Acute Lymphoblastic Leukemia

Sangyang Jia, Drs. James Jae, Cyrus Hsia.

Introduction: Diagnostic confusion can arise when acute lymphoblastic leukemia (ALL) patients present with intracytoplasmic granules which typically are found in acute myeloid leukemia (AML). Granular ALL is extremely rare in adults, and the natural history of this condition is not well described. We report a case of granular ALL in a 54-year old woman and review its clinical significance in adults reported in the literature.Case Description: A 54-year-old woman with history of myeloma treated 3 years prior presented with neutropenia which after work-up demonstrated morphologic AML with marrow blasts and cytoplasmic granules. However, flow immunophenotyping was positive for CD34, CD19, HLADR, and CD79a. CD 13, CD33, cytoplasmic CD3, CD10, and MPO were negative. These findings were consistent with a precursor B-cell ALL. Following the eight cycle of the intensification phase of the Dana Farber ALL Protocol the patient unfortunately developed sepsis and succumbed 9 months after the initial diagnosis of ALLDiscussion: It is currently unknown whether granular ALL is associated with a different clinical outcome. We performed a literature search of all cases of adult cases and found 18 additional patients. The complete remission rate to induction chemotherapy was 53% in these patients which is markedly lower than the rates reported in literature for non-granular adult ALL (80%-90%).Conclusion: Diagnostic confusion may arise in acute lymphoblastic leukemia with cytoplasmic granular inclusions resembling that of acute myeloid leukemia. An accurate diagnosis is critically important for treatment implementation and prognosis in acute leukemia.

Effect of Rapid Heart Failure Clinic Enrollment on Readmission Rates Post Initial Diagnosis in the Emergency Department

Sangyang Jia, Anna MacDonald, Dr. Stuart Smith.

Introduction: Heart failure patients have frequent and lengthy hospital stays. We aimed to investigate the effect of immediate heart failure specialist clinic enrollment post emergency department diagnosis on readmission rates.Methods: From September 2017 to January 2019, emergency physicians at LHSC were instructed to refer heart failure patients to immediate consultation at the heart failure clinic at St. Joseph's Hospital. Readmission rates were analyzed in the next month and three months. Results: 104 patients were referred from the emergency department with heart failure to the

heart failure specialty clinic. 91 patients attended the initial clinic. 77 patients were found to be in actual heart failure and were followed in subsequent clinics. The male to female ratio was 50:27 and the mean age was 75.5 ± 11.6 years. The mean initial ejection fraction was 46.7 ± 17.2%. The mean time from referral to first visit was 4.3 ± 4.1 days and the mean number of clinic visits in the first month was 2.1 ± 0.9. 87.0% of patients had medication changes during the first month of clinic and the mean number of medication changes in the first month was 3.5 ± 2.4. In the first month, 69 patients had no readmissions, and 8 patients had one readmission. In the first three months, 53 patients had no readmissions, 17 had one readmission, 4 had two readmissions, and 1 had three readmissions. Conclusion: Most heart failure patients who attended specialist clinic immediately post initial presentation did not have readmission in the short term.

Peritoneal Dialysis in Cirrhotic Patients Meta-Analysis

Sangyang Jia, Drs. Justin Zhu, Arsh Jain.

Introduction: Patients with cirrhosis represent on of the most fragile dialysis populations. Dialyzing this population is often fraught with clinical difficulties: including hypotension, volume control, ascites control. It is thought that PD may be more beneficial in this population due to its hemodynamic stability (decreased cardiac stunning, hypotensive episodes). In addition, it has been shown to have equivalent infection rates, and has been successfully used to bridge patients with cirrhosis to liver transplantation. We wish to explore the optimal dialysis modality for patients with cirrhosis; to see whether peritoneal dialysis may be better than our de facto solution of hemodialysis.Methods: EMBASE, COCHRANE, MEDLINE search performed by librarian for studies comparing PD vs HD in cirrhosis. Both RCTs and observational studies are included. Both prospective and retrospective designs are included. Outcome measures include mortality, rate of hospitalization, duration of hospitalization, rate of renal recovery, rate of transplantation, weight, diuretic use, frequency of paracentesis, renal function, MELD score, Child-Pugh, peritonitis, malnutrition (albumin).Results: Literature search and data abstraction completed. Analysis to be added.Conclusions: To be added.

Infection Risk in Apheresis

Sangyang Jia, Dr. Susan Huang.

Introduction: Infection risks may be increased when plasma containing immunoglobulin and complement proteins are replaced with albumin primarily. In one plasma exchange pass the amount of serum immunoglobulin can be decreased by 60% and the total body reservoir of immunoglobulins may be decreased by 20%. When many exchanges are carried out over a brief period, the effect may be amplified and persist for weeks, especially in the context where immunosuppressive agents are utilized. If FFP is used with apheresis, immunoglobulin and complement deficiency may be prevented. The incidence of infection in patients post plasma exchange is very variable and difficult to determine due to confounding factors such as granulocytopenia and immunosuppression therapy. There is only one prospective, randomized trial by Pohl et al. which found in 86 patients with lupus nephritis receiving cyclophosphamide and steroids with or without apheresis that there was no difference in the rate of infection or infection related deaths between the two groups. However, it is still possible that the deficiencies in immunoglobulins and complement may reduce the patient's ability to combat an ongoing infection, which may be of concern when the replacement fluid is virally contaminated or the vascular access presents a route of infection during treatment. Therefore, the aim of our study is to clarify the incidence and patterns of infections for patients undergoing apheresis in a tertiary care center to determine the proper clinical management and prevention of infectious complications if they arise.Methods: Single institution retrospective study.Results: To be added.

A Systematic Review of Factors Associated with Pulmonary Arterial Hypertension in Systemic Sclerosis

Yuxuan Jiang, Janet E Pope.

Background: Pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) is a lethal complication affecting approximately 8-15% of patients. Screening guidelines such as echocardiography and pulmonary function tests exist to triage patients for definitive diagnosis by right heart catheterization. Understanding the currently-unclear risk/associated factors of SSc-PAH could help stratify high-risk patients for regular screening. Methods: A systematic review was conducted to determine the risk/associated factors for SSc-PAH, including clinical/disease characteristics, antibody status, test results and biomarkers. The frequency of publications featuring a risk/association were reported. Results: Among 1351 articles returned, 605 case reports or non-English publications and 188 duplicates were removed, leaving 558 articles for manual screening. After excluding papers with small sample sizes or repeated publications from identical cohorts, 74 articles were eligible. 76 distinct risk factors/associations for SSc-PAH were identified, among which biomarkers (21) and patient characteristics (15) categories are largest and most diverse, while cardiovascular manifestations (5) and other labs (3) are the smallest. Lowered diffusing lung capacity for carbon monoxide (DLCO) and 6-minute walk score (6MW score), elevated N-terminal-pro-B-type Natriuretic Peptide (NT-proBNP), anticentrometic antibody (ACA) presence and limited subtype are most frequent risk factors. Conclusions: Risk factors for SSc-PAH such as limited-SSc, ACA, older age, longer disease duration and presence of ILD may enrich screening programs. Genes and other antibody profiles are inconsistent and requires further validation. Other PAH-complication-related data includes dyspnea, abnormal right heart deviation on echocardiogram, high BNP and short walk distance, although some of which might be manifestations rather than risk factors of SSc-PAH.

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

Radha Joseph MD, Jacqueline Torti PhD, Mark Goldszmidt MD, PhD, FRCPC

Background: Faculty and trainees are familiar with the clinical tasks required in providing care, but less familiar with the metacognitive tasks—reasoning tasks—that influence how we perform those clinical tasks. Reasoning tasks have been studied during clinical teaching unit admission case review. The purpose of this study is to explore the patterns of reasoning tasks used in academic ambulatory geriatrics clinics. **Methods:** Data consists of 13 audio-recorded case review discussions between 4 geriatricians and 7 trainees (medical students, residents and fellows). Using a previously validated list of 3 overarching and 20 supportive reasoning tasks, we are using constant comparison and template analysis to analyze these transcripts. **Results:** Our preliminary analysis of the case reviews (primarily comprehensive geriatric assessments) suggests that most reasoning tasks will be addressed during these discussions. We anticipate that trainees will emphasize precipitants to the current problem, and physical and psychosocial consequences of current conditions or treatment. Geriatricians will likely emphasize exploring the interplay between psychosocial context and management, weighing alternative treatment options, and implications of available resources on diagnostic or management choices. We expect that both trainees and faculty will assess patients' decision-making capacity, and explore collaborative roles for the patient and family. **Discussion:** Developing a shared language around the metacognitive tasks shaping geriatric encounters will allow for more meaningful feedback to trainees. Identifying common patterns of omission will help trainees better prepare for future encounters, and set goals for achieving expert-level assessment and decision-making. We can also use these reasoning tasks to design assessment instruments.

Cannabis for the treatment of Crohn's Disease and Ulcerative Colitis: Evidence from Cochrane reviews

Tahir S. Kafil, Tran M. Nguyen, John K. MacDonald, MA, and Nilesh Chande, MD, FRCPC.

We systematically reviewed the use of cannabis and cannabinoids for the treatment of Crohn's disease and ulcerative colitis. A literature search was conducted using MEDLINE, Embase, WHO ICTRP, AMED, PsychINFO, the Cochrane IBD Group Specialized Register, CENTRAL, ClinicalTrials.Gov and the European Clinical Trials Register. In the Crohn's disease review, three studies met inclusion criteria. One study (N = 21) showed 45% (5/11) of the cannabis group achieved clinical remission compared with 10% (1/10) of the placebo group (RR 4.55, 95% CI 0.63 to 32.56; very low certainty evidence). A second study (N = 22) showed no difference in clinical remission rates. A third study (N= 50) did not report on clinical remission or clinical response. GRADE analyses found that the certainty of the evidence was low to very low. In the ulcerative colitis review, two RCTs met inclusion criteria. One study (N=60) showed no difference in clinical remission rates. A second study (N=32) showed the effect on mean disease activity, CRP levels and mean fecal calprotectin levels was uncertain. This study did not report on clinical remission or clinical response. GRADE analyses of the UC review showed that the overall certainty of evidence ranged from low to moderate. Overall, the effects of cannabis and cannabinoids on Crohn's disease and ulcerative colitis were uncertain. Based on available evidence, no firm conclusions can be drawn regarding the efficacy and safety of cannabis and cannabinoids in adults with active Crohn's disease or ulcerative colitis.

A Case of BALLOON: Bronchiolitis and Allergic Alveolitis or an Opportunistic Organism Nesting?

Mikameh Kazem, Dr. Sherry Rohekar.

Background: Allergic Alveolitis, also referred to as hypersensitivity pneumonitis, is a group of lung diseases often resulting from inhalation of an antigen in the form of environmental or occupational exposure. Manifestations include a febrile reaction, malaise, and dyspnea. The onset of such symptoms in an immune-compromised host, such as any number of rheumatology patients, often triggers a concern for opportunistic infections in the setting of immune suppression.Objective: To describe a case of bilateral lung infiltrates in an immune-suppressed patientCase Presentation: We report a case of a 45-year-old male with Psoriatic arthritis, on methotrexate who presented with symptoms of dyspnea, rigors, fevers, and decrease exercise capacity and imaging consistent with bilateral, widespread miliary pattern nodules in the lungs. His infectious and environmental risk factors included a trip to the United States and inflating 200 balloons for a celebration. He was referred to respirology for further assessment and his methotrexate was stopped.Conclusion: This reported case of allergic alveolitis was likely precipitated from inhalation of the powdered substance from inflating many balloons. While hypersensitivity pneumonitis is on the differential for miliary lung disease, other causes such as different opportunistic infections must be ruled out.

Arthritis in Systemic Sclerosis

Mikameh Kazem, Dr. Janet Pope.

Inflammatory arthritis in systemic sclerosis (scleroderma) is common affecting at least 1 in 6 patients. It is heterogeneous and may mimic rheumatoid arthritis or have ankylosing or severe deformities or overlap with systemic lupus erythematosus. There are many other reasons for joint pain in scleroderma that are not from the disease (such as osteoarthritis, crystal arthritis, tendonitis) or are other manifestations of musculoskeletal problems without inflammatory arthritis (such as tendon friction rubs, hand contractures, calcinosis, tuft resorption). The diagnosis of inflammatory arthritis in scleroderma often requires a history, physical examination demonstrating joint swelling, lab tests to determine if there is seropositivity (such as

rheumatoid factor) and hand radiographs. The treatment is dependent on the severity and type of inflammatory arthritis and is often borrowed from rheumatoid arthritis treatment with use of methotrexate, antimalarials, low dose glucocorticoids and possibly biologics as warranted. There are likely emerging therapies that will help inflammatory arthritis that need to be tested in scleroderma using validated outcome measurements. Research is needed to phenotype patients with scleroderma and arthritis accurately with respect to the type of arthritis and potential prognosis and response to treatment. We have summarized some of the more recent developments in this area.

A Comparative Study of Hip Geometry in Older Patients with Acetabular versus Hip Fractures

Dr. Sara Kelly, Dr. Jennifer ThainDr. Amanda LorbergsDr. Richard Crilly.

Background: Acetabular fractures following a fall from a standing height or less are increasing in older adults. The role of osteoporosis in these acetabular fractures is unclear, but are compared to hip fractures, more common in men, other factors are likely involved. We explored if differences in hip geometry may influence the type of fragility fracture.Methods: The database of two acute care hospitals in London, Ontario from 2013 to 2015 was reviewed for acetabular and hip fracture patients aged 75+. Thirty patients with acetabular fracture were age and gender matched with 30 hip fracture patients. Digital X-rays were used to measure hip geometry. Results: Patients (35 women, 25 men) had a mean age of 86 years (range 75 to 98). Compared to those with hip fracture, patients with acetabular fracture had narrower neck shaft angle (126.7° vs. 129.6°, p = 0.029) and larger femoral shaft width (36.4 mm vs. 34.7 mm, p = 0.049). Hip axis length, femoral neck length, and femoral neck width measurements were similar between groups.Conclusion: We found that hip geometry differs between patients with acetabular fracture and hip fracture. The narrower neck shaft angle, which indicates that the femoral neck is approaching a right angle, may increase the propensity to sustain an acetabular fracture. It is unclear why the wider femoral shaft matters, unless it suggests increased femoral bone strength, which could explain the higher incidence in men. Future studies incorporating bone mineral density are needed to improve our understanding of factors associated with acetabular fractures.

A case of the syndrome of inappropriate antidiuretic hormone treated with non-invasive ventilation

Tanya Khaper, MD, Marcus Povitz, MD FRCPC.

We present a unique case of a 54-year-old female with muscle weakness, hypercarbic respiratory failure and euvolemic hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone (SIADH) that resolved with the use of non-invasive ventilation (NIV). The patient had no relevant past medical history or family history but experienced prior episodes of hyponatremia complicated by respiratory failure, which was left essentially untreated after acute stabilization. Following institution of chronic NIV therapy, hyponatremia resolved. Neurological assessment later identified a diagnosis of Limb Girdle Muscular Dystrophy with respiratory involvement. Thus far, there have been few cases of neuromuscular diseases causing SIADH reported, with Limb Girdle Muscular Dystrophy not yet being reported as one. This case further demonstrates the importance of chronic NIV therapy and evaluation of respiratory failure for respiratory muscle weakness.

Connecting Care to Home (CC2H) Early Supported Discharge Program for COPD Exacerbation: A Retrospective Cohort Study

Nicholson, J.M., **Khaper T.**, Appleton A., Schultz C., Gibson J., Lewis, J.F, Povitz M.

In Ontario, Canada nearly 12% of people have COPD but use 33% of all health services.

Approaches to care for this population that rely less on acute care resources are needed. A retrospective cohort study was done to compare outcomes between participants and non-participants of the Connecting Care to Home (CC2H) program which integrated disease management for COPD and provides a supported transition from specialty to primary care and from hospital to home. The CC2H aim is to provide continuous care and lower cost by reducing hospital length-of-stay (LOS), emergency department visits and readmissions. Individuals admitted to the pulmonology service or general medicine service with a diagnosis of COPD exacerbation, at Victoria Hospital or University Hospital in London, Ontario between October 6, 2015 and May 30, 2018 were eligible to participate. Main outcomes included hospital LOS, emergency department visits and hospital readmissions within 6 months of the index admission. The results from this study are pending further interpretation, however do suggest that multidisciplinary teams that support patients during their transition from hospital to home, following a COPD exacerbation, may be associated with reductions in hospital LOS risk of readmission and emergency department visits.

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

Nidhi Kulkarni, Sean E. Gill

Introduction: Disruption of microvascular endothelial cell (MVEC) barrier function in various pathologies is associated with organ dysfunction and death. MVEC-MVEC interactions are crucial for maintaining barrier function, as disruption of these interactions results in leak. Multiple mechanisms are known to mediate MVEC interactions, including MVEC binding to the extracellular matrix (ECM). Decreased MVEC-ECM interactions under pro-inflammatory conditions, indicated by reduced focal adhesion kinase (FAK) phosphorylation, is associated with decreased barrier function and leak. Tissue Inhibitor of metalloproteinases 3 (TIMP3) may regulate MVEC barrier function, as MVEC from Timp3-/- mice have increased leak; however, the underlying mechanism is unknown. Previous studies in the developing lung found that TIMP3 is also capable of mediating cell-ECM interactions. As such, we hypothesize that TIMP3 maintains MVEC barrier function by promoting EC-ECM interactions. Methods: MVEC isolated from wild type (WT) and Timp3-/- mice will be cultured on various matrices, and stimulated with PBS or pro-inflammatory cytokines. MVEC-ECM interactions will be assessed using adhesion assays and the XPERT-permeability assay. Finally, localization and activation/abundance of proteins associated with focal adhesions (e.g. FAK, paxillin) will be assessed by immunofluorescence and western blot respectively. Expected results/discussion: MVEC from Timp3-/- mice will have impaired MVEC-ECM interactions leading to increased permeability vs. MVEC from WT mice. Timp3-/- MVEC will have decreased MVEC adhesion to the ECM, and decreased abundance and altered localization of focal adhesion proteins vs. WT MVEC. These results could elucidate therapeutic targets to decrease MVEC permeability and maintain or rescue barrier integrity in pathological conditions, like sepsis.

Severe peripheral edema as only presenting symptom of intravascular large B-cell lymphoma - a diagnosis too frequently made on autopsy

Rachel Kyle, Gillian Mount, ShaoShi Li and Jenny Thain.

Intravascular large B-cell lymphoma (IVLBCL) is seen in less than one per million people and can be an extremely difficult ante-mortem diagnosis to make. We present a case of an otherwise healthy 74-year-old woman whose predominant symptom was pitting edema. She underwent extensive outpatient work-up, including abdominal ultrasound, bone marrow biopsy, doppler ultrasound of the legs, skin biopsy, echocardiogram and repeated blood work without clear etiology. After 15 months she presented to the emergency department with progressive leg weakness, pain and hypotension. Extensive inpatient investigations and subspecialty consultations did not bring her closer to a diagnosis. Unfortunately a week into her

admission she went into progressive renal failure with worsening hypotension and increasing leukocyte count. Dialysis was not within her goals of care and despite antibiotics and aggressive fluid resuscitation, she passed away. Post-mortem evaluation revealed large B cell lymphoma cells in her heart, lungs, skin, pancreas, liver, thyroid, peri-adrenal fat, bladder, kidneys and pituitary. The cells were confined to the capillaries and small blood vessels without any tissue invasion, giving the extremely rare diagnosis of IVLBCL. Due to the fact that the lymphoma cells can be in any organ, the potential presenting symptoms are diverse. Coupled with the difficulty in identifying the lymphoma cells in biopsies, a diagnosis of IVLBCL is often made on autopsy. This case illustrates the importance of autopsy in securing diagnosis, the potential advantage to repeating investigations and the need to consider rare diagnosis when appropriate investigations are non-diagnostic.

The Influence of Adjuvant Chemotherapy Dose Intensity on Five Year Outcomes in Resected Colon Cancer

Suganija Lakkunarajah, Daniel Breadner2, Frances Whiston3, Larry Stitt3, Stephen Welch.

Background/ MethodsThere is evidence that achieving a dose intensity > 70 - 80% in adjuvant colon cancer treatment improves survival. 192 consecutive patients with resected stage III colon cancer that received adjuvant chemotherapy at LRCP were retrospectively analysed. Patients who received at least 6 weeks of adjuvant therapy were included. The primary objective assessed the influence of dose index (DI) and relative dose intensity (RDI) on DFS and OS at 3 and 5 years in patients receiving fluorouracil-based doublet therapy with oxaliplatin (FU-OX), or capecitabine monotherapy. FU-OX regimens, CAPOX and FOLFOX, were not compared as a vast majority of patients received FOLFOX. Results66% of patients received FU-OX, while 34% received capecitabine alone. The capecitabine group's DFS rates for 3 and 5 years were 69.3% and 64.2% respectively. OS rates were 93.4% and 87.3% respectively. FU-OX showed DFS rates of 78.2% and 72.4% in 3 and 5 years, respectively while OS rates with FU-OX were 98.4% and 95.5% respectively. Median RDI was 74% for capecitabine and 77% and 86% for oxaliplatin and FU components within FU-OX, respectively. No significant difference seen in DFS or OS when comparing patients who achieved an RDI of above versus below the median/cut-offs at 70 or 80% nor any difference based on DI. ConclusionThis retrospective analysis of 192 patients that received chemotherapy for stage III resected colon cancer showed no significant difference in outcomes based on RDI or DI. Considering the evidence from the IDEA collaboration, pooling data from multiple institutions would be warranted.

Qualitative Analysis of Patient Preferences with Regards to Resuscitation in a Non-Dichotomous System

Rachelle Lassaline, Mark GoldszmidtRavi TanejaJacqueline Torti.

Poorly held conversations with patients about resuscitation status choice can lead to a discordance between patient preference and what gets documented on their chart. Part of this discordance may be due to an oversimplification of resuscitation status choice. There is a lack of research looking at how patients make decisions about their resuscitation status outside of the traditional dichotomy of Full Resuscitation or Do-Not-Resuscitate. The purpose of this study is to explore the nuances of resuscitation status choice in a non-dichotomous system, potentially reducing the discordance between preferences and care received. Patients admitted to the CTU were interviewed by RNs on an ACP consult service, and a clinical note documenting the conversation was recorded. These clinical notes were analyzed for emerging themes using a constant comparative method. A total of 57 clinical notes have been analyzed and the following five themes were found to have significant impact on patients' decisions surround resuscitation status: ability to engage in meaningful activity, health trajectory, previous experience with healthcare, patient perceptions of death and dying, quality of life.

An Atypical Case of Resistant Familial Dysbetalipoproteinemia Uncovered by Next-Generation Sequencing

Ryan Le, Minan Abbas, Adam D. McIntyre, Robert A. Hegele.

Familial dysbetalipoproteinemia (FDBL) is a rare autosomal recessive disorder associated with homozygosity for the apolipoprotein (apo) E2 isoform. Apo E is found on chylomicron remnants, VLDL, and IDL, and mediates clearance of these lipoproteins; the E2 variant has a cysteine at amino acid residue 158, impairing clearance. IDL accumulates abnormally in FDBL, resulting in equimolar elevated cholesterol and triglyceride (TG). Patients present with mixed dyslipidemia, tuberous/tuberoeruptive xanthomas, palmar xanthomas, and premature CAD and PVD. We describe a 48-year-old male patient with severe mixed dyslipidemia (total cholesterol 11.5 mmol/L and TG 21.4 mmol/L) and tuberous xanthomas on his elbows and knees starting in his early 20s. Except for BMI of 42 kg/m2, he had no secondary factor associated with FDBL. He had been trialed on multiple medications including rosuvastatin, ezetimibe, fenofibrate, and alirocumab. Unfortunately target cholesterol and TG levels never reached on these regimens. Remarkably he has avoided complications; specifically he had neither cardiovascular disease nor pancreatitis, and his carotid intima-medial thickness was at the 50th percentile, with no plaque. We used next generation sequencing to confirm the APOE E2/E2 genotype, but also uncovered multiple additional variants including a novel ultra-rare heterozygous APOC2 nonsense mutation (p.Q92X), a known ultra-rare APOE missense mutation (p.G145D) previously associated with dominant FDBL, and a high polygenic SNP score for hypertriglyceridemia (16/28; 82nd percentile). These multiple genetic hits on top of the classical APOE E2/E2 genotype likely explain the skewed TG to cholesterol ratio, and the overall severity and refractory nature of his dyslipidemia.

Awareness and Barriers to Access of a Ministry of Health Mandated â€˜Do Not Resuscitate' Confirmation Form: An Interim Analysis

Marc Ryan Lipkus, Thulasie Manokaran, Kristine Van Aarsen, Matthew Davis.

IntroductionMany elderly patients decide that if they have a cardiac arrest, they would want not want resuscitation. In Ontario, prehospital personnel must provide resuscitation to all patients regardless of previously stated wishes or legal documentation unless they are presented a Ministry of Health mandated 'Do Not Resuscitate' Confirmation Form (MOH-DNRCF). This study aimed to evaluate the awareness of this form as well as any barriers to its completion.MethodsPatients over 70 years of age presenting to the Emergency Department were approached to complete a short survey about their wishes regarding resuscitation, awareness of the MOH-DNRCF, as well as any barriers to completion. Standard descriptive statistics were summarized using median [IQR] and simple proportions.ResultsPreliminary data of 96 patients has been collected. The median [IQR] age of patients recruited was 81 [75-88] years and 54% were female. 49/96 (51%) have wishes to not be resuscitated in the event of cardiac arrest and of those 42 (86%) are not aware of the existence of the MOH-DNRCF. Of the 7 patients who were aware of the form only 1 had completed one. Barriers to completion included the patient being unsure where to access the form and difficulty in discussing the topic. ConclusionThe majority of patients with wishes to be DNR are unaware of the MOH-DNRCF. Strategies to increase awareness of the form as well as strategies to increase ease of access should be considered to avoid resuscitation that is against patient wishes.

Hip fracture in the frail elderly: Is there enough evidence to guide management?

Andre Maddison, Marko Mrkobrada, Shiraz Malik.

Objective: To analyze the current literature on outcomes after hip fracture among the frail elderly, comparing surgical vs non-surgical management. Specifically, is there sufficient

evidence to properly inform frail elderly patients with an acute hip fracture and their families regarding trajectory and prognosis after non-surgical management?Methods: A systematic literature search and review was undertaken by 1 clinical reviewer and 1 clinical librarian using medline database key terms. The initial search retrieved 733 articles, of which 717 were excluded after reviewing abstracts. In total, 16 articles were included in the systemic review.Results: 16 studies examined surgical vs non-surgical management of hip fractures in the elderly, of which there are 2 randomized control trials, 12 observational studies, and 2 meta-analyses. A Cochrane review from 2008 of randomized control trials identified no differences in mortality or long-term pain after hip fracture in frail elderly patients treated surgically vs non-surgically. Small observational studies examining frail elderly patients with hip fractures suggest increased short and long-term survival among those treated surgically, but without improved function, mobility, or pain control.Conclusion: Surgical management is the standard of care for acute hip fractures. However, as the population becomes older and more medically complex, there appears to be inconsistent evidence to support a universal recommendation for surgical management for all frail elderly patients with acute hip fracture. Despite current beliefs, studies suggest that a significant proportion of frail elderly patients treated non-surgically for an acute hip fracture will regain baseline mobility and have mild pain only.

The effect of a multimodal exercise intervention combined with computerized cognitive training on neuropsychiatric symptoms in older adults with mild cognitive impairment: A work in progress

Joel Mahon, Manuel Montero-Odasso.

Background:Exercise has been shown to reduce neuropsychiatric symptoms (NPS) in older adults; however, there is limited evidence surrounding the use of computerized cognitive training (CCT) to reduce NPS, especially in patients with mild cognitive impairment (MCI). This study evaluates whether a 5-month program combining multimodal exercise and CCT will provide a greater reduction in NPS and increase in quality of life (QOL), than multidomain exercise alone, in older adults with MCI.Methods: Data is obtained from the SYNERGIC trial, which is a 5-month randomized control trial. 200 participants, ages 60?, will be assigned to interventions for a progressive, multimodal exercise program alone or combined with a progressive CCT program. Participants will complete an assessment battery at baseline and following intervention. Measures taken include the ADAS-Cog 13, Geriatric Depression Scale-30 (GDS-30), Generalized Anxiety Disorder 7-Item Scale (GAD-7), and Short Form Health Survey (SF-36). Multiple regression will be used to assess the association among the measures.Results: Based on previous research, it is suggested that the group which receives both interventions will have a significant reduction in NPS, and greater increase in QOL, when compared to multidomain exercise alone. Reduction in NPS will be reflected through a decrease in GDS-30 and GAD-7 scores, while improved QOL will be seen by higher SF-36 scores.Conclusion: If the predicted results occur, they suggest that the combination of multimodal exercise and CCT may be more effective at reducing NPS and improving quality of life in older adults with MCI, than multidomain exercise alone.

Novel variants in NUDT15 identified in azathioprine-intolerant patients with inflammatory bowel disease of European ancestry

J Mailloux, UI Schwarz, RB Kim, A Wilson.

Azathioprine is a commonly used inflammatory bowel disease (IBD) treatment. However, azathioprine can cause severe myelosuppression which limits its use in clinical practice. Genetic variation in the thiopurine methyltransferase (TPMT), an enzyme involved in azathioprine metabolism, accounts for a portion of individuals with increased risk of azathioprine-induced myelotoxicity due to partial or complete TPMT deficiency. There are, however, a large number of at-risk individuals who remain unidentified. Recently, genetic variation in the nudix hydrolase (NUDT15) has

been linked to azathioprine-induced myelotoxicity in Asian populations; its role in patients of Caucasian ancestry is unknown. We aimed to identify novel and/or previously identified variants in the NUDT15 gene within a population of Caucasian IBD patients with a history of unexplained azathioprine-induced myelotoxicity. Blood samples from 373 IBD patients prescribed azathioprine were obtained for DNA analysis. Among those, 27 (7.2%) developed myelotoxicity defined as a leukocyte count ? 3.3 x109/L or a neutrophil count ? 1.0x109/L. All intolerant patients were TPMT wild-type. No patients were taking allopurinol. Sanger sequencing of the coding region was performed according to reported methods to determine NUDT15 genotype in those patients with myelotoxicity. We identified two rare NUDT15 variants including NUDT15 c.1A>G (Met1?), a novel coding variant resulting in the loss of the start codon, and NUDT15 g.682 G>A, a 3'UTR variant (rs61973267). Future studies will be performed using cell-based models with transient overexpression of NUDT15 wildtype compared to the NUDT15 c.1A>G mutant to determine its functional relevance and association with thiopurine-induced toxicity.

Determining predictors of Trastuzumab Cardiac Toxicity in HER2 positive Breast Cancer Patients

Usha Manian, Samuel C SiuRodigro BagurNikolaos Tzemos.

Background: Breast cancer is the commonest neoplasia in North America. Trastuzumab therapy has revolutionized the treatment and natural history of HER2+ breast cancer but not without limitations. Cardiotoxicity remains the most clinically important adverse effect and may lead to interruption or discontinuation of Trastuzumab. AimWe evaluated established echocardiographic parameters along with novel echocardiographic techniques amongst patients with HER2+ breast cancer to optimize care in this patient group.Methods: We prospectively included patients with HER2+ breast cancer eligible for Trastuzumab therapy. All patients underwent serial transthoracic echocardiograms with a dedicated protocol. Cardiotoxicity was defined as reduction of left ventricular ejection fraction (LVEF) below 50%. Trastuzumab therapy was held if patients developed cardiotoxicity and they were started on cardiac protective medications. Trastuzumab therapy was re-introduced once LVEF normalized. Results: 220 patients were followed for up to 18 months. Cardiotoxicity occurred in 10% of the population. 69% of these patients had recovery of their EF following introduction of cardiac protective medication. Mean reduction in 3D LVEF amongst patients who recovered function compared to those who did not recover function was 45% vs 40% ($p < 0.047$). Reduced left ventricular strain and reduced dissipation energy values were the strongest predictors of cardiotoxicity. Conclusion:Contrary to common belief we found that EF above 50% predicts good outcome in all patients independent of risk factors. Dissipation energy a novel echocardiographic parameter is a strong predictor of cardiotoxicity development along with strain imaging.

Low Prevalence of Fibrate Use in Patients with Established Diabetic Retinopathy at St. Joseph's Healthcare London: A Cross-Sectional Study

Justin Morein, Jeffrey L. Mahon, Artem Uvarov, Tamara Spaic, Irene Hramiak, Selina L. Liu.

BACKGROUND: Diabetic retinopathy (DR) is the leading cause of blindness in adults in Canada. Effective treatments to prevent/delay DR-related vision loss include glycemic and blood pressure control, laser photocoagulation, and fenofibrate, a fibrate agent. Current guidelines recommend considering fenofibrate (in addition to statins) to delay DR progression in those with type 2 diabetes and established DR. Despite this, fenofibrate is not widely used. This study's goal was to determine the prevalence of fibrate use and factors predictive of fibrate use in patients with known DR. METHODS: We performed a cross-sectional study of active adult diabetes patients with known DR followed by the St. Joseph's Healthcare London (SJHC) Diabetes Clinics. Descriptive statistics were summarized and logistic regression was used to determine

factors predictive of fibrate use. RESULTS: In 1341 subjects with DR, the prevalence of fibrate use was 3.0%. Factors predictive of fibrate use were type 2 diabetes (OR 3.30, 95% CI 1.03-12.57), ACE-inhibitor/ARB use (OR 2.79, 95% CI 1.17-8.05), dyslipidemia (OR 3.53, 95% CI 1.26-13.48) and serum triglyceride (mmol/L)(OR 1.36, 95% CI 1.11-1.64). Severe DR was associated with lower odds of fibrate use (OR 0.46, 95% CI 0.22-0.95). CONCLUSIONS: Despite strong evidence supporting the use of fenofibrate to delay DR progression, the prevalence of fibrate use in patients with known DR followed at SJHC is extremely low. This study highlights an important care gap in DR management. Further research is required to elucidate barriers to fibrate use in those with known DR.

Nobiletin corrects intestinal lipid metabolism in Ldlr-/- mice fed a high-fat diet

Nadya M. Morrow, Dawn E. Telford, Brian G. Sutherland, Jane Y. Edwards, Murray W. Huff.

Supplementation of the citrus flavonoid nobiletin to a high-fat, high-cholesterol (HFHC) diet in Ldlr -/- mice prevents obesity, insulin resistance, hepatic steatosis, dyslipidemia and atherosclerosis, in part, through enhanced hepatic fatty-acid (FA) oxidation. Intriguingly, Ldlr-/- mice fed a HFHC diet, but not chow, retain lipids in the jejunum of the small intestine, even in the fasted state. Addition of nobiletin to the HFHC diet prevents this lipid accumulation, which may contribute to the metabolic protection. To determine the mechanisms through which nobiletin prevents jejunal lipid accumulation, Ldlr-/- mice were fed HFHC (42% kcal fat, 0.2% cholesterol), or HFHC + nobiletin (0.3%w/w; n=16/group) for 10 weeks. Jejunal FA-synthesis and triglyceride (TG) synthesis were decreased, whereas jejunal FA-oxidation was unchanged. HFHC increased fasting (6 hr) plasma levels of total TG 2.5-fold, chylomicron TG 1.6-fold and apoB48 1.4-fold compared to nobiletin + HFHC. Postprandial experiments employing a poloxamer-407 injection and a 3H-TG-containing olive oil gavage showed that nobiletin increased TG mass and radioactivity secretion into plasma compared to HFHC alone. Additionally, nobiletin increased chylomicron-TG secretion 1.3-fold, although apoB48 secretion was unchanged, suggesting that nobiletin increases chylomicron-TG content. Nobiletin prevents HFHC-diet induced cytoplasmic lipid droplet formation within jejunal enterocytes 2 hours post-gavage. Nobiletin prevents HFHC-diet induced shortening of the small intestine and increases plasma levels of GLP-1, and likely its co-secreted, intestinotrophic peptide, GLP-2. In conclusion, nobiletin attenuates intestinal lipid accumulation through decreased de novo lipogenesis and increased chylomicron-TG secretion through improved intestinal insulin sensitivity and a possible GLP-2-dependent mechanism.

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

Omar Mourad, 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.

The impact of genetic varation in ABCC4 on azathioprine-induced myelotoxicity in patients with inflammatory bowel disease of European Ancestry.

Wilson, A.**, Nari,J.**, Kim,R.,B.

Background: Azathioprine, treatment for inflammatory bowel disease (IBD), is associated with a risk of myelotoxicity that can lead to morbidity and rarely mortality. Genetic variation in the TPMT gene, important for azathioprine metabolism, predicts a portion of individuals at risk of azathioprine-induced myelotoxicity; however, not all at-risk individuals are identified. The multi-drug resistance protein (MRP)-4 (ABCC4 gene) is involved in the cellular efflux of toxic azathioprine metabolites. Single nucleotide variations (SNVs) in ABCC4 have been linked to myelotoxicity in azathioprine-exposed cancer populations. We propose to evaluate the association between genetic variation in ABCC4 and the risk of azathioprine-induced myelotoxicity in IBD patients. Methods: A retrospective cohort study was carried out in 373 azathioprine-exposed IBD patients. All subjects underwent screening for four SNVs in ABCC4 (rs11568658, rs3765534, rs2274407 and rs3742106) using Taqman allelic discrimination and were assessed for azathioprine-induced myelotoxicity defined as a leukocyte count less than 3.3 x109/L or a neutrophil count less than 1.0x109/L.Results: Twenty-seven patients met the criteria for azathioprine-induced myelotoxicity. All subjects were TPMT wild-type. The minor allele frequencies for each SNV were 0.012 (rs11568658), 0.013 (rs3765534), 0.101 (rs2274407), and 0.466 (rs3742106) respectively. Univariate analysis did not reveal a correlation between any ABCC4 SNV and risk of azathioprine-induced myelotoxicity.Conclusion: Targeted SNVs in ABCC4 were not significantly associated with azathioprine-induced myelotoxicity in an IBD population. Given the large amount of genomic variability in ABCC4, a broader, rather than targeted, approach to assessing said variability and its link to myelotoxicity would better address this clinical question.

Cardiovascular Outcomes in Heart Failure Patients Undergoing AV-Nodal Ablation plus CRT versus AF Ablation: A Systematic Review and Network Meta-analysis

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Heart failure (HF) and atrial fibrillation (AF) often occur concomitantly and the combination portends a worse prognosis than either alone. While cardiac resynchronization therapy (CRT) may have some benefit in AF patients, the outcomes are still not as good as in patients in sinus rhythm (SR). As of now, it is still unclear whether AF ablation is more effective than AV nodal ablation plus with CRT in a HF population. We therefore aimed to do a systematic review and meta-analysis to compare cardiovascular outcomes among the following groups of HF patients with LV systolic dysfunction: 1. AF treated medically 2. AF treated with AV nodal ablation and 3. Sinus Rhythm. A literature search was conducted on Medline and Embase applying permutations on the search terms ‘ablation’ and ‘heart failure’. The study was conducted and reported in accordance with PRISMA6 guidelines. For our analyses, eligible studies will include a HF population with LV systolic dysfunction and compare outcomes between at least two of the following groups: 1. AF treated medically 2. AF treated with AV nodal ablation 3. Sinus Rhythm. We will exclude non-English language studies. The primary outcome was all-cause mortality. Secondary outcomes included cardiovascular mortality and HF-hospitalizations. Results indicate AF catheter ablation is super to AV nodal ablation plus CRT at reducing both all-cause and CV mortality as well as HF hospitalization in specifically chosen HF patients.

CEP Chemotherapy in Relapsed or Refractory Aggressive Lymphomas: A Retrospective Review

Brent Parker, Chai Phua, Lakshman Vasanthamohan, Selay Lam, Joy Mangel, Kang Howson-Jan.

Background:There is no standard of care for the management of patients with aggressive lymphomas in the relapsed or refractory settings. The combination of lomustine (CCNU), etoposide and prednisone (CEP) is an oral palliative chemotherapy regimen unique to the London Regional Cancer Program (LRCP) for relapsed or refractory aggressive lymphomas. CEP is a modification of previously established chemotherapy regimens including CEPP (cyclophosphamide, etoposide, procarbazine and prednisone) and LEMP (lomustine, etoposide, methotrexate and prednisone). There is no published data regarding the efficacy or safety of CEP in relapsed or refractory aggressive lymphoma.Methods:We conducted a retrospective review of patients treated between January 1, 2014 and May 24, 2018 at LRCP with aggressive lymphomas who received CEP at any point during their treatment. The primary endpoints included overall response rate and duration of response. Secondary endpoints included overall survival, progression-free survival and treatment safety. Data was analyzed using Student's t-tests, Cox proportional hazards models and Kaplan-Meier survival curves with p values < 0.05 considered significant. Results:79 patients who received CEP were screened and 50 were included in the final analysis. The median age of patients starting CEP was 76 and the median number of prior therapies was 2. Data analysis is currently in progress with final statistical analysis results pending.Conclusions:In summary, we hypothesize that CEP is efficacious and relatively well tolerated in patients with relapsed or refractory aggressive lymphoma. Further studies are necessary to compare the efficacy of CEP to other palliative chemotherapy regimens available in this setting.

Mitochondrial Permeability Regulates Heart Graft Ischemia-Reperfusion Injury and Rejection

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

A growing body of evidence indicates that mitochondrial permeability transition pore (mPTP) formation plays a crucial role in necroptosis - a programmed form of necrosis. Previously, we showed that inhibiting cyclophilin D (CypD), a critical regulator of mPTP, decreases necroptosis and that CypD-deficient heart grafts exhibit prolonged survival. In this study, we extended our findings to a clinically relevant scenario of cold ischemic organ storage followed by transplantation. To model ischemic insult in vitro, endothelial cells (ECs) were exposed to hypoxia in oxygen-depleted glucose-free medium. To model the reperfusion event, ECs were then transferred to a normoxic incubator in oxygenated glucose-rich medium. Necroptosis was induced using TNF? and a pan-caspase inhibitor and monitored by live cell imaging system and flow cytometry. For in vivo studies, C57BL/6 heart grafts were treated with cold ischemia for 4 hours before transplantation into BALB/c mice. Histopathological grading of ischemia-reperfusion injury (IRI) was done by a pathologist. Our data indicate that necroptosis plays a significant role in hypoxia induced EC death and that inhibition and silencing of CypD decreased hypoxia induced necroptosis. Our in vivo studies confirmed that CypD ablation in donor heart grafts attenuates transplantation associated IRI and donor heart graft rejection. Interestingly, apoptosis inducing factor (AIF) silencing also decreased hypoxia induced necroptosis. Following IRI, apoptosis inducing factor (AIF), a mitochondrial oxidoreductase, translocates to the nucleus and induces DNA fragmentation. Our studies indicate that CypD and AIF play significant roles in EC necroptosis following IRI and that AIF may be the downstream effector of necroptosis.

A Systematic Review of Risk Factors for Sleep Disruption in Critically Ill Adults

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Introduction: Sleep disruption is common in intensive care unit (ICU) patients and may have

deleterious effects. There has been no comprehensive exploration of all potential risk factors associated with sleep disruption in ICU patients. Objective: We conducted a systematic review of the literature to identify premorbid, illness-related, and ICU-acquired risk factors associated with disrupted sleep in ICU patients. Methods: We conducted a systematic search of the literature to identify relevant articles that assessed sleep quality in adult ICU patients and reported one or more risk factors for sleep disruption in ICU . We screened citations and conducted full-text review to identify relevant studies and extracted risk factors for their association with sleep disruption. Results: Of 5148 citations, we identified 67 that met our inclusion criteria. Among premorbid factors, poor sleep quality and use of sleep medications at home were associated with sleep disruption in ICU. Among illness-related factors, patients commonly reported pain and psychological distress as sleep disruptive. Delirium was also associated with sleep disruption in the ICU. ICU-acquired environmental risk factors included restricted mobility, care interventions, and noise. Corticosteroids and antipsychotics were associated with sleep disruption. In mechanically ventilated patients, pressure support ventilation and patient-ventilator asynchrony were risk factors associated with sleep disruption. Conclusion: These findings may be used to identify high-risk patients and develop targeted, evidence-based interventions to minimize sleep disruption in the ICU. Further research is needed to better stratify risk factor importance and determine the impact of strategies aimed at mitigating identified risk factors.

Impact of Propofol Sedation on Colonoscopy Quality - Findings of the Southwest Ontario Colonoscopy Cohort

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Background: The use of propofol during colonoscopy has gained increased acceptance due to deeper anesthesia compared to conscious sedation. Whether propofol sedation leads to improved colonoscopy quality is unknown and the aim of our study. Method:We examined the association between use of propofol sedation and colonoscopy quality metrics, including adenoma detection rate (ADR), polyp detection rate (PDR), cecal intubation, and perforation, using colonoscopy quality data prospectively collected by the Southwest Regional Cancer Program, a division of Cancer Care Ontario. All colonoscopies performed for any indication across 21 hospitals in Southwest Ontario between April 2017 and December 2018 were identified. Data collected included patient and endoscopist demographics, procedural indication, bowel preparation quality, type of sedation, cecal intubation, polyp detection, and histology. Multi-variable models were built to assess the relationship between propofol sedation and adenoma detection rate (ADR), polyp detection rate (PRD), cecal intubation, and perforation risk. Results: In total, 23,903 colonoscopies were identified, of which 8,533 (35.6%) procedures were performed with propofol sedation. There were no significant differences in ADR (22.6% vs. 21.6%, p= 0.156), PDR (43.9% vs. 42.6%, p=0.05), or cecal intubation rates (97% vs 96.7%, p-0.192) between the two groups on univariate or multivariate analyses. The event rate for perforation was too low for a meaningful comparison in this analysis (1 vs. 2 events).Conclusion: In this large colonoscopy cohort, propofol sedation was not associated with improved ADR, PDR, or cecal intubation rates.

Timing and Completion Rates of Adjuvant Chemotherapy Following Definitive Surgery for Pancreatic Head Adenocarcinoma

Sheikh Hasibur Rahman, Rachel Liu, Daniel Breadner, Sanjay VB Patel, Carlos Garcia-

Ochoa, Anton Skaro, Kenneth Leslie, Stephen Welch.

Background:Prognosis of resectable pancreatic adenocarcinoma improves with the use of adjuvant chemotherapy, however the importance of timing and chemotherapy completion is not well understood. Methods:A cohort analysis was performed on patients who underwent pancreatic resection for ductal adenocarcinoma from a single tertiary hospital between 2007 and 2016. Patients who completed adjuvant chemotherapy were compared to those who did not. Overall survival (OS) and disease-free survival (DFS) were assessed using a Cox proportional hazards model adjusting for confounding variables. A logistic regression analysis was performed to evaluate what factors may influence adjuvant chemotherapy completion rates following resection.Results:The cohort included a total of 150 patients eligible for chemotherapy, 98 received adjuvant chemotherapy with 54 completing treatment. DFS at 1-year was significantly improved with completing chemotherapy (HR 0.225, $p < 0.01$). However, this effect was not seen for overall DFS (HR 0.901, $p = 0.76$). There were no differences in 1-year survival (HR 0.997, $p = 0.99$) or OS (HR 0.993, $p = 0.98$) between these groups. Chemotherapy completion rates decreased with increasing age ($p < 0.01$) and improved in patients receiving adjuvant radiation ($p < 0.01$). The median time from surgery to chemotherapy was 64 days. Sub-group analysis showed chemotherapy completion improved with adjuvant radiation (OR 4.31, p= 0.001), however, these patients had a reduced 1-year DFS ($p < 0.01$). Conclusion:Completion adjuvant chemotherapy following pancreaticoduodenectomy appears to have an early and non-sustained DFS benefit, and survival did not appear to be adversely affected; complete and partial adjuvant chemotherapy have similar long-term benefits

Treatment outcomes in transplant ineligible multiple myeloma patients aged 80 and above treated with novel agents: A systematic review

Sadaf Rahman, Cody Sider, Martha Louzada, Chai Phua.

Background: Multiple myeloma is a plasma cell malignancy that is primarily a disease of the elderly, with an estimated one third of patients aged 75 or above1. Older patients are typically transplant ineligible, often have many comorbidities and may be frailer than their younger counterparts, making treatment decisions more complex. Novel therapeutic agents have demonstrated significant improvements in multiple myeloma outcomes, even in older age groups. Purpose: There is a paucity of data to guide treatment decisions in newly diagnosed multiple myeloma patients aged 80 or above1. Our systematic review assesses overall survival and progression-free survival in newly diagnosed, transplant-ineligible multiple myeloma patients aged 80 and above treated with a novel therapeutic agent. Methods: MEDLINE and EMBASE databases were searched until March 4, 2019 for retrospective, prospective or randomized controlled trials enlisting patients aged 80 and above with multiple myeloma who were treated with a novel therapeutic agent as first-line therapy. Screening and full text review was conducted by two independent reviewers.Results: A total of 1683 articles were retrieved. An initial 206 articles have been excluded as duplicates. Screening is ongoing, with a remainder of 770 articles to be sorted.Conclusions: TBD.

A Comparison of Liver Fibrosis and Simple Steatosis Assessment using Gadoxetic-acid Enhanced MRI with MR Elastography and MRI Fat Fraction

Rai, Rajbir, Tirona, Rommel Kassam, Zahra Beaton, Melanie.

BackgroundNAFLD is a spectrum of disease ranging from simple steatosis to steatohepatitis, with or without fibrosis. The gold standard for NASH diagnosis remains liver biopsy. Due to risks and sampling error, there has been an increased use of non-invasive modalities. MRI-fat fraction (MR-FF) is validated for assessment of

hepatic steatosis and MR elastography (MRE) for fibrosis. Both requires special software and MRE special hardware not readily available. As such, a more readily available modality known as gadoxetate enhanced MRI (GE-MRI), may be able to differentiate NAFLD.AimCan GE-MRI differentiate NAFLD from controls compared to MR-FF. Can GE-MRI differentiate simple steatosis from NASH compared to MRE.MethodThis cohort study comparing healthy controls and NAFLD patients. NAFLD patients were divided into those with simple steatosis or NASH based on liver biopsy or MRE. All patients underwent MR-FF, MRE, and GE-MRI.Results17 patients were studied. Five control and 12 NAFLD patients. 3 had biopsy proven NASH and 4 had fibrosis based on MRE, 5 had simple steatosis. GE-MRI was able to differentiate healthy patients from NAFLD with a mean enhancement difference of -35.07 Â± 11.66 (p=0.0088). GE-MRI was unable to differentiate hepatic steatosis from NASH with statistical significance, but there was a mean difference in enhancement of -18.67 between the groups.ConclusionThis study shows the difference in enhancement on GE-MRI is much lower in patients with fatty liver and liver fibrosis. Given the small patient size, specific cut-off values could not be established.

A Fungal Foe: Bilateral Adrenal Histoplasmosis Manifesting as Primary Adrenal Insufficiency

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Histoplasmosis is a fungal pathogen rarely associated with primary adrenal insufficiency.A 72-year old woman from Southwestern Ontario presented with a 2-month history of progressive weakness, nausea, presyncope, and 15-pound weight loss. Past history was significant for remote melanoma and ductal carcinoma in-situ, both in remission. She was on no prescribed medications. She was tanned (despite no recent travel) with a blood pressure of 94/65 mmHg and presyncope on standing. Serum sodium was 128 mmol/L (normal 137-145 mmol/L), potassium 4.1 mmol/L (normal 3.5-5.0 mmol/L), cortisol 50 nmol/L (133-537 nmol/L) and ACTH 187.9 pmol/L (1.98-12.47 pmol/L), consistent with primary adrenal insufficiency. Glucocorticoid and mineralocorticoid replacement were initiated. CT thorax/abdomen/pelvis revealed bilateral adrenal enlargement with heterogeneously enhancing adrenal masses suspicious for metastases but no other evidence of malignancy. Liver histology demonstrated multiple necrotizing granulomas with fungal spores consistent with Histoplasma capsulatum, despite negative fungal serology. Given the most likely cause of primary adrenal insufficiency being histoplasmosis, definitive therapy with itraconazole was initiated. Disseminated histoplasmosis causing primary adrenal insufficiency in an immunocompetent host is rare, with only 33 prior published cases. Most cases occur in endemic areas, such as Southwestern Ontario, possibly arising from a transient insult to cellular immunity. Although remission rates for H. capsulatum can be up to 90% with antifungal therapy, adrenal insufficiency rarely resolves. This case emphasizes two points: 1. Disseminated histoplasmosis can occur in an immunocompetent host in Southwestern Ontario and 2. The cause of adrenal insufficiency should be investigated thoroughly to determine appropriate management.

Recurrent Infective Endocarditis In People Who Inject Drugs

Laura Rodger, Meera Shah, Seyed Hosseini, Michael Silverman.

Background: Infective endocarditis (IE) is increasing among persons who inject drugs (PWID)(1) and has high morbidity and mortality (2). Recurrent IE in PWID is likely common, but not well described.Methods: Retrospective chart review between February 2007-March 2016. Included were adult inpatients (>18) at tertiary care centers in London, Ontario with definite IE based on the Modified Duke's Criteria. The main objectives were to characterize recurrent IE in PWID, identify whether fungal infections were more common in recurrent endocarditis and establish whether fungal infection was associated with a higher mortality.Results: 390 patients had endocarditis with 212/390 in PWID. 68/212 (32%) PWID had a second episode with 28/212 (12%)

having additional recurrences. Second episode IE is more common in PWID (14/179 [6.2%] vs 68/212 [24.3%]; p<0.001)). In PWID, fungal IE is more common in second episodes (1/212, 0.5% vs 5/68, 7.4%, p=0.004). Additionally, fungal infections were associated with mortality in second episode IE in PWID with an adjusted OR of 16.49 (95%CI 1.12, 243.17, p=.041). Despite recurrent infection, likely due to continued drug use, there was a low rate of referral to addiction treatment (14/68, 20.6%).Conclusions: PWID have a high risk of recurrent endocarditis, where episode characteristics are similar to their index infection. Fungal endocarditis is more common in second episode endocarditis and is associated with increased mortality. Empiric antifungal treatment should be further explored in recurrent IE in PWID.

IN VITRO FUNCTIONAL CHARACTERIZATION OF RARE GENETIC VARIANTS IN THE HEPATIC BILE ACID/DRUG TRANSPORTER NTCP

Laura E. Russell, Markus Gulilat, Ute I. Schwarz & Richard B. Kim.

Background: Sodium taurocholate co-transporting polypeptide (NTCP) is a liver membrane-bound transport protein. NTCP, encoded by gene SLC10A1, mediates hepatic bile acid and rosuvastatin uptake. The aim of this study is to assess transport of substrates taurocholic acid and rosuvastatin by rare genetic variants of NTCP. Additionally, in silico prediction algorithms will be compared for accuracy of functional prediction. Methods: Rare, missense genetic variants in SLC10A1 were identified using open-access genomic databases and targeted next-generation sequencing (NGS). Plasmids containing NTCP were mutagenized and transiently transfected into HEK293T cells. Uptake of taurocholic acid and rosuvastatin were assessed. Results: Thirty-four rare, missense variants with no associated functional data were identified in SLC10A1. Uptake of taurocholic acid was reduced by more than 75% for 7/34 variants. Uptake of rosuvastatin was reduced by more than 75% for 14/34 variants. One variant, p.G191R, displayed substrate specificity. All in silico algorithms categorized at least one loss of function variant as benign. Conclusions: Recent advances in technology have yielded large genomic datasets which show the abundance of rare genetic variation in the population. Accordingly, in silico models are becoming more critical to identify variants of potential clinical significance. Our study shows that concordance between in silico prediction and observed in vitro activity is not sufficiently predictive. Caution must be exercised while prioritizing variants based on predictive algorithms. Validation using cell-based assays remains the most accurate method to determine the effect of genetic variation on protein function.

A NOVEL GENETIC MUTATION ASSOCIATED WITH FAMILIAL HYPOCALCIURIC HYPERCALCEMIA: CASE REPORT

Sabreena Sadat, Amanda Berberich, Robert A. Hegele, Ruth McManus.

Introduction: Familial hypocalciuric hypercalcemia(FHH) is a rare, benign autosomal dominant genetic condition, characterized by mild hypercalcemia with a normal or mildly elevated parathyroid hormone [PTH] level. FHH must be considered in the differential diagnosis of primary hyperparathyroidism(PHPT). Low fractional excretion of urinary calcium is often sufficient to distinguish FHH from PHPT, but in cases where diagnostic uncertainty exists, genetic confirmation may be helpful to prevent unnecessary clinical concern, surveillance and treatment risk.Case report: A 62-year-old woman was referred with a 20 year history of asymptomatic hypercalcemia (albumin-corrected range: 2.6-2.8mM) with an inappropriately normal PTH (4.9pmol/L). She was not taking lithium or thiazide diuretics. She reported a sister with high serum calcium levels. Her laboratory investigations showed a 24 hour urine calcium of 7.16 mM/day with a 1.4% fractional excretion of urinary calcium. Her serum protein electrophoresis and bone scan were negative. Genetic testing identified a novel heterozygous missense mutation in calcium sensing receptor (CaSR) (c.647A>G; p.D216G).Discussion: CaSR protein plays an important role in regulating calcium homeostasis. A loss of function mutation

in the CaSR gene increases the set point for sensing calcium, leading to calcium hyposensitivity and resultant hypercalcemia. DNA sequencing of the CaSR gene in this patient revealed a missense mutation resulting in an aspartic acid being exchanged for a glycine at amino acid 216 in the extracellular domain of the CaSR. To our knowledge, this hasn't been previously reported, but is predicted to be disease-causing using in-silico prediction models.

Emergency Department-Performed Renal Point-of-care Ultrasound for the Assessment of Obstructive Uropathy: Accuracy and Impact of a Training Curriculum and Ongoing Educational Interventions

David Bastien, D. Thompson, F. Myslik, K. Van **Aarsen, J. Serhan**, B. Hassani.

Introduction--Hydronephrosis, the de facto measure of obstructive uropathy (OU), can be evaluated using renal Point-of-Care Ultrasound (rPOCUS). This educational initiative developed a rPOCUS curriculum for Emergency Department (ED) physicians and evaluated if feedback/quality assurance (QA), leads to improvement in image acquisition and technique and interpretation of hydronephrosis.Methods--Physicians were randomized into QA or control group (NQA) and attended a one-day training session. Participants then performed POCUS scans on ED patients where formal renal-US was clinically indicated. QA group received expert feedback on scans for 10 weeks. Sensitivity and specificity were calculated compared to formal scans using chi-square tests. Feedback was reviewed for future improvements. Participants completed surveys at study start and end regarding initiative effectiveness and barriers/comfort with POCUS measured with a Likert scale (Not at all(1)-Very(7)). Results--Fourteen ED physicians participated. Most common barrier to utilizing rPOCUS was lack of knowledge/training (78.6%). 63 scans were reviewed. Common feedback included breath-holding (69.7%), using color doppler (48.5%) and including transverse sweep (36.4%). Sensitivity and specificity were better in QA versus NQA group though not statistically significant. Ten post-surveys were completed; all reported improved comfort with rPOCUS (median [IQR]: ?+2 [1-3]). Comfort rating for using POCUS without formal scan remained low (median [IQR]: 3.50 [1.8-4.2]). The training initiative was rated highly (median[IQR]: 5.50 [4.8-7.0]). Conclusions--Although the initiative was rated highly effective and improved comfort, physicians did not feel comfortable solely using POCUS to diagnose OU. Further initiatives are needed before rPOCUS is used as the primary investigation.

Risk Factors of Infective Endocarditis in Persons Who Inject Drugs

Meera Shah, Ryan Wong, Laura Ball, Esfandiar Shojaei, Michael Silverman.

Background: Rising incidence of infective endocarditis (IE) rates in London has been a major concern, particularly among persons who inject drugs (PWID). The details of injection practices leading to this are not well characterized.Methods: A case-control study through one-on-one interviews was conducted to understand risk factors and injection practices associated with IE among PWID. Eligible participants had to have injected drugs within the last 3 months, be >17 years old and either never had or be currently admitted for an IE episode. Cases were recruited from the tertiary care centers and controls were recruited from addiction clinics and harm reduction services in London.Results/Conclusions: We had 33 cases (PWID IE+) and 107 controls (PWID but IE-). We found a non-significant association between Hydromorph Contin injections and IE with 90.9% of cases and 81.4% of controls reporting HMC use (p=0.197). We suspect that the very high prevalence of HMC use made our sample size too small to identify a significant association. Injection of methamphetamine was borderline protective with 78.4% in controls and 54.5% in cases (p=0.07). Injection into the feet (57.6% cases; 36.6% control; p= 0.034) and into the neck (63.6% case; 46% control; p=0.079) were also associated with IE. We suspect that the association of using alternative sites of injection and IE likely reflects the greater difficulty in

accessing these sites and thus a greater likelihood of contamination. This also may be a surrogate marker for more venous damage from previous injections and thus more frequent drug use.

Meta-analysis of 1st and 2nd generation Tyrosine Kinase Inhibitors in Anaplastic Lymphoma Kinase (ALK) Positive Non-Small Cell Lung Cancer

Dr Daniel Breadner, **Dr. Sumugan Shanmuganathan**, Dr. Jacques Raphael.

Background: Lung cancer remains the leading cause of cancer death in Canada. Approximately 20% of Canadians with metastatic non-small cell lung cancer (mNSCLC) have an oncogenic mutation which can be targeted, leading to better outcomes. Chromosomal rearrangements of the anaplastic lymphoma kinase (ALK) gene lead to drastic responses to tyrosine kinase inhibitors (TKI) targeting the ALK gene, and are present in 3% of mNSCLC. Crizotinib was the first approved ALK TKI for the treatment of ALK mNSCLC, there has since be a new generation of ALK TKIs approved.Methods: The databases of PubMed and Web of Science and the abstracts of major oncology conferences were searched for randomized controlled studies comparing ALK TKIs versus chemotherapy and 2nd generation ALK TKIs versus 1st generation ALK TKIs. Published hazard ratios for progression free survival (PFS) and overall survival (OS) were assessed, including for reported subgroups. Intracranial disease efficacy and adverse events were also examined using the random effects model and fixed effects model. Results: Nine randomized clinical trials were included in the analysis, all reported significant improvements in PFS, but no individual trials reported a significant improvement in OS, owed to limited follow-up and cross-over. Pooled OS data will be presented along with pooled subgroup assessments and comparisons of intracranial efficacy of 1st versus 2nd generation ALK TKIs.

The Validity of Established VO2peak Estimates in a Cardiac Rehabilitation Population

Sharma N, Hartley T, Faubert C, McKelvie R, Suskin N.

Cardiorespiratory fitness (CRF), expressed as peak oxygen consumption (VO2peak), is strongly predictive of mortality and morbidity. Patients entering the Cardiac Rehabilitation and Secondary Prevention (CRSP) Program at St Joseph's Hospital (SJH) undergo CRF assessment by a graded cardiopulmonary exercise test (CPET) to stratify residual risk post-hospital-discharge and to determine initial fitness to individualize CRSP exercise training. CPET measured VO2peak is also reported as a percentage of expected results, based on the Wasserman formula. The Wasserman formula was derived from small (approx. 75 and 300), healthy populations almost 40 years ago. The American Heart Association (AHA) has recognized the need for more appropriate reference formulas. One such formula has been derived from the "Fitness Registry and the Importance of Exercise National Database" (FRIEND), but excluded individuals with diagnoses and hence medications (such as beta-blockers) common in CRSP patients. This study aims to compare Wasserman and FRIEND formulas to measured CPET results from SJH, to determine if a population-specific equation has merit. Results from April 2017 to September 2018 were included, yielding a sample of 1033. The FRIEND prediction correlated moderately ($R=0.581$) and significantly ($p<0.001$) with measured VO2peak. The Wasserman prediction had a higher correlation ($R=0.687$, $p<0.001$). Both FRIEND and Wasserman tend to over-predict VO2peak in the CRSP patient population, although a small proportion (7.1% and 4.8%, respectively) achieved >100% predicted VO2peak. Given the known existence of CAD in the CRSP population, underperformance compared to predictive equations may be expected. The generation of a CRSP patient-specific equation is ongoing.

Role of Lgr5+ cells in tuft cell-derived colitis-associated colon cancer

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A major risk factor for colorectal cancer (CRC) is inflammatory bowel disease (IBD). However, the mechanism by which colitis leads to CRC is still unknown. We previously showed that Dclk1+ tuft cells serve as a cellular origin of CRC upon colonic inflammation. In this study, we explored the mechanism by which inflammation contributes to tuft cell-derived cancer initiation. We hypothesized that colonic inflammation leads to dedifferentiation of Dclk1+ tuft cells to an Lgr5-expressing stem cell state susceptible to tumor initiation.To conduct Dclk1+ cell lineage tracing and cell-specific knock-out of the tumor suppressor APC, we crossed Dclk1-CreERT2 mice to ROSA26-tdTomato and APCfl/fl mice. To examine the role of dedifferentiation in colonic tumor initiation, the mice were further crossed to Lgr5-DTR-eGFP mice (Lgr5DTR;Dclk1/APCfl/fl). These mice were given tamoxifen and dextran sodium sulfate (DSS) to induce colitis and subsequent tumorigenesis. The mice were additionally administered diphtheria toxin (DT) post DSS injury to ablate Lgr5+ cells.Ablation of Lgr5+ cells significantly reduced colonic tumors. Interestingly, two weeks post DSS-colitis, we could detect Dclk1+ cells that co-expressed Lgr5. Analysis of colonic mRNA levels revealed significantly reduced Lgr5 and increased RSPO1 and RSPO3 levels in DSS-treated mice.Upon DSS-induced colonic injury, Dclk1+ tuft cells express the stem cell marker Lgr5 prior to initiation of colonic tumorigenesis. These data suggest that dedifferentiation of Dclk1+ cells to a stem cell state may play an important role in the development of colitis-associated CRC and provides insight into the mechanism by which Dclk1+ cell derived colonic tumors arise.

Sex differences in Motor and Cognitive Trajectories before Dementia

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Motor and cognitive decline assessed using serial measures of gait speed and MoCAchanges have been associated with a higher risk for incident dementia versus cognitive decline or motordecline alone. Dual decliners (concurrent motor and cognitive decline) mayrepresent a different phenotype for dementia risk. However, how sex affects these interactions anddementia risk is unknown. We aim to examine the role of sex in cognitive and motor trajectories beforedementia. Data from the Gait and Brain Study, a longitudinal prospective cohort study with 10 years offollow-up, comprised of community-dwelling participants aged 65 and older free of dementia atbaseline were followed every 6 months.Males with purely cognitive decline progressed more to dementia(males:35.3% versusfemales:13.6%), while females with purely motor decline progressed more to dementia(females: 31.8%versus males: 23.5%). Females with dual decline had a greater percentage of progressing todementia versus males (40.9% versus 17.6%). Hazard ratios were higher for motor and dualdecliners in females (motor: HR:2.46, p=0.193; cognitive: HR:1.21,p=0.818.; dual: HR: 3.83, p=0.045) and for cognitive decliners in males(motor: HR:2.46, p=0.193; cognitive: HR:1.21, p=0.818.; dual: HR: 3.83, p=0.045). Cognitive decline may be a stronger predictor of progression to dementia in males, and gait speed and dual decline may be a stronger predictor in females. Sex affects motor and cognitive trajectories decline and may help increase accuracy of dementia risk prediction. Future studies are need to understand mechanisms underlying our findings.

A phase I study of fixed dose vinorelbine and escalating doses of ifosfamide in first-line advanced non-small cell lung cancer

Julian Surujballi, Daniel Breadner, Donald Morris, Anne O'Connor, Frances Whiston, Larry Stitt, Mark Vincent.

Objective: To examine vinorelbine and ifosfamide combination chemotherapy as a possible alternative to platinum doublet chemotherapy in chemotherapy-naïve patients with advanced NSCLC via phase I trial. **Methods:** The dose of vinorelbine was held constant at 25 mg/m^2 on days 1 and 8 of a 21-day cycle. Equal doses of ifosfamide were administered after vinorelbine on days 1 and 8 (escalated from 2.0 g/m^2 upward). Dose-limiting toxicities (DLT) were defined as grade 4 hematologic or grades 3 or 4 non-hematologic toxicities. Patients who died before receiving chemotherapy were analysed as having DLT. If no patients experienced DLT in cycle 1, the next cohort was recruited. If ≥ 2/6 patients experience DLT, that cohort's dose was declared the maximum tolerated dose (MTD). If ≤ 1/6 experience DLT in the cohort below the MTD, that was declared the recommended phase II dose. **Results:** The MTD was 2.25 g/m^2 and the recommended phase II dose was 2.0 g/m^2. Unfortunately, 58% of all patients suffered DLT. Dose limiting toxicities were largely hematologic, but higher doses of ifosfamide saw toxicities including confusion, memory loss, anorexia, and impaired motor function. There was no significant difference in overall survival between doses. 12-month survival was 21.3% (Kaplan-Meier estimate), lower than the previously described 33% for platinum doublet chemotherapy. 6 "excellent responders" were identified who survived between 20 and 45 months from registration. **Conclusion:** There was no significant evidence that vinorelbine and ifosfamide combination could provide an alternative to platinum doublet chemotherapy based on an inferior 12-month survival and high rate of DLT. The 6 incidentally identified "excellent responders" may be explained by chance or lead-time bias, but may also have been early evidence of favourable response to then unknown mutations, such as EGFR. Further study may be relevant to examine synergy between vinorelbine or ifosfamide with modern targeted therapies.

Bloodstream Infections in Persons Who Inject Drugs on Treatment for Infective Endocarditis

Charlie Tan, Esfandiar Shojaei, Meera Shah, Adeel Sherazi, Michael Silverman.

Objective: Persons who inject drugs (PWID) being treated for infective endocarditis (IE) remain at risk of bloodstream infections (BSIs). We sought to characterize BSIs in this population and determine clinical factors associated with their development. **Methods:** We conducted a retrospective cohort study of episodes of definite IE based on the modified Duke criteria in PWID ≥18 years of age, admitted to tertiary care centres in London, Ontario from March 1 2007 to March 31 2018. We characterized cases of new BSIs among this population and compared them against episodes of IE without BSIs. We also compared the incidence of inpatient versus outpatient BSIs. **Results:** There were 420 episodes of IE among 309 PWID, and 82 (19.5%) were complicated by BSIs. There were 138 BSIs with 266 unique isolates: 143 (50.4%) were gram-negative bacilli, 75 (28.2%) were fungi and 48 (18.0%) were gram-positive cocci. The most common bacteria included ESKAPE organisms associated with nosocomial resistance. Factors associated with BSIs in a multivariable logistic regression included inpatient treatment, previous IE, right-sided IE and ongoing inpatient drug misuse. BSIs were more commonly identified in inpatients (9.60 BSIs per 1000 days of intravenous access, 95% CI 7.95–11.5) than outpatients (5.23 BSIs per 1000 days of intravenous access, 95% CI 3.50–7.46). **Conclusion:** BSIs are common in PWID being treated for IE, and empiric therapy should cover resistant gram-negative bacteria and fungi. Although detection bias could have decreased outpatient BSI rates, carefully selected PWID with IE may be safely treated with outpatient parenteral therapy.

ADALIMUMAB FOR MAINTENANCE OF REMISSION IN CROHN'S DISEASE

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Background: Maintenance of remission of Crohn's disease (CD) is a clinically important goal. Objectives: To assess the efficacy and safety of adalimumab for maintenance of remission in patients with quiescent CD. Methods: EMBASE, MEDLINE, CENTRAL and the Cochrane IBD Group Specialized Register were searched from inception to April 2018. Randomized controlled trials (RCTs) comparing adalimumab to placebo or an active comparator were considered for inclusion. Data were analyzed on an intention-to-treat basis. Risk ratios (RR) and corresponding 95% confidence intervals (95% CI) were calculated for dichotomous outcomes. The primary outcome was the number of patients who relapsed. Results: Seven RCTs (n = 1229) were included. Five trials were rated low risk of bias and two were rated unclear risk of bias. Three studies (683 patients) included relapse at 52-56 weeks as an endpoint. Fifty-nine percent (252/430) of patients treated with adalimumab relapsed compared with 86% (217/253) receiving placebo (RR 0.69, 95%CI 0.63-0.76, P<0.05; moderate quality evidence). Two RCTs (302 patients) reported the number of patients who failed to maintain clinical or endoscopic relapse at 52-56 weeks among those who received prior TNF antagonist therapy. Sixty-nine percent (129/186) of adalimumab patients relapsed compared with 93% (108/116) receiving placebo (RR 0.76, 95%CI 0.68-0.84, P< 0.05; high quality evidence). Serious adverse events were seen in 8% (52/643) of patients who received adalimumab and 14% (53/368) receiving placebo (RR 0.55, 95% CI 0.38-0.79, P < 0.05; low quality evidence).Conclusions: Adalimumab is an effective therapy to maintain clinical remission.

The Role of GDF15 in T cell function

Vitali Veramkovich, Hao Zheng, Cuilin Zhu, Suyale, Xiufen Zheng.

Introduction:Elevated plasma levels of growth differentiation factor 15 (GDF15) have been observed in patients suffering from a wide variety of ailments. While GDF15 is implicated in immunomodulation, there is limited research on the effects of GDF15 on lymphocytes. In the present study, we attempt to characterize the effects and potential mechanisms involved in the activity of GDF15 on T cells. Hypothesis:GDF15 suppresses CD4 and CD8 T cell proliferation, increases T cell viability and increases CD4 T cell differentiation into regulatory T cells. In melanoma, GDF15 promotes tumor growth through immunosuppression resulting in reduced immune response.Methods: In order to evaluate the effects of GDF15 on T cell proliferation and differentiation we are using knockout and transgenic mouse models. A combination of flow cytometry, PCR and colorimetric assays is used to evaluate the cell differentiation and cytokine secretion profiles of CD4 and CD8 positive T cells.Results:Using GDF15 knockout (KO) and Wild Type (WT) mice we determined that lack of GDF15 promotes T cell proliferation in vitro. Furthermore, GDF15 enhances T cell viability and promotes the expression of Treg associated cytokines. In melanoma, GDF15 reduces tumor antigen response of T cells and GDF15 expression in mice promotes tumor growth. The expression of GDF15 in tumor cells results in reduced tumor growth.Conclusion:Preliminary data suggests that GDF15 is involved in T cell viability, proliferation and immunomodulation. Furthermore, GDF15 expression affects Treg cell populations and affects tumor growth.

How Do Medical Students Perceive Physician Leadership?

Albert Vo, Drs. Jacqueline Torti and Nabil Sultan.

The most notable change to the CanMEDs framework has been the revision of the manager competency to leader competency. Before implementing any changes to the medical curriculum to reflect this revision, it is important to address two gaps in the leadership literature. First, medicine specific leadership training and resources are limited and require further development. Second, there remains a need for an in-depth exploration of undergraduate medical students' perceptions of leadership. By studying these perceptions, this study can help inform leadership curricula. In this descriptive qualitative study, 22 interviews were conducted with medical students in their first three years of training. Interview questions covered topics such as effective and ineffective leadership as well as

character-based leadership. Following the audio recording and transcription phases, a preliminary thematic analysis was conducted. The effective leadership characteristics revealed in this analysis included effective communication, leading by example, and team management. In contrast, being demeaning, having an elitist attitude and lacking passion were examples of ineffective leadership characteristics. Most interviewed students agreed that competence, commitment and character play an important role in leadership. In particular, students who had been exposed to clinical learning provided the most descriptive examples of physician leadership and were more capable of identifying the importance of character-based leadership. Nevertheless, there were students who questioned the applicability of character-based leadership based on their stage of medical training. Overall, these perspectives on physician leadership will be important in future leadership education initiatives for undergraduate medical students.

Improving Accuracy of Dictation Medication Lists for Patients Discharged from CTU

Bingxi Alice Wang, Marilyn Phung, Dayna Butler, Rasha Abdul-Karim, Andre Maddison, Saira Zafar.

Medical errors are the third leading cause of death and morbidity in North America, and medication errors comprise a large proportion of overall errors.Medication reconciliation is a crucial step where medication errors can be mitigated. The introduction of the Patient-Oriented Discharge Summary (PODS) has improved this process at London Health Sciences Centre (LHSC). However, discrepancies still occur between the reconciliation and the discharge summary medication list. This can be a source of confusion for subsequent healthcare encounters.We compared the discharge medication reconciliation in the PODS to the discharge dictations to identify the frequency and severity of errors, followed by identifying key factors associated with errors. The next steps are direct observation of trainees, design of Pareto chart, and stakeholder interviews. This ongoing project will undergo PDSA cycles to work to achieve the target of reduction of errors by 30%.We reviewed 81 discharge dictations from CTU at LHSC over a 4-month period. 54% of dictations had clinically significant errors when compared with the PODS. The most serious errors were narcotics and antibiotics missing from the dictation or medication reconciliation. The most common errors were wrong medication dosages.Through a root cause analysis and table of frequencies, we identified that dictations performed by medical students have more errors. Medical students cannot independently complete medication reconciliations, which is likely a contributing cause.Medication errors can be decreased by simplifying the discharge process, such as faxing the PODS document directly to family physicians and by educating medical students about medication reconciliation.

A-LURT: Acquisition and Retention of Lung Ultrasound Skills by Respiratory Therapists: a point-of-care lung ultrasound curriculum for respiratory therapists

Amanda Young, MD FRCPC; **Derek Wu, BMSc**; Dr. Vincent Lau, MD FRCPC; Dr. Frank Myslik, MD CCFP(EM); Dr. Dany Burke, MD FRCPC; Dr. Robert Arntfield, MD FRCPC.

BACKGROUND: Point-of-care ultrasound (POCUS) is a versatile bedside tool used by acute care physicians in the management of critically ill patients. Lung ultrasound in particular is a POCUS technique with superb diagnostic accuracy in the identification and treatment of those with respiratory failure. As respiratory therapists (RTs) are routinely involved in caring for those with respiratory failure, there is good rationale for their adoption of lung ultrasound however no training standards have been defined. OBJECTIVES: To develop and implement a training program for RTs to achieve and sustain competence in lung ultrasound. METHODS: Ten RTs completed a lung POCUS curriculum consisting of didactics (video and in-person) and a single 3 hour hands-on training session. After training, RTs were tasked with independently completing ten lung ultrasound

exams on patients with the images and interpretations recorded on our centre's POCUS quality assurance software, Qpath™. All exams were remotely and blindly overread by a local expert in lung ultrasound, providing interim feedback around each exam as necessary. After 6 weeks, each RT will carry out 3 additional exams which will be subject to the same workflow. The judged quality of image generation and interpretation in the initial phase and at the 6 week mark formed the basis of competence determination and skill retention. RESULTS: RTs were able to acquire interpretable images 96.4% of the time and accurately interpret their images 86.1% of the time. Confidence levels were marked as high or moderate for 80.1% of the images taken.

Characteristics of Takayasu Arteritis Patients with Severe Ischemic Events

Richard Yu, Roaa AlSolimani, Nader Khalidi, Christian Pagnoux, Lillian Barra1,and CanVasc.

Objective: Takayasu arteritis (TAK) is a rare large vessel vasculitis with a high risk of developing severe ischemic events (SIE). Outcomes for TAK patients with SIE are poorly understood. We aim to describe the characteristics of TAK patients experiencing SIE. Methods: All TAK patients with at least one follow-up visit seen between 1988 and 2015 were included from 3 academic centres in Ontario, Canada. Diagnosis was based on American College of Rheumatology (ACR) criteria, physician opinion and vascular imaging. SIE were defined as cerebrovascular accident (CVA), acute coronary syndrome (ACS), ischemic cardiomyopathy, ischemic blindness and/or ischemic bowel or limb requiring surgery. Results: Of the 52 TAK patients included in the study, 51 (98%) were female and 22 (42%) were Caucasian. The mean age was 31 at the time of diagnosis (SD12) and the follow-up time was 6 (SD 5) years. Fifteen (29%) experienced a SIE: 5 CVA, 5 ACS, 1 ischemic cardiomyopathy and 4 limb ischemia. 13/15 (87%) SIE occurred at or before diagnosis. Patients with SIE were more likely than those without SIE to be started on corticosteroids combined with immunosuppressants (p=0.03) and anti-platelet agents (p=0.0003). SIE were not associated with disease activity scores or traditional cardiovascular risk factors. Outcomes including disease activity and damage scores were similar between patients with and without SIE.Conclusion: SIE are common in patients with TAK and occur early in the disease. With aggressive treatment, patients with SIE had a favourable prognosis.

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