



Western University
Schulich School of Medicine & Dentistry
Department of Medicine

RESEARCH DAY

Thursday, May 11, 2017
Best Western Lamplighter Inn
591 Wellington Road South
London, Ontario N6C 4R3

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 (hours).

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.

**Department of Medicine
Resident Research Day 2017
Thursday May 11, 2017
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	9:20	Translational Research and You: A Clinical Approach to Basic Science Dr. Aze Wilson (Crystal Ballroom North) <i>30 min presentation 10 min Q&A</i>	
9:20	10:00	Quality Improvement: The Next Evolution in Research and Care Dr. Alan Gob (Crystal Ballroom North) <i>30 min presentation 10 min Q&A</i>	
10:00	11:00	BREAK	Poster Presentation and Judging (Crystal Ballroom South)
11:00	11:45	Infections in Persons Who Inject Drugs in London. What the *!#! is going on here? Keynote - Dr. Michael Silverman (Crystal Ballroom North) <i>40 min presentation 5 min Q&A</i>	
11:45	13:45	LUNCH	Poster Presentation and Judging (Crystal Ballroom South)
Afternoon Session – Highlight Research by Department of Medicine Trainees			
14:00	15:00	Trainee Oral Presentations (Crystal Ballroom North) <i>10 min presentation 5 min Q&A</i>	
15:00	15:15	REFRESHMENT BREAK	
15:15	16:30	Trainee Oral Presentations (Crystal Ballroom North) <i>10 min presentation 5 min Q&A</i>	
16:30	16:45	Presentation of Awards (Crystal Ballroom North)	
1645	1655	Closing Remarks(Crystal Ballroom North)	
1655	17:00	<i>Completion of Participant Evaluation Form Please drop your completed form at the Registration Desk on your way out.</i>	

Oral Presentations

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2:30pm	Alexander Hofkirchner	MD Student	Determining whether Citrullinated and Homocitrullinated Lipoproteins Have a Role in Rheumatoid Arthritis-Associated Atherosclerosis by Promoting Proinflammatory Cytokine Release from Macrophages	32
2:45pm	Kathryn McIntyre	PGY-5	Decreasing Inappropriate Referrals to The Urgent Medicine Clinic	42
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3:30pm	Elena Qirjazi	PGY-6	Educational Workshop on Goals of Care Discussions in Nephrology	47
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Assessing the Quality of ICU Transfers to the Medicine Ward at University Hospital

Rasha Abdul-Karim, Dr. Alan Gob.

Background Once a patient is stabilized in the medical intensive care unit (ICU), it becomes important to initiate the transfer process to medicine floor. This study addressed concerns regarding the quality of the transfer process and the presence of medication reconciliation. Over 60 percent of inpatient medication errors occur during times of transition. **Methods** The study consisted of two parts. The first part assessed the request for transfer phase. This was conducted through phone survey to the senior medicine resident (SMR) using handover probes (diagnosis, present state of patient, recent changes and anticipation in changes of condition or treatment, what to monitor along shifts, and warning signs). The second part investigated the presence of a transition record and if it included the minimal set of information necessary; principle diagnosis and problem list, medication reconciliation, major procedures and tests performed during inpatient stay, summary of test results/pending results, and principal diagnosis at discharge. **Results** SMR was usually contacted by the unit clerk who would provide patient's name and identification number (12 out of 13 requests). Reviewing charts showed the absence of a dedicated transition record from the ICU team and the lack of transfer medication reconciliation. Both were being completed by the SMR who was not involved in patient's care while in ICU. **Conclusion** Transition process by which a patient is transferred from the ICU to the medicine ward at University Hospital is found to be lacking the essential elements necessary to ensure a safe transfer, especially medication reconciliation.

COPD Imaging Biomarkers to Guide Bronchoscopic Lung Volume Reduction: A Cautionary Note

Colin Adams, Dante PI Capaldi, Robert DiCesare, David G McCormack, Grace Parraga.

For patients with severe emphysema, bronchoscopic-lung-volume-reduction (BLVR) is employed to improve quality-of-life. While thoracic x-ray computed-tomography (CT) identifies specific lobar targets based on quantitative measurements of emphysema, inhaled-gas magnetic-resonance-imaging (MRI) also provides quantitative biomarkers of regional ventilation and emphysema. We hypothesized that CT and MRI would provide different regional targets in COPD patients eligible for BLVR and retrospectively evaluated 22 patients from the TINCan cohort who were eligible for BLVR (DLCO=37±12%predicted, FEV1=34±7%predicted, TLC=131±17%predicted, RV=216±36%predicted). CT-derived relative area < -950 Hounsfield-units (RA950) (RA950=20±10%) and MRI ventilation-defect-percent (VDP) (VDP=33±9%) were generated for each lobe and independently used to rank the severity of disease in individual lung lobes. CT and MRI classification of the most- and second-most diseased lobes showed weak-to-moderate inter-biomarker reliability (Cohen's κ =0.40-0.59). Moreover, the spatial overlap of CT emphysema and MRI ventilation defects was modest (Dice-similarity-coefficient=29±12%). In seven of 22 COPD patients, there were differences in CT and MRI predictions of the most-diseased lobe while in some patients, there were ventilation defects in non-BLVR target lobes, suggesting that in these patients, BLVR might not improve outcomes. In summary, in this proof-of-concept demonstration, quantitative MRI ventilation and CT emphysema measurements may provide different targets for BLVR in some patients.

The Efficacy of Colonoscopic Balloon Dilation in Stricture Crohn's Disease

Waleed Alghamdi, Nilesh Chande, Jamie Gregor.

Background: Stricture formation is a common complication of Crohn's disease. Management options include medical therapy, surgical resection or strictureplasty. A more common middle ground approach is colonoscopic balloon dilation (CBD). **Aims:** Examining the efficacy of CBD in a patient population with symptomatic

strictures. Methods: Retrospectively, patients in our IBD practice with symptomatic Crohn's strictures who underwent CBD between January 2006 and March 2016 were reviewed. Demographic data were collected and technical and clinical success determined to compare the results between primary and anastomotic strictures. Technical success was defined as subjective improvement in the stricture and the ability to pass the scope through it. Clinical success was defined as subjective clinical improvement at follow up visits. Pearson's chi-squared test was used to compare relative efficacy. Results: 98 patients were identified with 108 strictures dilated. The mean age of the patients was 45.2 years. 64.3% of the patients were females. An adult Olympus colonoscope (diameter 13.2 mm) was used in 86.1% of cases. The most common balloon diameter was 15 mm (24.1%). Technical success was achieved in 62% and clinical success in 84.3% of the patients. One patient experienced post colonoscopy bleeding. Comparison of primary and anastomotic strictures demonstrated a statistically significant difference in technical success (73.1% vs 51.8%, $p=0.023$) but not clinical success (86.5% vs 82.1% $p=0.531$). Conclusions: CBD of Crohn's strictures appears to be feasible and clinically efficacious in most patients with symptomatic Crohn's strictures. Complication rates, though not insignificant, appear to be acceptably low.

The Utility of Separate Distal and Mid-Esophageal Biopsies in the Diagnosis of Eosinophilic Esophagitis (EoE)

Maan Alkhattabi, Kubica M, Driman D, Gregor J.

Background: EoE is an increasingly recognized cause of upper gastrointestinal symptomatology particularly dysphagia. The gold standard for diagnosis is the presence of increased eosinophils on esophageal biopsies. To distinguish EoE from esophageal eosinophilia due to gastroesophageal reflux disease (GERD), many physicians routinely separate biopsies from the mid and distal esophagus, theorizing that eosinophils will be more numerous in the distal esophagus in GERD and more diffusely distributed in EoE. The aim of our study was to determine if this approach was truly helpful in

clinical practice. Methods: All endoscopically obtained biopsies of the esophagus taken at London Health Sciences Centre between July 1, 2011 and June 30, 2014 were eligible for review. Patients were only included if they were 18 year old or older and biopsies were taken from the mid and distal esophagus for non-neoplastic findings and separated for review. The pathology was then reviewed by a pathologist blinded to diagnosis and a mean eosinophil count per high-power field (hpf) was calculated for each area. A delta eosinophil count (DEC) was calculated by subtracting the mean count in the distal esophagus from the mean count in the mid-esophagus. If multiple endoscopies were performed, only the first biopsy after the study initiation date was used. Results: 603 patients were included in the analysis. Of these 138 (22.9 %) had a final diagnosis of GERD, 124 (20.6 %) EoE and 341 (56.5 %) normal. The most common predominant symptoms in GERD were heartburn 99 (71.7 %) and dysphagia to solids 70 (50.7 %). The most common predominant symptoms in EoE were dysphagia to solids 90 (72.6 %), atopic symptoms 41 (33.1 %), heartburn 40 (32.3 %) and food impaction 38 (30.6 %). The most common endoscopic findings in EoE were furrows 81 (65.3 %), trachealization 70 (56.4 %) and stricture 29 (32.4 %). The mean eosinophil count in the distal and mid-esophagus respectively was 6.6 and 2.8 in GERD, 80.4 and 76.9 in EoE and 0 and 0 in normal patients. The DEC was positive in 20.3 % of GERD patients and 41.1 % of EoE patients. The mean DEC was -3.8 in GERD patients and -3.5 in patients with EoE. Conclusion: Mucosal eosinophilia is significantly more pronounced in patients with EoE although the difference between eosinophil counts in the mid and distal appears to be of only marginal value in distinguishing between the two diagnoses. Separating specimens for analysis does not appear to be necessary.

Is Hepatocellular Carcinoma Rare in Non-Cirrhotic Hepatitis C Patients?

Ammar Alotaibi, Waleed Alghamdi, Karim Qumosani.

Background: Hepatocellular carcinoma (HCC) is one of the feared complications of cirrhosis.

Hepatitis C virus (HCV), unlike hepatitis B virus, rarely causes HCC in the absence of cirrhosis. Case reports, systematic and retrospective reviews show a prevalence of HCC between 0% to 68% in this patient population. Further studies are needed to describe this population. Aim: Our analysis aims to determine the prevalence of HCC among liver transplant patients with hepatitis C virus in the absence of histologic cirrhosis. Methodology: We did a retrospective charts review of transplant patients in our center between January 2006 and June 2016. We included all adult HCV patients who had HCC before transplant. We reviewed the histopathology reports of all explants to determine the fibrosis stage. Liver fibrosis was staged using Batts-Ludwig and Ishak histologic scoring systems. Results: We included 98 hepatitis C patients in our analysis. 91.8% of the patients were males. The mean age was 57.1 ± 5.3 years (range 44-68). Hypertension and Diabetes were the most common co-morbidities among the patients, 24.5% and 16.3%, respectively. 13.3% of the patients were having a viral load of $> 3 \times 10^6$ IU/mL. The most common HCV genotype was 1 (61.2%). Alcohol was the most common co-factor contributing to cirrhosis(27.5%). Two patients (2%) were found to have fibrosis stage 2 and 3. Conclusion: HCC is not that rare among non-cirrhotic hepatitis C patients. The prevalence is likely higher in non-liver transplant population.

Prognostic Performance of the American Thyroid Association (ATA) Risk Classification for Pediatric Differentiated Thyroid Cancer – a Canadian experience.

Raad Alwithenani, Sarah Debrabandereb, Irina Rachinskyb, Danielle MacNeilc, Mahmoud Badreddineb, Stan Van Uuma.

Introduction: Differentiated thyroid Cancer (DTC) is the most common endocrine malignancy in children. Retrospective studies show conflicting results regarding predictors of persistent and recurrent disease after initial therapy. The ATA recently proposed a clinical classification system to identify patients at risk for persistent/recurrence disease. Material and Methods: We retrospectively included all patients

in our registry diagnosed with DTC at ≤ 18 years of age. We analyzed the prognostic performance of this risk classification and other risk factors for predicting response to initial treatment and final outcome in pediatric DTC. Results: We included 42 patients, 35 women and 7 men, diagnosed with DTC at a mean (SD) age of 16.1 (1.9) years. 41 patients had papillary thyroid cancer, 1 had follicular thyroid cancer. Based on the ATA pediatric risk classification, patients were categorized as low (62%), intermediate (9%) or high risk (29%). The median follow up period was 7.7 (0.7-41) years. Disease free was achieved in 81%, 50%, and 33% of the low, intermediate and high risk groups, respectively ($P < 0.01$). At the last visit persistent disease was present in 12%, 25% and 33%, respectively ($P = NS$). Assessing other risk factors, only the presence of distant metastasis resulted in increased presence of persistent disease ($P = 0.03$). Conclusion: This study supports the clinical relevance of the ATA risk classification for predicting the response to initial treatment, while no difference was found with respect to disease status at the last visit. This may be due to limited power due to small number of patients.

Infertility in female patients treated with cyclophosphamide for non-cancerous indications: a meta-analysis.

May Alzahrani, Lillian Barra.

BACKGROUND: Cyclophosphamide (CYC) is an alkylating agent that is used to treat various autoimmune diseases with severe organ involvement. A serious adverse event of CYC is infertility, reported in 50% of patients who received CYC for cancer treatment. The risk of infertility in autoimmune diseases where lower doses of CYC are used is unclear. OBJECTIVE: to summarize fertility outcomes in patients treated with CYC for non-cancerous indications. METHOD: We searched PubMed, EMBASE and Cochrane library. Inclusion criteria were studies of females of childbearing age who received CYC for autoimmune rheumatologic, neurologic, ophthalmologic, pulmonic, renal or dermatologic diseases and reported on fertility outcomes (premature ovarian failure, transient amenorrhea and infertility). Random effects meta-analyses (DerSimonian and Laird methods) will be

performed. RESULT: 76 of 315 papers met the inclusion criteria (a total of 1543 patients). Most of the studies were of patients with systemic lupus erythematosus and were observational (sample sizes ranged from 4 to 99 subjects). The studies were highly heterogeneous: mean ages of study subjects ranged from 12 to 42 years, CYC cumulative doses from 4 to 40 g and disease duration from 0 to 127 months. Outcomes were also variable, but the majority reported that infertility and premature ovarian failure occurred in <50% of cases. The proportion of subjects with transient amenorrhea ranged from 0% to 42%. CONCLUSION: Prevalence of premature ovarian failure in patients with autoimmune disease exposed to CYC is significant; however, studies are variable and the risk depends on age and cumulative CYC dose.

The effect of a high-fat diet on arthritis using a mouse model of Rheumatoid Arthritis

Nick Anand, St. John J, Huff M, Pickering G, Bell D, Cairns E, Barra L.

Background: Rheumatoid Arthritis (RA) is a chronic autoimmune disorder characterized by the production of antibodies that target citrulline, a post-translational modification catalyzed by isoforms of peptidylarginine deiminase (PAD). Obesity is a risk factor for RA. We aim to investigate the effect of a high fat diet on arthritis using a mouse model of RA. Methods: Mice expressing human leukocyte antigen DRB1*0401 (DR4tg) will develop arthritis starting at day 45 after immunization with PAD2-citrullinated fibrinogen (CitFib). We fed DR4tg mice a high-fat, high-cholesterol (HFHC) diet or standard CHOW for 70 days, and immunized them at day 0 and 21 with PBS, fibrinogen or PAD4-CitFib. Mice were monitored weekly for weight gain and joint swelling (change in ankle width using calipers). Serum IgG anti-CitFib antibody responses were measured using an ELISA. Protein sequences determined by mass spectrometry of PAD2-CitFib were compared to PAD4-CitFib. Results: HFHC-fed DR4tg mice (n=13) did not gain more weight than CHOW-fed mice (n=13). Caloric intake and antibody levels did not differ among groups. At day 70, there was no swelling or

histologic signs of arthritis in any mouse group (n=20). PAD2-CitFib was found to have 19 more citrulline residues than PAD4-CitFib. A citrullinated peptide known to bind to DRB1*0401 and initiate T and B cell responses was not present in the PAD4-CitFib. Conclusions: Short-term feeding of a HFHC diet did not induce obesity or increase arthritis severity in PAD4-CitFib-immunized DR4tg mice. Future work will investigate the impact of longer exposures to a HFHC diet in PAD2-CitFib-immunized DR4tg mice.

Patient centered approach to disease modification in scleroderma: Results from the faSScinate trial of tocilizumab compared to placebo in active diffuse cutaneous systemic sclerosis

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Objectives: Patient Acceptable Symptom State (PASS) as an absolute state of well-being and has shown promise as an outcome measure in many rheumatologic conditions. We assessed whether PASS may be an effective in active diffuse cutaneous SSc. Methods: Data from the faSScinate trial were used, which compared tocilizumab vs. placebo over 48 weeks followed by an open-label tocilizumab period to 96 weeks. Three different types of PASS questions were evaluated at weeks 8, 24, 48 and 96 including would a current state be acceptable over time as yes vs. no response, and Likert scales about how acceptable a current state is if remaining over time. Additional outcomes assessed included mRSS, HAQ-DI, MD and Pt global VAS, CRP and ESR. Results: At baseline, the placebo group consisted of 44 patients, and tocilizumab group had 43 patients. At baseline, 33% achieved PASS for all three PASS questions, with the proportion increasing to 69%, 71% and 78%, respectively at 96 weeks. Changes in PASS scores showed a moderately negative correlation with HAQ-DI, Pt and MD global VAS. PASS asking 'Considering all of the ways your

scleroderma has affected you how acceptable would you rate your level of symptoms?’ showed significant correlations with patient-reported outcomes and differentiating placebo vs. tocilizumab at 48 weeks (P=0.023). Conclusions: PASS may be used as patient-centered outcome in SSc especially as a 7-point Likert scale. Further validation through larger clinical trials is required before being able to apply this concept to clinical practice.

Recurrent Hepatocellular Carcinoma after Liver Transplantation: Validation of a Pathological Risk Score on Explanted Livers to Predict Recurrence

Salman Aziz, Paul Marotta, David Driman, Jeremy Parfitt, Karim Qumosani.

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide. A curative treatment option is liver transplantation, although recurrence occurs in 8-20% of patients. An HCC recurrence risk score was developed by Parfitt et al. which stratified patients into low, intermediate or high risk of recurrence. The aim of this study was to validate this risk score in a cohort of patients. Methods: We retrospectively evaluated 124 patients over a ten-year period that underwent liver transplantation for HCC. Using explanted pathology, patients were assigned the recurrence risk score. Within our cohort of patients, we determined the 1, 3, 5, and 7 year rates of HCC recurrence. Z test was used to compare recurrence in our cohort and Parfitt et al. Results: Out of 124 consecutive liver transplants for HCC, recurrence occurred in 15 patients (12%). 10 (8%), 21 (17%), and 93 (75%) patients were stratified into high, intermediate, and low risk of recurrence, respectively. At one year, HCC recurrence occurred in 67%, 20% and 5% in the patients considered high, intermediate, and low risk. From a validation perspective, low (p=0.62) and intermediate risk (p=0.14) were consistent with Parfitt et al. 2007 but high risk recurrence rates (p=0.00) were not consistent possibly due to a small sample size. Specificity was 91% and sensitivity was 50% with an area under the receiver operator characteristic curve of 0.8. Conclusions: The recurrence risk score can help tailor a surveillance strategy for early detection or

early adjuvant therapy to improve long-term survival.

ACTH-Independent Cushing’s Syndrome Diagnosed during Pregnancy- Successful Medical Management with Metyrapone

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Cushing syndrome is rarely diagnosed in pregnancy and limited literature is available to guide therapy. If left untreated, it is associated with significant maternal and fetal complications. Case: 24 year old female at 25weeks gestation, was assessed for concerns of excess cortisol. Her first pregnancy was complicated by an eclamptic seizure requiring emergency C-section. Elevated 24hour urine cortisol at 1141 nmol/day (normal <275) and loss of diurnal salivary cortisol variations (8am-8pm levels of 44.5 and 61.1nmol/L, respectively) confirmed Cushing syndrome, which was ACTH-independent (ACTH <0.3pmol/L). Abdominal MRI revealed a 3.7cm left adrenal adenoma. Although literature would favour early surgical adrenalectomy, this patient was considered high risk due to morbid obesity and gravid uterus, approaching third trimester. She was treated with metyrapone. Her overall condition including gestational diabetes and hypertension improved with successful control of hypercortisolism (based on saliva cortisol). Planned C-section at 35 weeks was uncomplicated with delivery of a healthy child. Post-partum, transition to ketoconazole therapy was well tolerated with laparoscopic left adrenalectomy planned for the near future. This case report illustrates the additional complexity of Cushing syndrome management when detected in late pregnancy. In a high risk surgical patient, literature on medical therapy is sparse. Key endocrine points required exploration including safety of medical treatment in pregnancy, availability and effectiveness of

metypapone in pregnancy and unknown fetal risk. We discuss the establishment of a monitoring and titration protocol for this medication to avoid potentially detrimental effect to mother and fetus, and considerations for a planned caesarean section.

Reducing Inflammation Associated with Bacterial Lung Infections using a Host Defense Peptide

Brandon Baer, Ruud Veldhuizen and Cory Yamashita.

Background: Recent studies indicate that an inability to control excessive inflammation associated with bacterial pneumonia, represents a key factor associated with poor outcomes. It has been postulated that the release of pro-inflammatory mediators induced by killed bacteria may be partly responsible for the maladaptive immune response. Host defense peptides (HDPs) are components of the innate immune system, which serve important immunomodulatory functions. Previous work done in our laboratory shows that a chicken derived HDP, CATH-2, can effectively downregulate the pulmonary inflammation associated with killed bacteria in vitro. **Hypothesis:** CATH-2 can downregulate the pulmonary inflammation associated with antibiotic killed bacteria in vivo. **Methods:** To test the effects of supplementing conventional antibiotics with CATH-2, a mouse model of lung inflammation, induced by the bacterial toxins from antibiotic treated bacterial pneumonia was employed. Mice received an intratracheal instillation of antibiotic, antibiotic-killed bacteria, or antibiotic-killed bacteria supplemented with CATH-2. A bronchoalveolar lavage was then performed and analyzed to determine the inflammatory response within the lung. The response was quantified by counting the number of neutrophils in the lavage, and by using an immunoassay to measure the concentration of the pro-inflammatory cytokine TNF- α . **Results/Conclusion:** Our results indicated that mice treated with antibiotics supplemented with CATH-2 showed a significant reduction in the concentration of TNF- α and in the number of neutrophils recruited to the lung. With antibiotics

at the core of clinical treatment for pulmonary infections these results suggest that CATH-2 could be used therapeutically, to prevent the inappropriate activation of the immune system.

Safety and efficacy of actual weight adjusted dose of Low molecular weight heparin in short term and long term vs warfarin vs Direct oral anticoagulant a retrospective cohort study.

Safwan Bakhsh MD, SBIM , Michael J.Kovacs, MD, FRCPC , Alejandro Lazo-Langner, MD , FRCPC, Lenicio Siqueira,BSc and Martha L Louzada, MD, MSc.

Background: Warfarin has been used as the standard of care for treatment of patients with venous thromboembolism(VTE) over 100 years. Since 2010, direct oral anticoagulants (DOACs) have been available for treatment of VTE. DOACs are appealing because they have a very stable pharmacokinetics and pharmacodynamics, as such, do not need frequent blood work monitoring and are given at fixed daily doses. However, their efficacy and safety have not been adequately studied in obese patients with acute VTE. **Methods:** This is a single center, retrospective cohort study conducted in (London, Canada) of obese patients referred to our thrombosis clinic from January 2010 until December 2015. We included all obese patients assessed at the thrombosis clinic. Obesity was defined as weight above 90 kg or BMI of 30 kg/m² or more. All included patients have proven acute VTE. Deep venous thrombosis (DVT) diagnosis was confirmed by ultrasound of the lower extremities that showed evidence of thrombus in the calf trifurcation or more proximal veins and /or Pulmonary embolism (PE) was confirmed when the ventilation-perfusion lung scan showed at least large mismatched defect or CT pulmonary angiography which showed at least one segmental intraluminal filling defect. Patients were started on anticoagulants. We compared the efficacy and safety of different anticoagulant strategies used by the attending physicians:long-term low molecular weight(LMWH) vs DOAC vs warfarin . Our primary outcome measure, VTE recurrence rate, was assessed during the first 6

months of anticoagulation. It was defined as a new symptomatic VT event or extension of the former event. Our secondary outcome measure was total and major bleeding rates during the anticoagulant period. We assessed bleeding during the first 10 days of anticoagulation and up to 6 months thereafter. Major bleeding was defined as hemoglobin drop >20g/L, , bleeding requiring 2 units or more of packed red blood cells, a hemorrhage requiring permanent cessation of anti-coagulation, or retroperitoneal or intracranial bleeding. Results: In total, 147 obese patients met our eligibility criteria. In the study 52% were males and 48% were females. Mean age was 58 years old (range). mean BMI of 37.3 (range). 84 (xx%) patients had a proximal DVT and 79 (xx%) had a PE. Of those, 26 (xx%) patients had both DVT and PE. Overall, VTE recurrence occurred in xxx patients (9.46%). When we stratified the VTE recurrence events according to treatment strategy, we found that VTE recurred in 5 of 70 (7.1%) patients on recurrence long-term LMWH; in 4 of 34 (11.4%) patients on warfarin and 5 of 43 (10.7%) patients on DOAC . We did not find a statistically significant difference between LMWH and oral anticoagulants (RR= 0.95 (95%CI: 0.871 – 1.051); p=0.387). A subgroup analysis of patients on oral anticoagulants also did not demonstrate any difference (RR= 0.99 (95%CI: 0.863 – 1.151); p=0.986). Bleeding occurred in xxx of aaa (FF%) patients. Major bleeding was present in only 1 (1.4%) patient on long-term LMWH; none in the warfarin group and 3 (6.9%) in the DOAC group. One patient on LMWH arm had bleeding on full dose while five patients had recurrent VTE all were on full dose on LMWH arm.

The efficacy of BLES+CATH-2 against *Pseudomonas aeruginosa* in models of bacterial pneumonia

Brandon Banaschewski, Brandon Baer, Teah Jazey, Johan Delaport, Edwin Veldhuizen, Henk Haagsman, Cory Yamashita, Ruud Veldhuizen.

In cystic fibrosis patients, spontaneous respiratory infections often develop into multi-drug resistant bacterial infections, with no novel therapeutic treatments available. Previous studies have shown bactericidal activity of CATH-

2 in suspension with the surfactant BLES. There is currently no data to investigate the potential of BLES+CATH-2 against clinically isolated bacteria, or efficacy of BLES+CATH-2 in vivo. Hypothesis: BLES+CATH-2 will have effective antimicrobial activity against clinical isolates, and treatment of BLES+CATH-2 in models of bacterial pneumonia will improve overall clinical outcomes. Bacteria were isolated from adult cystic fibrosis patient sputum samples by the London Health Science Center clinical microbiology lab. Bacteria were incubated with BLES+CATH-2 for three hours to assess bactericidal activity. In vivo, ~2x10⁶ CFU/ml of *P. aeruginosa* was administered to mice, followed by treatment. The mice were left for four or eighteen hours, before determining bacterial recovery. In rats, ~1x10⁹ CFU/ml of *P. aeruginosa* was administered to ventilated rats, followed by treatment one hour after inoculation. Mechanical ventilation was continued for three hours before lavage and tissue sample collection. BLES+CATH-2 exhibited bactericidal activity against 8/9 isolates tested. In mice, BLES+CATH-2 showed bactericidal activity at four hours. In ventilated rats, BLES+CATH-2 did not significantly reduce bacterial recovery, but caused a significant increase in oxygenation at the end of ventilation. BLES+CATH-2 has shown effective bactericidal activity in vitro against multiple drug-resistant bacteria derived from cystic fibrosis patients, and can improve clinically relevant outcomes in pneumonia models, such as oxygenation. Future directions will investigate altered compositions in order to optimize therapeutic potential.

Retrospective chart review of rates of resistance and intolerance to hydroxyurea in patients with polycythemia vera

Arvand Barghi, Anargyros Xenocostas, Alejandro Lazo-Langner, Selay Lam, Alan Gob, Michael J. Kovacs, Joy Mangel, Kang Howson-Jan, Ian Chin-Yee, Chai Phua, Bekim Sadikovic, Christopher Hillis, Cyrus C. Hsia

Hydroxyurea (HU) is a generally well-tolerated oral cytoreductive therapy used in patients with polycythemia vera (PV). Ruxolitinib, an oral non-

specific Janus kinase (JAK)1/2 inhibitor, is a new therapeutic option for patients who fail HU. We aim to determine the proportion of PV patients who meet the European LeukemiaNet (ELN) criteria for resistance or intolerance to HU in the real-world setting and determine if ruxolitinib was offered as an alternate therapy. In a preliminary retrospective chart review, a total of 88 JAK2 positive PV patients managed with HU were identified. 557 patient-years were reviewed with 20% (112 patient-years) representing disease that was resistant or intolerant to HU. The rate per patient-year of composite outcome of venous thrombosis, progression to myelofibrosis or acute leukemia, or death, was 5.3% vs 3.4% in resistant/intolerant vs controlled patients respectively ($p = 0.193$). The rate of stroke or myocardial infarction was 2.6% vs 2.2% ($p = 0.399$), and of major bleed was 1.8 vs 1.5% ($p = 0.439$), for resistant/intolerant vs controlled patients, respectively. For cases of resistance or intolerance to HU, only two patients were offered ruxolitinib. The rate of resistance or intolerance to HU was 20% in this preliminary real world PV patient cohort. Ruxolitinib was rarely offered to these patients. There was no significant difference in rate of venous thrombosis, major bleeding, stroke, myocardial infarction, and transformation to myelofibrosis, acute leukemia or death between PV patients resistant or intolerant of HU versus those who were controlled on HU. Acknowledgement: Peter Xenocostas for ongoing data collection.

Improving the Quality of Goals of Care Discussions at LHSC

Lavanya Bathini, Andrew Smaggus.

Accurate documentation of goals of care discussions is crucial to the delivery of patient-centred care. The goal of this quality improvement pilot study was to examine patterns of completion of Goals of Care forms at University Hospital for patients admitted to the Clinical Teaching Units (CTU). A convenience sample of 100 patient admissions between February and April 2016 were audited to determine the characteristics contributing to changes in goals of care during an inpatient admission. We looked to see if there were any references on the form to

the specific content of the discussion and if there were any specific wishes outlined in addition to what is mentioned on the form. Descriptive statistics were used, and the results analysed to identify themes. There were few cases (8/100) in which a patient's goals of care form was updated during admission. Deteriorating health status appeared to be the most important factor contributing to changes in code status documentation. While these results suggest that the documentation of goals of care does is not a major factor in the majority of CTU admissions, they also reinforce the importance of re-addressing philosophy of care with any change in health status." (Results and conclusion of this study are pending)

Drug-eluting stents compared to coronary artery bypass grafting for unprotected left main coronary artery disease: systematic review and meta-analysis

Nicolas Berbenetz, Matthew Chong.

Traditionally, coronary artery bypass grafting (CABG) has been the intervention of choice for revascularization of left main coronary artery disease (LM-CAD). However, since the development of drug-eluting stents (DES), some patients have opted for percutaneous coronary intervention (PCI). Importantly, the evidence supporting this practice has come from small studies with limited follow-up. Given the recent publication of two large randomized controlled trials (RCTs) with extended follow-up, we conducted an updated systematic review and meta-analysis of CABG and PCI for unprotected LM-CAD. Methods: We searched the Cochrane Library, MEDLINE, and EMBASE for RCTs that compared PCI to CABG in adult patients with unprotected LM-CAD. For inclusion, studies had to report data on major adverse cardiac and cerebrovascular events (MACCE). Results: Six RCTs comprising 4700 patients were included. Four RCTs evaluated first-generation DES. PCI increased the risk of MACCE compared to CABG (OR 1.30, 95% CI 1.10-1.53; $P=0.002$, $I^2=10.6\%$, $NNT=26$). There were no significant differences in all-cause mortality (OR 1.00, 95% CI 0.75-

1.34), myocardial infarction (OR 1.37, 95% CI 0.83-2.28), and stroke (OR 0.76, 95% CI 0.36-1.58). The quality of evidence was moderate. Conclusions: The available evidence suggests that CABG is superior to PCI for the treatment of LM-CAD, with significantly lower rates of MACCE. Most patients would benefit from CABG rather than a first-generation DES. Additional studies investigating next-generation DES may alter this recommendation.

ordered) in October 2015 to 6 units per month (5.6% of total transfusions ordered) in November 2016. Conclusion: The reduction in proportion of two pRBCs ordered was secondary to the proposed intervention, and was sustained over a period of six months. These initiatives highlight a novel way of limiting overutilization at the level of front-line providers and healthcare system.

Decreasing overutilization of two red cell unit transfusions on an inpatient oncology ward

Anurag Bhalla, Ian Chin-Yee and Alan Gob

Asthma Phenotypes in Adult Survivors of Premature Birth Using Functional Magnetic Resonance Imaging

Anurag Bhalla, Anurag Bhalla, Khadija Sheikh, Heather M Young, David G McCormack, Thuy Mai Luu, Sherry Katz and Grace Parraga.

Introduction: Choosing Wisely Canada was introduced in 2014 to help guide conscious healthcare practices to reduce unnecessary tests, procedures and treatments. As part of the campaign, Canadian Society for Transfusion Medicine recommends one over two packed red blood cell unit (pRBCs) transfusions. Objective: Aim of the study was to devise strategies to limit unnecessary two pRBCs transfusions. Methods: We conducted real-time and retrospective audits, and survey of front-line staff on oncology inpatient ward at London Health Sciences Centre to identify factors associated with two pRBCs transfusions. Based on the surveys, we implemented two main targeted interventions including educating healthcare providers through posters and bulletins, and removal of automatic two pRBCs computerized transfusions orders. We monitored number of pRBCs ordered on a monthly basis from October 2015 to November 2016. Results: After implementation of proposed strategies in April 2016, there was a 50% reduction in proportion of two pRBCs ordered in May 2015. In addition, the reduction in 2 pRBCs ordered was sustained for remained of the monitoring period. The number of 2 pRBCs transfusion decreased by 89% from 71 units per month (51.1% of total transfusions

RATIONALE: Prematurity results in a disruption of normal neonatal-lung-development and is a risk factor for chronic-lung-disease. Adult survivors of premature-birth often report persistent respiratory symptoms and are frequently diagnosed with asthma, although the underlying pathophysiology is likely atypical. Our objective was to evaluate adults born preterm and those born full-term with a clinical diagnosis of asthma using inhaled-gas-hyperpolarized-3He-magnetic-resonance-imaging (MRI). We hypothesized that asthmatics born preterm would have significantly greater ventilation-defects and abnormally enlarged lung-microstructure that is unresponsive to bronchodilator. METHODS: Participants provided written-informed-consent to an ethics-board approved protocol and were evaluated using pulmonary-function-tests and MRI at baseline, post-Methacholine-bronchial-challenge (MCh) and post-salbutamol. MRI was performed to generate the ventilation-defect-percent (VDP) and apparent-diffusion-coefficients (ADC). SPSS 23.0 software was used to evaluate differences between preterm and term-born subjects. RESULTS: Asthmatics born preterm (n=3, age=28±3yrs, GA=29±2wks) as compared to those born full-term (n=5, age=22±2yrs, GA≥40wks) had significantly lower (p<.05) pre-salbutamol FEV1 (term=89±11%pred, preterm=37±8%pred), greater RV/TLC (term=25±5%, preterm=48±8%), and greater (p<.05) pre-salbutamol VDP

(term=2.4±0.4%, preterm=6.4±1.5%). Preterm asthmatics reported greater mean ADC (term=0.20±0.02cm²/s, preterm=0.37±0.01cm²/s). There was no ventilation-defect reversibility following bronchodilation in the preterm asthmatics. Full-term participants underwent MCh and had significantly improved (p=.04) VDP post-salbutamol (post-MCh=5.7±1.7%, post-salbutamol=2.3±0.7%). Premature subjects did not undergo the MCh (due to low FEV₁)⁵ and did not have significantly (p=.2) improved VDP post-salbutamol (pre-salbutamol=6.4±1.5%, post-salbutamol=7.4±2.7%). **IMPLICATION:** Asthmatics born preterm had significantly worse lung-function without post-bronchodilator reversibility. This highlights the importance of understanding mechanisms leading to abnormal pulmonary function in adults with a diagnosis of asthma and in those survivors of preterm-birth.

Linking Competency Based Medical Education and Professional Identity Formation through a Threshold Concepts Lens

Chirag Bhat, BMSc (Hons), Sarah Burm, PhD, Tricia Mohan, Saad Chahine B.Ed, M.Ed, PhD, Mark Goldszmidt, MD, FRCPC, PhD.

Supporting medical trainees' professional identity formation (PIF) is increasingly recognized as an essential component of physician training. The role of PIF in the context of competency based medical education (CBME) is not understood. While not explored in medicine, threshold concepts (TC) - 'troublesome' concepts - play an important role in PIF. The purpose of this study was to identify and explore the types of TC that medical trainees (senior medical students and junior residents) may encounter during their internal medicine clinical rotation. Constructivist grounded theory was used to guide data collection and analysis. Data sources included: 1) direct observation and field interviews with seventeen medical trainees and; 2) in-depth interviews with thirteen attending physicians to elaborate on findings from the observational component of the study. The theory of threshold concepts was used as a sensitizing concept. Ten TC were identified and thematically grouped

under the headings: developing as a professional, providing patient care and working collectively. TC where made visible through trainee behaviors, the rationales trainees provided to explain their behaviours, and the inferences attendings drew from their observations of trainees' behaviors. While attendings did not have an explicit language for describing specific TC, they appeared to have a shared understanding of thresholds strong students had crossed and weaker students struggled with. Trainees varied in the thresholds they crossed and struggled with. The identified TC provide new insight into a potentially important component of PIF. They offer a language for guiding trainee development and may be beneficial in improving CBME.

High aldosterone levels, hypertension and adrenal adenoma in a 36 year-old pregnant patient: Is this primary aldosteronism?

Amanda Brahm, MD, Deborah Penava, MD; Dongmei Sun, MD; Arlene MacDougall, MD; Stan Van Uum, MD, PhD

A 36-year-old woman with no history of hypertension presented at 16 weeks gestation with hypertensive urgency. Potassium was intermittently low (3.1mmol/L). Aldosterone was elevated (3000pmol/L (N <1118 standing)), renin was unsuppressed (40.7ng/L (N1.7-23.9)), with aldosterone to renin ratios in the reference range. An adrenal MRI scan demonstrated a 1.8 x 1.4 cm left adrenal adenoma. She was managed conservatively, with close maternal and fetal surveillance, and treatment with labetalol and nifedipine. She achieved reasonable blood pressure control, with no obstetric complications. Post-partum blood pressures remained elevated with normal aldosterone (539 pmol/L), unsuppressed renin (5.2 ng/L) and normal aldosterone-to-renin ratio (104 (N<144)), suggesting primary hypertension with an incidental finding of an adrenal adenoma, which was confirmed by normal saline suppression test results post-delivery. Suspected primary aldosteronism is challenging to diagnose and manage in pregnancy. Outside of pregnancy, the accepted screening test is the aldosterone to

renin ratio, with confirmatory tests including a saline suppression test, captopril challenge or salt/fludrocortisone load. However, these tests lack validated pregnancy reference ranges or are contraindicated. Moreover, pregnancy has significant effects on the renin-angiotensin-aldosterone pathway leading to physiologic elevations in both aldosterone and renin. Progesterone competitively binds to aldosterone receptors, the ovaries and placental tissues secrete renin and estrogen stimulates angiotensinogen production. While primary aldosteronism has been associated with poor pregnancy outcomes, optimal management in pregnancy is not clearly established. Conservative treatment with traditional antihypertensives, cautious use of mineralocorticoid receptor antagonists, or surgical adrenalectomy are all possible treatment options reported in the literature.

Improving the Timing of Inpatient Diabetes Education to Prevent Delayed Discharges

Alescia Azzola, MD; **Amanda Brahm, MD**; Christopher D'Sylva, MD, Kristin Clemens, MD.

Due to the increased monitoring and routine investigations conducted in the hospital setting, the need to initiate insulin in patients with diabetes is often recognized during a hospitalization. These patients require teaching from a diabetes nurse educator prior to discharge. Delays in receiving this teaching may lead to a delay in discharge from hospital. During a collection period of approximately 4 months, 25 patients were identified whose discharge from hospital was delayed or their teaching was rushed due to a consult request on the day of discharge. Combined, this resulted in 13 avoidable inpatient days. Overwhelmingly, the most common factor contributing to the delayed discharge or rushed teaching was a delay in the initial consult to the educator (18/25 cases). Lack of educator availability (6/25 cases) and patient factors (6/25 cases) were also minor contributors. We hypothesized this was due to a delay in MRP recognition of patients who would require diabetes education prior to discharge. To address this, we created guidelines to help identify

patients requiring education earlier in their hospital course, to be applied to every patient whose discharge status was changed from red to yellow or green. Our intervention also includes education of the nursing staff and other discharge facilitators regarding these guidelines and increasing their awareness of which patients may need education prior to discharge. We will be piloting this intervention on one closed unit and assessing its impact on the rate of delayed discharges or rushed teaching related to the requirement for inpatient diabetes education.

Phase 2 Trial of Capecitabine plus Erlotinib Versus Capecitabine Alone in Patients with Advanced Colorectal Cancer

Daniel Breadner, Mark Vincent, Stephen Welch, Michael Sanatani, Mary-Jane MacKenzie, Paul Klimo, Larry Stitt, Frances Whiston, Anne O'Connell.

Background: Capecitabine monotherapy as palliation for aCRC is generally well tolerated by elderly or unfit patients. EGFR TKIs might improve efficacy of capecitabine alone in patients not appropriate for combination chemotherapy. We conducted a randomized phase 2 trial investigating the novel combination of capecitabine and erlotinib in these patients. Methods: Between 2004 and 2008, 82 elderly or unfit patients who were deemed inappropriate for 1st-line combination chemotherapy were enrolled and randomized to capecitabine alone (Arm 1) or capecitabine with erlotinib (Arm 2). Primary endpoint was time to disease progression (TTP); secondary endpoints included safety and overall survival (OS). KRAS status, where possible, was retrospectively analyzed. Results: Median TTP for arm 2 was 9.2 versus 7.9 months for arm 1 (P=0.89). KRAS-WT patients on arm 2 experienced a trend towards greater TTP (median 11.7 vs. 8.4 months on arm 1, P=0.449). Conversely, patients with KRAS mutations had significantly worse median TTP when treated in arm 2 versus arm 1, 1.9 to 7.4 months (P=0.023). Arm 2 KRAS-WT patients with left-sided primary masses had a non-significant improvement in OS (16.0 vs. 12.1 months) compared to patients with right-sided tumours. Conclusions: The addition of

erlotinib to capecitabine increased TTP by 3.2 months in KRAS-WT pts, although this difference was not statistically significant. This study suggests that erlotinib harms patients with KRAS-mutated aCRC while it may provide benefit to those with KRAS-WT CRC. Further study of EGFR-TKIs in patients with KRAS-wild-type CRC, with left-sided primary tumours, is warranted.

Phase II trial of dose reduced capecitabine in elderly patients with advanced colorectal cancer

Daniel Breadner, Mark Vincent, Stephen Welch, James Biagi, Christine Cripps, Derek Jonker, Larry Stitt, Frances Whiston

Background: Combination chemotherapy results in improved outcomes in trials of selected fit patients with advanced colorectal cancer (aCRC). For older patients, combination chemotherapy is associated with greater toxicity and less benefit. Capecitabine monotherapy is a reasonable option for these patients but the optimal dosing remains controversial. Methods: A multicentre phase I/II trial of reduced dose capecitabine 2000mg/m² was conducted in 221 patients in one or more of the following subsets: age 65 years, ECOG performance status 1, elevated LDH, prior pelvic radiation. Patients with prior pelvic radiation received 1500mg/m² based on phase I results. Results: Median age was 72 years. A median 5 cycles were given (range 0 to 50). Grade 3/4 toxicity occurred in 25% of patients during the first 3 cycles (8.1% hand-foot syndrome, 7.7% diarrhea). Response rate was 13.6%, with 69.7% disease control rate. Median PFS was 5.6 months. Median overall survival for all patients is 14.3 months. Median survival was significantly higher for baseline ECOG 0 vs. ≥1 and normal vs. elevated LDH. Conclusions: This report suggests dose reduced capecitabine has less toxicity than historical full dose, with only a small tradeoff in efficacy seen as a lower ORR. Its improved tolerability may lead to an increased number of cycles of therapy, and the PFS appears consistently higher at the lower dose. This should be viewed as compelling evidence in the absence of a head to head clinical trial that

2000, or even 1500 mg/m², is an appropriate dose in elderly or frail patients with aCRC.

Pain management practices surrounding lumbar punctures in children: a national survey of emergency physicians.

Victoria Brzozowski, Samina Ali, Amy Drendel, Antonia Stang, Stuart Harman, Naveen Poonai.

Background: Less than a third of paediatric ED (PED) physicians adhere to societal analgesic recommendations when performing lumbar punctures (LPs). We sought to explore barriers behind this knowledge to practice gap. Methodology: A novel survey was disseminated to physicians listed on either the Paediatric Emergency Research Canada (PERC) or the Canadian Association of Emergency Physicians (CAEP) databases from May 1 to August 1, 2016. Participants were presented with three scenarios of children requiring an LP: a 3-week old male, 16-year-old female, and 3-year-old male. The primary outcome was willingness to provide analgesia for LPs. Results: Response rates were 150/222 (67.6%) for PERC and 272/1362 (20%) for CAEP. For the three-week-old male, 123/144 (85.4%) PED and 231/262 (88.2%) GED physicians reported a willingness to provide analgesia. The most common reason cited by PED physicians for withholding analgesia was that analgesia produced additional discomfort (13/21, 61.9%). The same reason was cited by GED physicians (12/31, 38.7%) along with unfamiliarity surrounding analgesic options (13/31, 41.9%). For the 16-year-old female, willingness to provide analgesia was endorsed by all but one GED physician. For the 3-year-old male, provision of analgesia was almost universal among PED (142/144, 98.6%) and GED physicians (256/262, 97.7%). Conclusions: Compared to older children, willingness to provide analgesia to young infants is suboptimal among GED and PED physicians. In young infants, barriers include perceptions that analgesia produces additional discomfort. GED physicians identify a lack of knowledge surrounding the most appropriate analgesics.

What Makes an Effective SMR On-Call: The Little Things Matter

Sarah Burm, Dr. Saad Chahine Dr. Mark Goldszmidt.

The role of on call Senior Medical Resident (SMR) in internal medicine (IM) represents a key milestone in trainee development. Identifying the core on-call tasks and practices of the SMR role and the range of ways SMRs enact these remains challenging. To support training, we require the perspectives of the broader health care team who can illuminate different components of SMR practice and what it means to competently enact the on-call role. Constructivist grounded theory guided data collection and analysis. Five medical students, 5 junior residents, 5 IM consultants, 5 ER consultants and 5 ER nurses conducted observations of their on-call interactions with SMRs over a period of 1-7 shifts. Participants were subsequently interviewed and asked to describe the SMRs they observed as well as comparative reflections on the practices of past SMRs they worked with. Participants identified a spectrum of behaviours and practices on-call SMRs enacted overnight. Three components of practice differentiated a perceived stronger SMR from a perceived ineffective SMR: communication, collegiality, and compassion. A strong knowledge base and clinical acumen was important, but more commonly, the “little things” SMRs did overnight (eg. introducing themselves, answering pages in a reasonable time, good bedside manner) resonated with participants’ conceptualization of a strong SMR. This critical perspective can be used by training programs to develop more effective, formative, assessment tools and SMR development initiatives.

Hemochromatosis: No iron overload with major symptoms?

Samer Chehade, Paul Adams

Introduction. Hereditary hemochromatosis (HH) has been defined as condition where iron overload leads to complications such as cirrhosis,

arthropathy, and diabetes. More recently, clinicians have begun challenging this dogma, as cases have been identified where patients without iron overload develop severe arthropathy. Our goal was to identify the prevalence of patients without excess iron overload who developed significant arthropathy. Methods. 108 charts of C282Y homozygotes were reviewed to study the relationship of iron overload (defined by liver iron concentration, serum ferritin, and transferrin saturation) to symptoms of arthropathy. No patients had alcoholism or chronic viral hepatitis. A potentially toxic liver iron concentration was considered to be > 280 µmol/g, normal 0 - 35. (Adams PC, Am J Gastro 2001;567). Results. 10 patients were identified who developed significant arthropathy without evidence of toxic iron overload. An 18 year C282Y homozygous man presented with typical hemochromatosis arthropathy requiring bilateral knee replacements by age 36. A woman who was diagnosed as a C282Y homozygote by screening had normal bloodwork, but developed type 2 diabetes and hip arthropathy requiring bilateral hip replacements. In 17 years of follow-up, her ferritin and Transferrin saturation were always in the normal range. Bilateral knee xrays in 2015 showed severe medial femoral and tibial joint space narrowing with osteophytes. Discussion. The clinical course of HH remains unpredictable. These cases challenge the dogma that iron overload is responsible for arthropathy and other HH complications. The role of co-modifying genes in the clinical expression of hemochromatosis is being studied using exome sequencing.

Factors Influencing Two-Unit Blood Transfusions: a quality improvement study

Samer Chehade, Anurag Bhalla, Alan Gob.

Introduction. Choosing Wisely guidelines on blood transfusion have clearly stated that in the case of anemic, stable patients, blood transfusions should be given one unit at a time, and hemoglobin checked prior to a second transfusion. At London Health Sciences Centre, clinicians aimed to study if these guidelines were being followed on a general medical ward, and on

a hematology/oncology ward. **Methods.** In cases of two-unit transfusions, factors influencing the decision by clinicians were identified through a retroactive and quasi-prospective review on both wards. The retroactive review involved examining charts of patients who were given a two-unit transfusion. The prospective review involved the researcher being informed when a two-unit transfusion was ordered, and then interviewing the ordering physician, and examining the chart. **Results and Discussion.** On the Oncology ward, the major factor influencing two-unit transfusions was an electronic order programmed into the EMR which allowed nurses to automatically transfuse two units when hemoglobin dropped below a specified level. The ordering physician was not actively making the order for two units. The pre-programmed order was changed to a one-unit transfusion, and this corrected adherence to guidelines almost completely. On the general medical ward, a pre-programmed order did not exist. Factors such as level of trainee, patient's hemoglobin, and indication did not seem to have an influence on the two-unit transfusion. A solution such as the one for our oncology ward was not identified; however, education regarding the guidelines for both staff physicians and residents may be of benefit.

Paramedic 12-lead ECG and the Frequency of STEMI in Chest Pain and Other Symptoms

Jason Cheng, Michelle Welsford.

BACKGROUND: Prehospital 12-lead ECG (PHTL) are performed for patients showing symptoms consistent with acute myocardial infarction (AMI) as it has been shown to reduce mortality in STEMI patients. The purpose of this study is to determine the frequency of STEMI for different presenting symptoms that may represent myocardial ischemia. **METHODS:** We performed a retrospective review of paramedic calls where a PHTL was performed in one Canadian EMS agency during an 18 month period between October 2013 and March 2015 – the first four months are included in this initial analysis. Data was abstracted from the paramedic medical records (PMR), final diagnosis of STEMI or other cardiac/medical was

determined by in-hospital chart review. **RESULTS:** 219 cases were included, with 80 (37%) being performed for chest pain. The four most common presenting concerns are chest pain, other medical, general weakness and dyspnea. The frequency of STEMI for each category are: chest pain (15%), other medical(5%), general weakness(0%) and dyspnea(5%). With 75% of all STEMIs presenting with chest pain. A chi-squared test showed a significant difference ($P=0.0078$) between the frequency of STEMI in chest pain patients. **CONCLUSIONS:** This initial analysis suggests there is a significantly higher frequency of STEMI in patients presenting to paramedics with chest pain in comparison with other symptoms. Despite 63% of the PHTLs being performed for patients without chest pain, fewer than 25% of STEMIs presented in these patients. The frequency of STEMI in patients without chest pain may be so low that the benefit of a PHTL may be limited.

Insulin Induced Lipohypertrophy: A Case Report

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Introduction: Lipohypertrophy (LH) is the most common skin complication associated with insulin injections, which can be easily overlooked. It can have significant negative impact on the patient's glycemic control, leading to erratic glucose levels. We describe a patient with type 2 diabetes (T2D) who presented with Diabetic Ketoacidosis secondary to LH. **Case reports:** An 85-year-old man with well controlled T2D started to develop worsening glycaemic control with a HbA1C of 9.8 % and 10.5%. He presented to emergency department with DKA and was found to have two areas of thickened discolored skin measuring 3cm in his abdomen, in keeping with lipohypertrophy. During the hospital admission, he developed recurrent severe hypoglycaemic episodes since insulin was injected to his arms or legs where absorption was not impeded. His insulin doses were subsequently decreased and he was counselled about the importance of rotating the injection sites, examining injection sites frequently for evidence of lipohypertrophy especially if increasing insulin requirements. This

patient was diagnosed with T2D 26 years ago and had not recently seen diabetes educators and his insulin injection technique was not formally reviewed prior to hospital admission. Conclusion: LH is a frequent complication of long-term insulin use which leads to reduced insulin absorption and poor glycaemic control. Close attention should be paid to routine examination of injection sites and patients education especially in elderly patient who have suddenly developed difficulties with glycaemic control.

Treatment of asymptomatic UTI in older delirious medical in-patients: A prospective cohort study

Monidipa Dasgupta, Chris Brymer, Sameer ElSayed.

Objectives: Asymptomatic bacteriuria (ASB) in older people is frequently treated. A common reason for treating ASB is a change in mental status. We sought to determine how often asymptomatic UTI is treated in older delirious medical in-patients and its association with functional recovery. Methods: Consecutively admitted older (≥ 70 years old) medical in-patients were screened for delirium and followed in hospital. Treatment for asymptomatic UTI was defined as treatment of UTI with antibiotics, without documented concurrent infectious or urinary symptoms. The primary outcome was functional recovery at discharge or 3 months post-discharge. Poor functional recovery was defined by any one of death, new permanent long-term institutionalization or decreased ability to perform activities of daily living. Results: Out of 343 delirious in-patients, 237 (69%) had poor functional recovery. Ninety four (27%) were treated for asymptomatic UTI. Asymptomatic UTI treatment was associated with poor functional recovery compared to other delirious in-patients (RR 1.30, 95% CI: 1.14-1.48 overall) in both univariable and multivariable analyses (controlling for baseline factors associated with poor recovery). Similar results were seen when the analysis was restricted to only bacteriuric delirious individuals (RR 1.34, 95% CI 1.08-1.66). Seven (7.5%) individuals treated for asymptomatic UTI developed *Clostridium difficile* compared to 8 (3.2%) in the remainder of the

delirious cohort (OR 2.45, 95% CI: 0.86-6.96). Conclusions: Results suggest that treatment of asymptomatic UTI in older medical in-patients with delirium is common, and of questionable benefit. Further evidenced-based guidelines are needed to minimize over-treatment of UTI in older delirious in-patients.

Inter-rater reliability of the retrospectively assigned Clinical Frailty Scale score in a geriatric outreach population

Jasmine Davies, Jennifer Whitlock, RN, Iris Gutmanis, PhD, Sheri-Lynn Kane, MD, FRCPC,.

Background: Frailty, a common clinical syndrome in older adults associated with increased risk of poor health outcomes, has been retrospectively calculated in previous publications; however the reliability of such retrospectively assigned frailty scores has not been determined. The aim of this study was to determine if the Clinical Frailty Scale (CFS) could be reliably assigned retrospectively, based on information in client charts. Methods: Patients undergoing an initial consultation with a nurse clinician from the Southwestern Ontario Regional Geriatric Program from August 15, 2013 onward were invited to participate in this study. As per standard practice, a CFS score (CFS-I) was assigned during the initial consultation. After patient consent was obtained, a medical student researcher, blinded to the initial score, assigned a CFS score (CFS-C) based on the initial consultation note. The inter-rater reliability of the CFS-I and CFS-C was then determined. Results: Of the 41 patients consented, 39 had both a CFS-I and CFS-C score. The median CFS score was six, indicating patients were moderately frail and required assistance for some basic activities of daily living. Cohen's kappa coefficient was 0.64, indicating substantial agreement. Conclusion: CFS scores can be reliably assigned retrospectively thereby strengthening the utility of this measure.

Mortality from potassium tablet aspiration in an elderly patient: lessons learned

Jasmine Davies, Dr. Anurag Bhalla and Dr. Sheri-Lynn Kane.

In the elderly, cognitive impairment is one of the risk factors for swallowing difficulties, which predisposes patients to a host of pulmonary complications. There have been a number of case reports highlighting the significant morbidity associated with pill aspiration. However, these studies primarily focus on post hoc investigations and treatment strategies. There are limited articles that emphasize appropriate screening and prevention of pill aspiration in elderly patients admitted to inpatient services. We present a case of a 94-year-old male admitted to the inpatient Acute Care of Elderly (ACE) service with confusion secondary to acetaminophen toxicity and sigmoid volvulus. At baseline, he was independent for activities of daily living and had no prior history of dysphagia or cognitive impairment. Unfortunately, he aspirated two potassium chloride (K-Dur 1500 mg) tablets, which resulted in occlusion of both main stem bronchi and subsequent death from asphyxiation. This Morbidity and Mortality (M&M) case report utilizes the Ottawa model to draw attention to the cognitive and systems issues related to pill aspiration in elderly patients. Our experience stresses the importance of prevention by appropriate screening swallowing assessments, posture, bolus modification and oropharyngeal rehabilitation.

Reversible Non-Ischemic ECG Changes Post-Adrenalectomy for Pheochromocytoma

Christopher D'Sylva, Tamara Spaic, Tisha Joy.

BACKGROUND: While the classic triad of pheochromocytoma consists of episodic headaches, diaphoresis, and palpitations, its presentation can be atypical. With the high prevalence of alternate or co- diagnoses, the manifestation of pheochromocytoma is often not

readily apparent. **CASE:** A 53-year-old female with a history of hypertension and type 2 diabetes presented to the emergency department with exertional dyspnea in the absence of chest pain. Electrocardiogram (ECG) showed ST segment depression in the anterolateral leads, with a mildly elevated high sensitivity troponin. Cardiac catheterization did not reveal any flow-limiting disease; however, ST segment changes persisted on ECG. During preparation for a cardiac CT, she received intravenous metoprolol and became profoundly hypertensive at 200/110 mmHg. A right 6.6 cm adrenal mass was noted on the study, with subsequent urine studies confirming a pheochromocytoma. Following staging and medical optimization, she underwent successful laparoscopic right adrenalectomy. Post-operatively, her ST segment changes resolved and all anti-hypertensive medications were discontinued. Her glycemic control improved and she was able to discontinue her insulin, achieving an HbA1c of 6.0% on oral medications alone. **DISCUSSION:** Hypertension and tachyarrhythmias are the most common cardiovascular manifestations of pheochromocytoma. Although limited to ST segment changes in this case, other ECG abnormalities of pheochromocytoma include QT prolongation and deep T-wave inversions, independent of atherosclerotic disease. Proposed mechanisms for these changes include oxidative and calcium induced myocardial damage, as well as vasoconstriction. Our case demonstrates the importance of considering pheochromocytoma in the differential diagnosis of ischemic ECG changes without obstructive atherosclerotic disease.

Investigating the role of citrullinated protein in the development of atherosclerotic plaque using animal models of atherosclerosis and rheumatoid arthritis

Bailey Dyck, Lillian Barra, Murray Huff, Ewa Cairns.

Objectives: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease (CVD), particularly in

patients expressing autoantibodies targeting citrulline-containing proteins (ACPA). Citrullinated proteins (CitP) are present in human atherosclerotic plaque. We hypothesize that in RA, ACPA bind to CitP in plaque promoting cardiovascular events. In this project, we use established mouse models of CVD and RA to determine whether CitP is expressed in the aortic plaque of these mice. Methods: Protein lysates were prepared from dissected aortas of: (1) low density lipoprotein receptor knockout (LDLR^{-/-}) mice (CVD model); (2) HLA-DR4 transgenic (DR4Tg) mice (RA model), (3) LDLR^{-/-} crossed with DR4Tg mice. All mice were fed a high fat, high cholesterol diet (HFHC) or regular chow. Western blot (WB) utilizing anti-modified citrulline (AMC) antibody (Millipore) was performed to identify and quantify CitP. Homogenized mouse skin (known to have CitP) was also used. Results: WB analysis of aortic lysates from LDLR^{-/-} mice (n=23) fed either HFHC or chow for 70 days did not detect the presence of CitP. As expected, homogenized mouse skin expressed high levels of CitP. Results from the other two mouse groups are in progress. Conclusions: CitP were not identified in aortas from LDLR^{-/-} mice fed 70 days of HFHC diet. Expression of CitP may be low or absent at this earlier stage of atherosclerosis compared to advanced plaque; future studies of mice fed diet for 6 months are underway. Understanding the role of ACPA and CitP in atherosclerosis may elucidate new mechanisms of CVD in RA.

Intranasal ketamine for procedural sedation in children undergoing fracture reduction: a randomized controlled pilot study

Sharlene Elsie BHSc, Kyle Canton BSc, Gary Joubert MD, Amit Shah MD, Mike Rieder MD, Naveen Poonai MD

Purpose: Procedural sedation and analgesia (PSA) is a common indication for intravenous (IV) insertion in the emergency department (ED). IV ketamine, the most frequently used agent, can also be given intranasally; obviating a painful IV. Our objective was to explore the feasibility of intranasal ketamine (INK) for PSA in children. **Methods:** This was a randomized, blinded,

controlled, trial comparing the effectiveness of INK versus intravenous ketamine (IVK) in children 4-17 years, < 40 kg, with a non-shortened distal forearm fracture requiring PSA for closed reduction. Participants received (i) INK 8 mg/kg + IV saline OR (ii) IVK 1 mg/kg + IN saline. The primary outcome was the proportion with adequate sedation as defined by a University of Michigan Sedation Scale (UMSS) score of > 3 of 4. Results: Fifteen participants (7 INK and 8 IVK) were recruited from March 1, 2016 to Feb 1, 2017. Adequate sedation was achieved by 4/7 (57.1%) versus 7/8 (87.5%) participants in the INK and IVK groups, respectively. The median (IQR) time to sedation was 10 (11.3) versus 5 (0) minutes in the INK and IVK groups, respectively. Adverse effects were seen in 4/7 (57.1) versus 2/8 (25%) of participants in the INK and IVK groups, respectively. Conclusion: The adequacy of sedation for INK 8 mg/kg is inconsistent for closed reduction of distal forearm fractures in children. Greater sedative efficacy may be achieved with a higher dose, consistent with demonstrated effectiveness in other studies of PSA in children.

Depression Increases the Risk of Injurious Falls In Individuals with Mild Cognitive Impairment: Results from The “Gait And Brain Study”.

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Background: Depression, falls, and gait impairments are highly prevalent in older individuals with Mild Cognitive Impairment (MCI). However, it is currently unknown whether the presence of depression in individuals with MCI could exacerbate their risk of falls and whether gait impairments are worse in these individuals. **Aims:** We aimed to prospectively evaluate the effect of depression and depressive symptoms in the risk of falls and to sustain injuries from falls in older adults with MCI. We also aimed to evaluate gait performance of groups at baseline. **Methods:** Ninety seven participants aged 65 and older (mean age 74±8; 61% women) were included in a three year cohort study. Study sample was stratified by Controls (n=25), MCI without

depression (MCI, n=50); and MCI with depression (MCI-D, n=22). ANCOVAs were performed to compare groups' gait data at baseline. The association between depression and falls was evaluated using unadjusted and adjusted Cox-Regression analyses including several covariates. Results: Both MCI groups walked significantly slower than Controls (MCI-D=98 cm/s; MCI= 106 cm/s; Controls= 122 cm/s). Despite clinically significant differences, no statistical differences were found between the MCI groups for gait velocity. The risk to sustain injuries from falls was up to 4 times higher in MCI-D than MCI [HRadjusted: 4.45; 95%-CI (1.74 – 15.39), p=0.017] while the risk of falls without injuries was similar across groups. Conclusions: Depression increases the risk to sustain injuries from falls in older individuals with MCI. Injuries due to falls may be linked to gait slowness in this population.

The Role of Keratin-19 Positive Stem Cells in Colonic Epithelium Regeneration post Colitis

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The intestinal and colonic epithelia are rapidly renewed every 3 to 5 days. In the intestine, at least two principal stem cell pools, comprised of rapidly cycling crypt based columnar (CBC) Lgr5+ cells and slower cycling Bmi1-expressing cells located above the crypt base, have been described. In the colon however, we have identified an additional, spatially distinct, Lgr5-negative stem cell pool that expresses Krt19. The goal of this study was to determine whether the Krt19+ colonic stem cell pool is responsible for colonic crypt regeneration during colitis. To study the lineage of Lgr5+ and Krt19+ stem cells and determine whether Lgr5 and/or Krt19 marks colonic stem cells that contribute to epithelial regeneration upon colonic injury, we crossed Krt19-BAC-CreER transgenic mice to Lgr5-DTR-GFP and the ROSA26r-Tdtomato reporter line. Mice were then treated with tamoxifen followed by water (control) or DSS (in the drinking water x 7 days) to induce colitis. Lgr5+ and Krt19+ cells were studied in the context of normal homeostasis or following DSS-induced colonic

injury. Our results demonstrate that Lgr5+ stem cells are sensitive to DSS-induced colonic injury. Krt19 marked long-lived cells above the crypt base that were resistant to DSS-induced colonic epithelial injury and gave rise to Lgr5+ cells in the newly regenerated crypts. Using Lgr5-DTR-GFP;K19-BAC-CreER; ROSA26r-Tdtomato mice, diphtheria toxin induced ablation of Lgr5+ cells further demonstrated that Lgr5+ stem cells are not required for colonic epithelial regeneration following DSS-induced colitis. Our data suggest that more than one stem cell population is important for regeneration in colitis.

Intracellular pH regulates TRAIL induced-apoptosis and necroptosis in endothelial cells

Benjamin Fuhrmann, Ingrid Gan, Alexander Pavlovsky, Xuyan Huang, Zhuxu Zhang and Anthony M. Jevnikar

During ischemia or inflammation, intracellular pH is quickly reduced if production of acid exceeds the cell's buffering capacity. The resulting acidosis can alter pH-dependent intracellular mechanisms that mediate cell death. We have previously shown that silencing caspase-8 in an in vivo ischemia reperfusion injury (IRI) model results in improved organ function and survival. However, caspase-8 loss in the donor organ paradoxically results in enhanced receptor interacting kinases (RIPK) 1/3 regulated necroptosis and accelerated graft loss following transplantation. In our current study, TRAIL (TNF-related apoptosis inducing ligand) induced cell death in vitro at neutral pH and caspase-8 inhibition enhanced RIPK1-dependent necroptotic death was confirmed. In contrast, both caspase-8 inhibition and RIPK1 inhibition attenuated cell death at a cell pH of 6.7. Cell death was attenuated with Mixed Lineage Kinase Domain-Like (MLKL) silencing, indicating that MLKL membrane rupture, a distinctive feature of necroptosis, occurs regardless of pH. These results highlight the complexity of modulating cell death and that therapeutic strategies may need to consider different consequences on cell death dependent on the model.

Mitochondrial permeability can regulate endothelial cell necroptosis and promote cardiac allograft rejection

Ingrid Gan, Jifu Jiang, Dameng Lian, Xuyan Huang, Winnie Liu, Aaron Haig, Anthony M. Jevnikar, Zhu-Xu Zhang.

Transplant injury is invariably associated with programmed cell death (PCD) resulting in delayed graft function and organ rejection. Many forms of PCD have been described including apoptosis, pyroptosis, ferroptosis, and necroptosis. They are induced by various death receptors (DRs) including tumor necrosis factor receptor-1 (TNFR1), DR4/5, and Fas engagement. We were the first to describe receptor-interacting serine/threonine protein kinase 3 (RIPK3) mediated necroptosis in transplant injury, where tissue necrosis and graft rejection were attenuated in RIPK3 null heart allografts following transplantation. Until now, the effect of mitochondrial dysfunction in the necroptotic pathway remains controversial – it is suggested that mitochondrial dysfunction may promote necroptosis in some studies but not in others. Here, our goal was to determine if mitochondrial injury participates in cardiac cell necroptotic death and accelerates graft rejection. We found that TNF α and caspase-8 inhibition triggered cells to undergo RIPK1/3-dependent necroptosis in vitro and this cell death was attenuated by MPT inhibition. Furthermore, cardiac allografts deficient in MPT regulator protein cyclophilin D (CypD) had prolonged survival compared to wild type grafts (MSD=85 versus 31 days, $p < 0.0001$). Our study shows that mitochondrial permeability may be an important mechanistic mediator of necroptosis, and that targeting the mitochondria-mediated cell death to reduce cardiac graft rejection may hold therapeutic promise.

Do serum adalimumab level correlate with disease severity in patients with Crohn's disease?

Mandark Gandhi, Larry State & Jamie Gregor.

INTRO: Tests measuring serum adalimumab levels are not widely available. We aim to evaluate whether serum adalimumab levels correlate with disease severity in patients with Crohn's disease. Additionally, we aim to see if clinical and biochemical markers can be used as a surrogate for adalimumab levels. **METHODS:** A retrospective chart review was performed on Crohn's disease patients that had a measured adalimumab level. Sixty-five patients were identified between January 2015 and January 2016. Disease severity was determined using the Harvey-Bradshaw Index. Patients were stratified by dosing intervals. **RESULTS:** For patients with weekly dosing ($n=16$), 8 were in remission. Mean trough adalimumab levels for remission and active disease groups were 8.8 and 7.3 respectively. There was no statistically significant relationship between trough adalimumab level and disease severity, weight, CRP or albumin. For patients with biweekly dosing ($n=49$), 32 were in remission. Mean trough adalimumab levels for remission and active disease groups were 8.5 and 6.1 respectively. The correlation between trough adalimumab level and weight was -0.44 ($p=0.002$). Similarly, the correlation between trough adalimumab level and CRP was -0.39 ($p=0.031$). Trough adalimumab level did not have a statistically significant relationship with albumin or disease severity. **CONCLUSION:** In patients with biweekly dosing, higher drug levels correlated with lower patient weight and lower CRP values. Empiric weekly dosing may be needed to obtain higher trough levels in heavier patients with higher disease burden. Ultimately, larger studies with prospective data are needed.

Assessing Comprehension of Acute and Chronic Illnesses in the Hospitalized Elderly Population

Dr. Amanda Giffin

Primary objective: To assess and describe hospitalized seniors' understanding of their medical conditions. **Secondary objective:** To identify characteristics associated with poor understanding of medical conditions and compare to frequency of 3 month re-admission rate. **Methods:** This was a pilot study. The first part involved developing an interview tool to

assess seniors' understanding of their acute and chronic medical conditions, and assessing reliability of this tool. This interview tool was administered to enrolled patients. Patients were enrolled if they met the following criteria: a) admitted to a CTU team; b) at least 70 years of age; c) anticipated to be within 72hrs of discharge; d) have one of four chronic illnesses (CHF, COPD, DMII, CKD) and e) have a clear admission diagnosis at the time of enrolment. Patients with known dementia were excluded. Other information collected included demographics, functional dependence, frailty level, cognitive function and co-morbidity. Results: Reliability on interview questions was acceptable ($\kappa > 0.75$, $n = 6$). The 13 patients (6 female) enrolled had an average age of 86. Most used a gait aid (12), 7 needed assistance with stairs, and 11 needed help with at least 2 IADLs. All patients interviewed knew 40% or less of their medications by name, and 9 patients could name 40% or less of their medical conditions. Conclusions: Understanding of medical conditions and their treatments appears sub-optimal in frail hospitalized seniors, even without overt cognitive impairment. Further research is required to characterize determinants of poor health literacy, and to improve understanding of health conditions.

Disseminated Nocardiosis with pulmonary and hepatic involvement in a 57-year-old female with CLL and drug-induced pneumonitis

Dan Gillett, Lise Bondy.

Nocardia spp. is a Gram-positive aerobic bacillus of the genus *Nocardia*. Infections resulting from pathogens of this genus are rare, typically occurring in immunocompromised patients. Risk factors for developing such infections include cellular immunity depression as in patients who have undergone transplantation, patients with leukemia, acquired immune deficiency virus or prolonged treatment with corticoids or cytotoxic therapy. The aerosol route is the most common site of entry, with lungs the most common site of infection. We report a 57-year-old female patient with a history of CLL in remission on chronic prednisone for drug-induced pneumonitis

secondary to chemotherapy with rituximab and cyclophosphamide presenting with a right lower lobe paratracheal mass. She underwent endobronchial ultrasound-guided transbronchial aspiration (EBUS-TBNA) and subsequently presented febrile and hypotensive and was found to have multiple liver abscesses. Ultrasound guided aspiration of her liver abscess was performed and culture was positive for *Nocardia farcinica*. Subsequent stains performed on the EBUS-TBNA sample for acid-fast bacilli showed a focal collection of positive filamentous organisms. The patient was started on oral sulfamethoxazole/trimethoprim (800/160mg mg every 8 hours) and intravenous imipenem (500 mg every 6 hours). Total mortality rates from *Nocardia* infections are high, with in-hospital mortality up to 20%. Early diagnosis and treatment of this infection is important to reduce mortality rates.

Initial use of subcutaneous methotrexate in early rheumatoid arthritis is associated with decreased biologic use: results from the CATCH cohort

Stephanie Gottheil, Janet Pope.

Optimal treatment for moderate-severe early rheumatoid arthritis involves using a MTX-based, treat-to-target strategy aiming for remission. Reducing the need for expensive biologic therapy may be possible by optimizing initial DMARD therapy. Our objective was to compare time to biologic use between early RA patients started on MTX monotherapy versus MTX combination therapy. Data were obtained from a multi-center prospective cohort study of early RA patients. We included participants who met 1987/2010 ACR criteria, with <12 months symptom duration, moderate-high disease activity, biologic naive and treated with MTX. Patients were followed until biologic start, loss to follow up or the end of the 3-year study period. Cox proportional hazards survival analysis was used to estimate effects of oral MTX monotherapy, scMTX monotherapy, and MTX combination therapy adjusting for age, gender, education, symptom duration, pain, erosions, DAS28, and corticosteroids. 1189 patients were included with 207 first events of biologic use. Median time to biologic start was 9

months. At baseline, 865 (71%) were female with mean (sd) age 54 (15) years, symptom duration 6 (3) months, and DAS28 5.45 (1.2). In fully adjusted Cox models, patients treated with scMTX monotherapy had a significantly reduced biologic start compared to oral MTX monotherapy (HR = 0.53, p = 0.02). Treatment with scMTX monotherapy was associated with reduced biologic initiation. This may be due to increased treatment efficacy compared to oral MTX. This study suggests that early use of scMTX can potentially delay the need for more expensive biologic therapies.

How do you solve a problem like data mining? How do you make a code to fit them all?

Amanda Grant-Orser, Marcus Povitz, Eric Frechette

In the progressive era of electronic health records, administrative data has been an evolving source and focus of research projects. The process varies, but generally a validation study is required to confirm the correct algorithm is in place to data mine the vast array of information available. Some areas of medicine have been very successful at accessing and utilizing this gold mine of data, while others are only starting to investigate its possibilities. This work attempted to identify a cohort of patients diagnosed with malignant pleural effusions (MPE). Through a variety of approaches including ICD10 criteria, CCI procedure codes, and OHIP billing information we attempted to create an algorithm, which was both sensitive and specific. What we found was while administrative data was easily accessible, thorough and consistent, this did not translate into being useful for our purpose. After multiple attempts it was determined that such an algorithm was not possible for this specific patient population. Moving forward, this opens the discussion to the increasing role administrative data plays in health care research and poses the question - what are the limits to administrative data?

A retrospective study comparing the efficacy and safety of prednisone versus dexamethasone for the treatment of patients with immune thrombocytopenia (ITP)

Manika Gupta, Kulraj Singh, Selay Lam, Joy Mangel, Alan Gob, Ian Chin-Yee, Chai Phua, Cyrus Hsia.

Background: Immune thrombocytopenia (ITP) is a common benign autoimmune hematological condition characterized by decreased platelet counts and an increased risk of bleeding. There has been significant variation in clinical treatment practices relating to ITP including choice of oral prednisone or dexamethasone. Objective: We will compare these corticosteroid agents for time to initial response, best response achieved, sustained response, and safety in the treatment of ITP patients. Methods: All adult patients, diagnosed with ITP between January 1, 2010 and December 31, 2015 treated with these two corticosteroids will be reviewed. Patients will be stratified according to severity of initial presentation based on clinical bleeding score (0 to 4). Time to initial response (within seven days or greater than seven days), best response achieved, and time to first relapse will be determined for patients in each treatment group. Types of responses include complete response (CR) (platelets >100x10⁹/L), partial response (PR) (platelets >30x10⁹/L) and no response (NR)(platelets =<30x10⁹/L). Results: 348 adult patients with ITP have been identified. 139 of these patients were treated with prednisone, 13 patients were treated with dexamethasone and 11 patients were treated with both regimens for ITP. Preliminary data suggests that amongst patients treated with dexamethasone, 3 patients achieved CR, 7 patients achieved PR, and 3 patients had NR. Comparison of treatment responsiveness for patients treated with prednisone will be completed. Conclusion: The research work will enable clinicians to have a well-supported risk-benefit discussion when discussing potential corticosteroid options for management of ITP.

Efficacy Of Ondansetron In The Prevention And Treatment Of Post-operative Delirium – A Systematic Review

Nihal Haque, Raza M Naqvi, Monidipa Dasgupta.

Background/Purpose: Post-operative delirium (POD) affects up to 50% of surgeries. It is associated with higher rates of functional decline and death. Serotonin may play a role in POD. Ondansetron is a serotonin antagonist with a favourable safety profile, and could represent a therapeutic and preventive option in POD. **Methods:** We performed a systematic review of MedLine, EMBASE, CENTRAL and PsychINFO from inception to December 2015. Initial screening identified 622 abstracts and three randomized controlled trials (RCTs) met inclusion criteria. **Results:** Two RCTs examined ondansetron for the treatment of POD. One study administered haloperidol 5mg or ondansetron 8mg intravenously (IV) as a single dose to 80 delirious patients post cardiac surgery (mean age 71). Both had similar reductions in their average delirium score and patients with persistent delirium. Another study administered ondansetron 4mg or haloperidol 5mg IV twice daily to 96 postoperative delirious patients for three consecutive days (mean age 31). Both groups had similar delirium rates after administration. However the ondansetron group received a higher total dose of rescue haloperidol. Finally, one RCT examined prophylactic ondansetron versus placebo to prevent POD in 106 orthopedic patients (mean age 71). They administered 8 mg of ondansetron or placebo IV once daily for five days postoperatively. There were significantly less delirious patients in the ondansetron group starting on day 3 and persisting to day 5. **Conclusions:** Ondansetron appears to be an efficacious agent for the prevention and treatment of POD. Further large RCTs of high quality are needed to confirm these results.

Innovating Curriculum with Interprofessional Patient Safety and Quality Improvement Projects to Deliver the Leadership, Advocate and Professional Competencies in UME

Juliya Hemmett, Ramiro Arellano, Robert Sibbald, Scott McKay, Neil Merritt, Monica Staley, Jason Elzinga, Brandon Chau, Teresa VanDeven, Wally Liang, Gary Tithecott, Nabil Sultan..

Background: Patient safety (PS), quality improvement (QI), leadership and medical ethics are key objectives of undergraduate medical education (UME) critical to health care. Instilling the importance of QI and PS is a national objective and challenge facing educators. Professional identity as a concept is becoming increasingly recognized as an important aspect of medical education. Providing students with tools to shape their identity as professionals and leaders, while understanding the important role of patient safety and quality improvement (PSQI) in patient care is key to competency. Through a longitudinal year 2 courses, we integrated this learning through a mentored team approach. **Methods:** Our school has undertaken a novel approach to educate by removing the artificial barriers of past individual courses. Using mentored small group, lecture and independent learning while focusing students on a team based one year PSQI project coached by interdisciplinary faculty in hospital and clinic settings, we delivered curriculum on leadership, PSQI, ethics, systems and financial learning in patient care prior to Clerkship. **Results:** We describe our inaugural cohort experience and recommendations for educators. Our approach delivering the leadership, advocate and professional competency within the lens of a team designed and delivered PSQI project with health care mentors will support schools revising curriculum. We advocate for early introduction to PSQI integrated learning focused on real care scenarios prior to formal Clerkship. Our approach supports students in a firm foundation to their professional identity as future physicians.

Diagnostic Utility of Lung Ultrasound for Heart Failure in Dyspneic Patients: A Systematic Review

Hailey Hobbs, Robert Arntfield Ian Ball Claudio Martin.

Introduction: First described in the 1980's, lung ultrasonography is now a well established diagnostic modality with superior accuracy and inter-observer reliability than current bedside diagnostic techniques. The objective of this review was to assess the available literature to determine the diagnostic accuracy of lung ultrasound for heart failure in adult patients presenting to an acute care setting with undifferentiated dyspnea. Methods: Literature review was conducted with the help of a hospital librarian. Embase and OVID of Medline databases were searched from inception through November 2016. Included studies assessed adult (age >18) patients who underwent lung ultrasound as part of the workup for acute undifferentiated dyspnea. To be included, studies had to have an independent assessor blinded to lung ultrasound results make a diagnosis of heart failure. Studies that did not report diagnostic accuracy of lung ultrasound alone, studies comparing only to chest X-ray or BNP, studies in chronic heart failure or dialysis patients were excluded. Risk of bias was assessed using the QUADAS2 methodology. Main Results: The primary literature search identified 1835 titles, after duplicates were removed 1438 titles were screened by two reviewers for inclusion and 99 were selected for full text screening: 20 papers were included in full text review. Full text analysis currently ongoing and expected to be complete prior to presentation date.

Improving ECG Diagnostic Accuracy in Emergency Medicine Services Personnel

Dr. Ashlay Huitema, Mistre Alemayehu, Sabrina Wall, Jay Loosely, Dr. Shahar Lavi.

Accuracy of ECG interpretation is important for identification of ST-elevation myocardial infarctions (STEMI) by Emergency Medical

Service (EMS) personnel who recognize STEMIs in the field and activate the coronary catheterization lab (CCL). Based on our previous research there is improvement in diagnostic accuracy of STEMIs for healthcare providers that read an average of >20 ECGs per week. This study evaluated the effectiveness of online ECG education modules on improving ECG diagnostic accuracy. EMS personnel received 25 ECGs per week to interpret via an online program. Evaluation for effect on improvement in diagnostic accuracy was assessed via completion of an ECG evaluation package before and after the intervention. Data was collected regarding job satisfaction to determine if the educational initiative had any significant impacts. A total of 64 participants completed the education modules and accompanying evaluation packages. Overall, there was a significant improvement in ECG diagnostic accuracy from 51 to 62% (CI 8-13%, $p < 0.0001$). Specifically there was statistically significant improvement in the diagnosis of STEMI (8.5% (4.9-12.3), $p < 0.003$) and supraventricular tachycardia (SVT) (39% (17.2-60.8, $p < 0.008$), with the trend toward improvement in all other diagnoses. Improvement was seen regardless of EMS personnel's employment experience and training. There was no significant impact on job satisfaction. ECG exposure remains an important factor in improving the accuracy of ECG diagnosis in EMS personnel. Online education modules provide an easily accessible way of improving ECG interpretation with the opportunity for positive downstream effects on patient outcomes and resource utilization.

Determining whether Citrullinated and Homocitrullinated Lipoproteins Have a Role in Rheumatoid Arthritis-Associated Atherosclerosis by Promoting Proinflammatory Cytokine Release from Macrophages

Alexander Hofkirchner, David Bell, Ewa Cairns, Bryan Heit, Murray Huff, Geoffrey Pickering, Lillian Barra.

Objective: Rheumatoid arthritis (RA) patients are at increased risk of developing cardiovascular

disease (CVD), although the pathogenetic mechanism in RA is unknown. The majority of RA patients express antibodies targeting citrullinated proteins. Citrulline is structurally similar to homocitrulline, and homocitrullinated (carbamylation) low-density lipoproteins (HcitLDL) have been identified in atherosclerotic plaques. However, the effects of citrullinated LDL (CitLDL) and HcitLDL on cytokine release from human macrophages are unknown. We aim to investigate whether macrophages exposed to CitLDL or HcitLDL secrete pro-inflammatory cytokines, namely TNF-alpha and IL-6. Methods: Cells from a human monocyte cell line (THP-1) were plated and differentiated to M1-type macrophages. Macrophages were treated with 10µg/mL CitLDL, HcitLDL, LDL, acetylated LDL (AcLDL), or lipopolysaccharide (LPS). Cell supernatants were collected at varying time points, and TNF-alpha and IL-6 cytokine concentrations were measured in duplicate using commercial ELISA kits. Results: Compared to baseline LDL treatments, significant ($p < 0.05$) secretion of TNF-alpha occurred at 6 hours for AcLDL (1.17ng/mL) and LPS (1.71ng/mL) treatments, while significant secretion of IL-6 occurred after 24 hours for AcLDL (0.15ng/mL) and LPS (0.70ng/mL). At 10µg/mL, LDL, CitLDL, and HcitLDL did not induce TNF-alpha or IL-6 secretion at any time point. Conclusion: In a human monocyte cell line differentiated to an M1-macrophage phenotype, significant secretion of TNF-alpha and IL-6 occurred 6 and 24 hours after AcLDL exposure, respectively. At the same concentration, CitLDL and HcitLDL did not induce release of these cytokines. Future work will examine whether different concentrations of CitLDL and HcitLDL elicit pro-inflammatory cytokine release.

The outcome of an integrated care intervention at a tertiary hospital for patients with chronic obstructive pulmonary disease: a retrospective, single center, cohort study of the Connecting Care to Home Program.

Jessica Jackson, Dr. Marcus Povitz Caitlin Schultz.

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide representing an increasing economic and social burden. Globally, this burden is projected to increase in coming decades because of continued exposure to COPD risk factors and the aging population. Despite the clear burden on healthcare systems both globally and here in Canada, there are few interventions that have been shown to reduce length of stay for COPD-related hospitalizations. It is well understood that optimal care for patients with COPD requires an individualized, patient-centered approach that recognizes and treats all aspects of the disease and integrates medical care both in hospital and in the community. The purpose of this study was to evaluate the effect of the Connecting Care to Home (CC2H) Program at London Health Sciences Center on length of stay for COPD-related hospitalizations. The Connecting Care to Home (CC2H) Program is a program offered to patients admitted to Victoria Hospital with a diagnosis of COPD. CC2H is a multi-disciplinary team consisting of a COPD Navigator (a respiratory therapist), community care coordinators and nursing staff that help to facilitate discharge from hospital and continue care at home. This study was a single-center retrospective cohort study examining patients offered enrollment in the Connecting Care to Home program at LHSC between October 2015 and January 2017. The study is current in the data collection stage and results are pending. Results of this study will help inform further program advancement and development.

Impact of occupational mechanical stress in clinical outcomes in patients with axial spondyloarthritis

Maysam Khalfan, Sherry Rohekar.

Axial spondyloarthritis (axSpA) is an inflammatory arthritis that has been thought to be affected by environmental factors such as mechanical stress. While previous work has shown that heavy physical activity can worsen functional outcomes in patients with ankylosing spondylitis, a subtype of axSpA, there is little work that looks at this effect across all subtypes of axial spondyloarthritis. This research project

looks at a Canadian cohort of patients with axial spondyloarthritis and examines the effect of occupational mechanical stress on patient reported outcomes. Patients answered questions about the type of physical activity encountered at work, for example lifting, bending and squatting, and this information was correlated with their scores in validated patient reported outcome tools such as the Health Assessment Questionnaire. We expect this study to help inform patients and care providers on the contribution of specific physical activities encountered in the workplace towards disease outcome.

Weight Loss as an Initial Manifestation Of Cushing's Syndrome

Parul Khanna and Tisha R. Joy.

BACKGROUND Cushing's syndrome is a disorder of hypercortisolism that is typically characterized by truncal weight gain, easy bruising, purple striae, glucose intolerance/diabetes, and hypertension. Ectopic secretion of adrenocorticotropin hormone (ACTH) from tumours is rare, accounting for 10% of cases of Cushing's syndrome. **CASE:** A 51 year-old man (BMI 18.3 kg/m²), non-smoker, presented with a history of weight loss in the setting of new-onset diabetes. Although his blood sugars improved with the use of insulin, he had ongoing weight loss. History of proximal muscle weakness and erectile dysfunction prompted further biochemical testing. In addition to secondary hypogonadism and hypothyroidism, he had an elevated ACTH level of 22.95 pmol/L with a 24 hour urine cortisol of 13184 (normal <346) nmol/d. Imaging documented a right upper lobe lung mass measuring 3.5cm x 3.6cm and multiple metastatic lesions to the brain, pituitary and liver as well as bilateral adrenal enlargement. Histology confirmed the diagnosis of large cell neuroendocrine tumor with primary lung origin. **DISCUSSION:** Although diabetes and Cushing's syndrome are often associated with weight gain, weight loss rather than weight gain may occur in the setting of ectopic Cushing's syndrome. This case therefore demonstrates the importance of keeping a broad differential for patients with ongoing weight loss.

The Effects of Intra-uterine Growth Restriction (IUGR) on the Pulmonary Surfactant and developing Lung Injury

Reza Khazaei, Lynda McCaig, Daniel Hardy, Cory Yamashita, Ruud Veldhuizen.

Introduction: Intra-uterine growth restriction (IUGR) is defined by a low birth weight and contributes to a variety of adult-onset diseases. There are potential shared mechanisms between these diseases and acute respiratory distress syndrome (ARDS), which is defined as severe lung dysfunction. The lung dysfunction results from alterations to surfactant; a lipid-protein mixture coats the inside of the lung and maintains the lungs' ability to expand easily during respiration. There is evidence that IUGR affects the lung function, however, whether this happens through surfactant alterations and may predispose the host to the development of ARDS is unknown. This study investigates IUGR effects on the surfactant system and lung function during postnatal life. **Hypothesis:** IUGR is a risk factor for ARDS through alterations of surfactant system. **Methods:** We used an IUGR rat model induced by maternal low protein diet. Offspring were sexed in each dietary group following birth. We assessed surfactant content, lung compliance, and airway resistance for 1, 7 and 21-day offspring. **Results:** There was no significant difference in surfactant content between the IUGRs and controls. Lung compliance in 21-day female IUGRs significantly decreased while airway resistance increased significantly in 21-day male and female IUGRs. **Discussion:** No changes in surfactant content suggest that the lower lung compliance in females potentially happened through alterations of surfactant biophysical properties. Increases in airway resistance could affect the development of surfactant system and lung injuries. In future experiments, to further evaluate the ARDS susceptibility, we will assess surfactant function and lung histology in adult IUGRs.

Development of a personalized competency based assessment tool (PCAT) for Internal Medicine trainees

Meherzad Kutky, Mark Goldszmidt, Saad Chahine.

Background: The recent shift towards competency based medical education has created a need for new assessment tools. Internal Medicine trainees are currently evaluated using the Mini-Clinical Evaluation Exercise (mini-CEX). While the mini-CEX is a validated tool to assess global competence, it does not assess competency for a specific task. The purpose of this study was to create a personalized competency based assessment tool (PCAT) for Internal Medicine trainees that could provide a global competency score for an encounter and focused feedback for the trainee. **Methods/Results:** Using the Ottawa Surgical Competency Operating Room Evaluation Score Based (O-Score) as a template. We designed a prototype encounter assessment tool with similar global competency anchors such as “I had to repeat (Level 1) or I did not need to be there (Level 5)”. Through consultations with residents and faculty, six key attributes that would be useful to help trainee’s progress to the next global level of competency were identified. Additionally, pre-generated comments based on clinical reasoning tasks were created for each attribute, allowing for ease of use and focused feedback. **Conclusions:** The PCAT provides a global assessment of competency for an encounter, followed by feedback on key attributes trainees need to improve upon in order to progress to the next competency level. The current version of the PCAT will be used in a pilot study across consult services at LHSC and the data will be used to further refine and assess its use in other clinical settings.

ReCoM: The Development of the Resident Communication Manual

Rachel Kyle, Raza Naqvi.

The overall objective of this project was to produce a manual that will provide guidance to beginner residents on quality communication with patients in order to improve their skills with difficult conversations. Communication is an important skill for physicians, and yet medical education is lacking around concrete skills. The manual, written in colloquial language, is meant to be a functional reference for residents using tangible examples, the personal experience of the authors, and the evidence-based shared decision making model to address the common communication problems faced by residents in their everyday practice. The presentation and interpretation of statistics are one of the common pitfalls tackled in the manual. Using a real life example to show the sometimes dramatic consequences of how statistics are presented, we address how statistics can be used to practice evidence-based medicine and preserve patient autonomy. The evidence behind the shared decision making model is presented, as well as a practical approach to using it in everyday practice. Using code-status discussions as a familiar example, a mock conversation is presented to demonstrate how this approach can help to facilitate a difficult discussion with patients. The framing and wording of the conversation is then reflected upon and discussed, along with common patient responses and how to address them. The manual also addresses some of the common knowledge gaps around survival, outcomes and the process of resuscitation itself. Efficacy and readability of the manual has been evaluated by surveys completed by residents and CTU staff.

Relatedness of antibodies to peptides containing homocitrulline or citrulline in patients with Rheumatoid Arthritis

Patrick Lac, Maud Racapé, Lillian Barra, David A. Bell, Ewa Cairns.

Background. Rheumatoid arthritis (RA) is an autoimmune disorder that is characterized by joint inflammation. Anti-citrullinated protein antibodies (ACPA) target proteins containing citrulline (post-translationally modified arginine), are specific for RA and are arthritogenic. RA has also been associated with anti-homocitrullinated

protein antibodies (AHCPA) which target proteins containing homocitrulline (post-translationally modified lysine), which shares structural similarity with citrulline. The relationship between ACPA and AHCPA is poorly understood. We examined the expression and cross-reactivity of ACPA and AHCPA using molecules with equal numbers of citrulline and homocitrulline residues, CitJED and HomoCitJED. Methods. Serum from RA patients (n=137), healthy subjects (n=51), Systemic Lupus Erythematosus patients (SLE; n=37) and Psoriatic Arthritis patients (PsA; n=37) were screened for IgG anti-CitJED and anti-HomoCitJED antibodies by Enzyme-Linked Immunosorbent Assay (ELISA). Cross-reactivity of these antibodies was examined by inhibition with various concentrations of CitJED and HomoCitJED. Results. Antibodies to CitJED and HomoCitJED were detected in 69/137 (50%) and 78/137 (57%) of RA patients respectively. These antibodies were 77% concordant and their levels were correlated (Spearman $r=0.6676$). Sera from 25/27 (93%) RA patients with adequate antibody levels, were inhibited by both CitJED and HomoCitJED with equal or higher affinity for the cognate (homologous) peptide. Conclusion. Anti-CitJED and anti-HomoCitJED antibodies frequently occurred in RA, but not in SLE or PsA, suggesting that these antibodies are specific for RA. Cross-reactivity between anti-HomoCitJED and anti-CitJED antibodies suggests that ACPA and AHCPA are derived from the same B cell population and both may contribute to RA pathogenesis.

Patient, Family and Physician Satisfaction with Discharges Directly Home from Intensive Care Units – Direct from ICU Sent Home (DISH Study)

Joyce Lam, Vincent Lau, Fran Priestap, John Basmaji, Ian Ball.

Background : With decreasing hospital bed availability, there is an increasing rate of discharges directly to home (DDH) from intensive care units, despite sparse literature evaluating this practice. Objectives: To evaluate patient, family and ICU attending physician satisfaction with DDH from the intensive care unit (ICU); and intensivists' current DDH practices and

perceptions. Methods: Prospective cohort study of adult patients undergoing DDH from an ICU between February 2016 and February 2017, using a modified FS-ICU 24 satisfaction survey completed by patients, family members, and attending physicians at the time of patient discharge home from ICU. Results: A majority of patients (89%) and families (78%) were satisfied or very satisfied with DDH. Conversely, ICU physician satisfaction varied, with only 5% very comfortable with DDH and the majority (50%) only somewhat comfortable. 31% of staff physicians felt patient and family discomfort would be barriers to DDH. Compared to physicians and allied health professionals, nurses were identified as the most helpful members of the healthcare team in preparation for DDH by 98% of patients and 92% of family members. The estimated annual number of DDH patients per ICU physician varied widely (2-30, median 5). DDH rates have increased for the past twelve years in our ICUs, but declined during the study period. Conclusions: Patients and family members are satisfied with the practice of direct discharge home from ICU, although ICU physician satisfaction is more variable. Physician comfort may be improved by data informing which patients may be safely discharged directly home from the ICU.

Critical Care Point-of-Care Transesophageal Echocardiography Indications and Usage Patterns: A Single-Centre Observational Study

Dr. Yves Landry, Dr. Vincent Lau Dr. Robert Arntfield.

Background & Rationale: Point-of-Care transthoracic echocardiography has become an integral tool in managing the critically ill. POC transesophageal echocardiography (POCTEE) remains largely underutilized in critical care. In December 2012, a formal POCTEE program was established in LHSC ICUs, complete with image archiving and report quality assurance. It was crucial to analyze our local compilation of POCTEE studies to better understand the indications and usage patterns of this modality. Objective: To analyze the indications and usage patterns of POCTEE studies in the ICUs at LHSC,

since program inception in December 2012. Design: Single-centre, retrospective observational analysis of the POCTEE studies stored in the QPATH database (Qpath, Telexy Healthcare, Maple Ridge, BC, Canada) at LHSC. Study period from December 1st 2012 to December 31st 2016. Methods: POCTEE studies were obtained via direct search in the QPATH database. Patient demographics, source and reason for admission were obtained. Study information obtained included study date, indication, and proposed change in patient management. Results: 273 POCTEE studies with full reports obtained. 73% of studies performed at CCTC (Victoria Hospital). The most common indications were hemodynamic instability, cardiac arrest, and infective endocarditis. A change in patient management was proposed following ~80% of POCTEE studies. ~40% of POCTEE studies were performed on weekends or weekday evenings (16:30-08:00) when formal cardiology TEE studies are less available. Conclusions: POCTEE usage in the critical care setting is increasing over time at LHSC. A better understanding of indications and usage patterns will promote further acceptance and implementation of this modality internationally.

Kidney Injury Molecule-1 Mitigates Tissue Damage From Transplant Renal Ischemia Reperfusion Injury

Ji Yun Lee, Ola Ismail, Xizhong Zhang, Aaron Haig, Dameng Lian, Lakshman Gunaratnam.

Ischemia reperfusion injury (IRI) at the time of organ harvesting is unavoidable, may cause delayed renal graft function, as it is associated with premature graft loss. Kidney Injury Molecule-1 (Kim-1) is a well-known biomarker for acute tubular injury but its biological function in transplantation is unknown. Kim-1 upregulation on renal tubular epithelial cells (TECs) during acute injury allows them to clear apoptotic and necrotic cells, reducing inflammation in native kidney IRI. Our objective was to determine if Kim-1 can protect against the severe cold and warm IRI that occurs during renal transplantation. We performed single syngeneic kidney transplants (cold ischemia time 35 minutes) from either C57BL/6 Kim-1+/+ or C57BL/6 Kim-1-/- donor

mice into C57BL/6 Kim-1+/+ mice. We evaluated serum creatinine, survival, histology, tubular obstruction, cell death, inflammation, expression of pro-inflammatory cytokines and Kim-1 expression. Kim-1 protein was upregulated in TECs exposed to cold and warm hypoxia in vitro, and in kidney grafts in vivo. Compared to recipients of Kim-1+/+ kidneys, recipients of Kim-1-/- kidneys had significantly more renal dysfunction (creatinine = 15+/-3 vs. 162+/-40 umol/L); mortality (0/5 vs. 9/12 deaths); tubular obstruction (score = 0.3/5 vs. 4.0/5); tissue damage (injury score = 0.7/5 vs. 3.7/5); infiltrating macrophages (3.8 vs. 10); graft inflammation (relative fold-change expression of IL-6= 11.3 vs. 45.1; relative fold-change expression of MIP-2= 29.5 vs. 108.6); and apoptosis (cleaved caspase-3= 0.3 vs. 4%). Our data suggest that Kim-1 upregulation in kidney grafts protects against transplant-related IRI and may serve as a therapeutic target for improving graft outcomes.

Genotype Analysis of Hyperlipoproteinemia Type 3 Using Next-Generation Sequencing

JooHo Lee, Jian Wang, Robert Hegele.

Background: Unlike other dyslipidemias, hyperlipoproteinemia (HLP) type 3 is a disorder for which the underlying genetic basis is partially understood. This case-control study sought to better characterize the genotypic differences that can potentially explain the HLP type 3 phenotype. Methods: Patients with confirmed HLP type 3 had sequencing of candidate genes for VLDL overproduction or impaired clearance as well as abnormal LDL clearance using the LipidSeq panel, as described elsewhere. Variants were filtered by rarity and predicted likelihood of causality by in silico algorithms predicting the degree of deleterious change. Candidate variants were tallied and compared to a healthy control population and to variants known in the literature to be causative. Polygenic risk scores were generated using genetic markers from the original lipid GWAS study and compared between the HLP type 3 population and healthy controls. Results: 53 HLP type 3 patients and 43 controls were evaluated. 37 patients were homozygotes for APOE E2/E2, 44 patients had deleterious variants associated with VLDL overproduction.

26 patients also had variants predicting poor LDL clearance. HLP type 3 patients had more mutations than normolipidemic controls, as well as strongly statistically significant triglyceride-weighted polygenic risk score. Conclusions: The genetic architecture of HLP type 3 is characterized by both monogenic and polygenic variants that can cause impaired VLDL clearance and overproduction. Larger sample sizes and more detailed understanding of annotated rare variants can lead to better understanding of the key players in VLDL metabolism, which may further identify target pathways and molecules for new therapies.

Sirtuin 6 Knockdown Causes Severe Degeneration of the Elastic Media in a Mouse Model of Spontaneous Aortopathy

Jason J Lee, Sharon Leung, Hao Yin, J. Geoffrey Pickering.

Background: Cardiovascular disease is the number two cause of death in Canada. This mortality risk increases with age, but the exact mechanism of disease is not yet known. Sirtuins are a class of Nicotinamide Adenine Dinucleotide (NAD) dependent enzymes that regulate various cellular processes like cellular aging and inflammation. Here, we aim to investigate the relationship between the sirtuin enzyme SIRT6 and its' effect on structural vessel wall integrity. **Methods:** To study the role of SIRT6 in vascular smooth muscle cells (VSMC) within the media of elastic vessels we created a novel strain of inducible VSMC-specific SIRT6 deficient mice. Non-invasive in vivo measures, including tail-cuff blood pressure measurements and cardiac ultrasounds were performed at weekly intervals. At 6 months of age tissues were harvested under pressure fixation using 4% paraformaldehyde. Finally, these tissue sections were stained and analyzed using light and fluorescent microscopy for changes in the vascular architecture. **Results:** Eight SIRT6 deficient mice were aged to 6 months of age without any overt changes in their physical phenotype compared to their controls (n = 8). In the ascending aortas of aged SIRT6 deficient mice, there was a substantial increase in the number of elastin breaks in the medial layer

(35.5 +/- 2.6 vs. 19.6 +/- 4.1, p < 0.03). Clinically, these structural changes were associated with a spontaneous 10%-15% dilatation in the ascending aorta and a 10 mmHg decrease in blood pressure. **Conclusions:** The SIRT6 enzyme in the VSMC appears to play an important part in the homeostasis of the structural integrity in the mouse aorta. Deficiency in this nuclear enzyme lead to a spontaneous degeneration that resulted in clinical changes in aorta diameter and blood pressure.

Causes of Delay in Planned Discharge in Internal Medicine Inpatient Services

Zhe Li, Alan Gob.

BACKGROUND: The Internal Medicine Inpatient Unit is a high volume service with rapid turn-over. Delays in discharge leads to impaired work flow, and results in inefficiency in the utilization of healthcare resources. Given the heterogeneous nature of different hospital systems, there are limited formal reports describing causes of discharge delays. While anecdotal experience within individual institutions can be informing, and a quality improvement strategy to identify these causes of delay is important. While our institution has adopted the colour-coded predictive discharge system, targeted discharge time of 11am is often not met. **AIM:** The goal of this project is to examine the causes of discharge delay in patients who were planned for discharge. **METHODS:** Prospective data was collected was done over 4-week period. Delayed discharges from the University Hospital CTU teams were tracked by the Patient Care Facilitators, descriptive data was collected to inform the causes for delays. **PRELIMINARY RESULTS:** Results over 2-week period demonstrated preventable delayed discharge in 36% of all cases (total N=46). Forty-six percent of the delays were due to delayed patient transportation. Delayed assessment/order by the medical team accounts for 35% of all delayed discharge. **CONCLUSIONS:** There was a significant number of preventable discharge delays during our collection period. Two major contributors were delays in patient transportation and medical team assessment. Our data will provide data for future interventional step; and

inform discharge check list that is currently being developed.

Surviving a hemoglobin of 28: A case of a Jehovah's Witness patient with severe GI bleed

Andre Maddison, Marko Mrkobrada.

Managing severe acute anemia among patients who refuse blood products is clinically and ethically challenging and requires a multi-disciplinary approach. This case describes a 59-year-old female presenting to emergency department with melena, hematemesis and syncope, 10 days after elective right total hip arthroplasty. She had been discharged from orthopedics on Aspirin 325mg and was taking non-steroidal anti-inflammatories as needed. On presentation to emergency department her hemoglobin was 28 g/L. She clearly stated that she wished to avoid human blood products due to her religious beliefs. Her wishes were respected. She underwent extensive investigation, including esophagogastroduodenoscopy, push enteroscopy, flexible sigmoidoscopy, CT angiogram, tagged RBC scan, meckel's scan, and capsule endoscopy, but a source of bleeding was not identified. She was co-managed by internal medicine, hematology, gastroenterology, and critical care. She received prohemostatic agents, parenteral iron, erythropoietin-stimulating agents, and was electively intubated and cooled to reduce metabolic demands. She was discharged after 22 days with a hemoglobin of 78 g/L, and 6 months later her hemoglobin was normal and she lives a normal life. In fact, she recently underwent an uncomplicated laparoscopic cholecystectomy and is planned for a left total hip arthroplasty. This case explores the physiology of severe anemia, the management of GI bleeding in patients who refuse blood transfusions, the risk and benefits of elective intubation for severe anemia, and the ethical/practical considerations in caring for Jehovah's witness patients.

Short but sweet? A review of admissions to medical wards lasting less than 12 hours.

Dr. Mary Mahler, Dr. Stephanie Gottheil, Dr. Mary Lu.

OBJECTIVE/BACKGROUND: There is a paucity of literature surrounding short (<12 hour) admissions to general medicine wards. This study aims to examine the prevalence and contributing factors of these short admissions. **METHODS:** We conducted a retrospective chart review of all patients admitted for less than 12 hours to the general medicine wards in two centres in London, ON over a 45-day period. Baseline characteristics, such as patient age, time of admission, admitting facility, admitting physician, and reason for admission were examined. Two authors independently reviewed the data. We also collected outcome data of 30-day readmission rates. **RESULTS:** 46/1069 patients during this period were admitted for <12 hours over 45 days. 59% (27/46) were male and 67% (31/46) over age 50. Victoria Hospital accounted for 68% (31/46) of short admissions, with the majority (68%, 31/46) admitted between 0100 and 0900. We classified the cases into 8 different admission categories based on reasons for hospitalization and/or discharge: death (3/46, 6.5%), leaving against medical advice (8/46, 17%), awaiting assessment by allied health (4/46, 9%), requiring medical care (15/46, 33%), awaiting diagnostic imaging (3/46, 6.5%), patients too frail to be discharged in the middle of the night (3/46, 6.5%), appropriate for ambulatory clinic (7/46, 15%), and patients unable to be categorized as no discharge dictation complete (3/46, 6.5%). None of the patients appropriate for ambulatory clinic were readmitted within 30 days. **CONCLUSION:** The largest proportion of patients admitted for less than 12 hours required acute medical care, while only 15% of short admissions (7/46, or 0.01% of all 1069 admissions) were identified as potentially appropriate for avoiding admission in lieu of outpatient management.

Appropriateness of In-patient Transthoracic Echo Ordering

Dr. Usha Manian, Dr. Richard Matiasz, Faisal Khan, Dr. Kiran Sidhu, Dr. Kareem Ballut, Dr. Neville Suskin and Dr. David McCarty.

Background: Imaging is an important contributor to increasing healthcare costs. Inappropriate use of echocardiograms is a waste of resources and can have a negative impact on patient care. This Quality Improvement (QI) project hopes to reduce inappropriate routine inpatient transthoracic echocardiograms (TTE) to improve throughput through the echocardiography labs at London Health Sciences Centre (LHSC). Methods: A retrospective review of all echocardiograms performed at LHSC between May 2012 and September 2015 demonstrated how many repeated TTE were performed and the time intervals between them. From this we established a screening time of 3 months, under which all inpatient TTE requests would be reviewed. The QI project was conducted with consecutive pre-intervention and post-intervention periods between April 25th 2016 and May 8th 2016 at University Hospital (UH) site only. A call was made to the ordering physician and cancelled if deemed inappropriate per current guidelines during the intervention week. Results: At LHSC across three hospital sites over 3.4 years, 3625/6254 (58%) of the inpatient TTE were performed less than 3 months from a previous scan. During the QI project in the pre-intervention period 25/62 (40.3%) repeat inpatient TTE were performed with a previous less than 3 months prior. 8/25 (32%) were considered inappropriate. Following the intervention 24 requested inpatient TTE were screened and 10 TTE's were cancelled. Conclusions: This project identifies that screening all inpatient TTE with a previous scan less than 3 months prior is feasible and can reduce unnecessary TTE allowing more timely appropriate TTE requests to occur.

Ethnic Variations in the Length of Hospital Stay in patients with Type 2 Diabetes

Dr. Bharat Markandey, Dr. Rahul Potluri.

Background & Aims: Type 2 Diabetes Mellitus (T2DM) is a common condition worldwide and a major contributor to length of hospital stay (LOS). It is significantly more common in South Asian patients. We aimed to explore the influence of ethnicity on LOS in hospitalized patients with T2DM. Methods: We examined LOS and ethnic variations in patients with T2DM using anonymous data of adult patients admitted across several hospitals across Greater Manchester, North West England, between 2000 and 2013 using ACALM study protocol. Results: Out of a total sample of 929465 adult patients, there were 68084 patients with T2DM. LOS was significantly lower in South Asian and Mixed-race patients compared with Caucasian patients after adjusting for variations in age, sex and presence of co-morbidities. LOS was significantly higher in Afro-Caribbean patients. Conclusions: A greater proportion of South Asians are admitted to hospital with T2DM and have significantly shorter LOS in comparison to Caucasians. We briefly discuss these findings and their implications for healthcare.

The metalloproteinase-dependent role of TIMPs in regulation of pulmonary microvascular endothelial cell barrier function during sepsis

Marcello G. Masciantonio, Sanjay Mehta, Lefeng Wang, Marta Rohan, Cynthia Pape, Sean E. Gill.

Sepsis, a systemic inflammatory response to infection, is a serious disease with significant mortality characterized by injury and dysfunction of pulmonary microvascular endothelial cells (PMVEC). Mechanisms protecting against septic PMVEC dysfunction are unclear; however, the tissue inhibitors of metalloproteinases (TIMPs), which regulate metalloproteinase activity, may be one such mechanism. Metalloproteinases, are associated with inflammation and tissue damage. My hypothesis is that murine septic PMVEC barrier dysfunction is due to disruption of the balance between metalloproteinases and TIMPs leading to increased metalloproteinase activity.

Analysis of metalloproteinase and TIMP expression by qRT-PCR revealed a significant alteration in TIMP and metalloproteinase expression in vitro following stimulation with cytomix and lipopolysaccharide. Additionally, metalloproteinase activity, specifically ADAM17 activity, was increased in PMVEC following septic stimulation and treatment with a global metalloproteinase inhibitor, Batimastat, reduced albumin flux across the PMVEC monolayer. Further, while septic stimulation increased cell surface intracellular adhesion molecule (ICAM) 1 on wild type (WT) PMVEC, Timp3^{-/-} PMVEC had significantly less cell surface ICAM1 vs. WT PMVEC under basal and septic conditions. Additionally, this decrease in ICAM1 was associated with significantly impaired PMVEC-neutrophil (PMN) adhesion in Timp3^{-/-} vs. WT PMVEC. My data demonstrates that the balance between metalloproteinases and TIMPs in PMVEC is altered under septic conditions leading to increased protein leak. Furthermore, disruption of this balance is also associated with impaired PMVEC-PMN interaction. Taken together, my studies highlight the critical role of metalloproteinases and TIMPs in septic PMVEC dysfunction, and understanding these mechanisms may provide insight into potential therapeutic interventions in human sepsis.

Prehospital Adverse Events Associated with Nitroglycerin Use in STEMI Patients with Right Ventricle Infarction

Allison McConnell, MD, MKin, BScK, Matthew Davis, MD, MSc, Kristine Van Aarsen, MSc, Melanie Columbus, PhD, Michael Lewell, MD.

Paramedics in our region do not perform 15-lead ECGs. Therefore, patients experiencing a Right Ventricular Infarct (RVI) may receive nitroglycerin (NTG). Often, paramedics do not administer NTG to inferior STEMI due to concern for RVI. The purpose of this study is to determine if there is a difference in prehospital adverse events (AEs) associated with NTG administration in patients with unrecognized RVIs compared to those with an inferior STEMI. Ambulance Call Records (ACR) of patients with prehospital STEMI between Jan 1, 2012 and Dec 31, 2015 were analyzed for the incidence of NTG administration.

AEs were defined as HR < 60 bpm, systolic BP < 100 mmHg or drop of 1/3, drop in GCS, syncope, arrest or death. Hospital records were reviewed to determine patients diagnosed with an inferior STEMI with or without RVI. Of the 334 ACRs that were manually reviewed, 144 were excluded resulting in 189 patients that had a prehospital STEMI (mean 66.9 +/-13.5 years, 70.6%, male). Of 189 STEMI patients, 82 (42.9%) received NTG. Nineteen (41.3%) of these patients were subsequently diagnosed with RVI and 27 (58.7%) had inferior STEMI without RVI. For patients receiving NTG, AEs occurred in 11 (57.9%) within the RVI group, and 10 (37.0%) within the inferior group (Δ 20.9%, 95% CI -7.8% to 45.4%, p=0.2). Cardiac arrest or death did not occur in either group. Results of this study suggest no difference in the rate of AEs between patients with inferior STEMI and STEMI with RVI when NTG is administered in the prehospital setting.

Emergency Department Utilization of Point-of-Care Ultrasound in the Assessment and Management of Shock

McGuire J., Van Aarsen K., Thompson D., Hassani B.

Purpose: To determine the rate of POCUS use, characterize data collection methods and determine rate of quality assurance in both the ED and Intensive Care Unit (ICU). Methods: Included were all ED patients from Jan-Jun 2015 that were transferred to the ICU, and were in shock, as determined by sBP <90, diagnostic code or vasopressor use. Patient charts, electronically archived studies and formal online worksheets were reviewed to determine if POCUS was performed, and how the results were recorded. For worksheets completed it was determined if a management change was recommended, if quality assurance was completed and if any improvement was recommended. Results: POCUS was performed in roughly half of the shock patients (53% ED, 41% ICU) with no statistical difference in usage (Δ 12, 95% CI -0.01 to 0.25; p =0.06). Most ED studies (87%), were documented, however few (9%) had a formal worksheet completed. In comparison 71% of ICU studies had formal worksheets. Of these formal ICU reports 77%

recommended a management change as a direct result of scan findings. Furthermore, of worksheets submitted for quality assurance (88%), over half the reviews (55%) suggested improvement. Conclusion: Currently POCUS is only utilized in about half of the shock cases in ED and ICU. Given that the majority of the formally reported ICU studies over-read for quality assurance found areas for potential improvement and given that the majority of ED studies were reported informally, it stands to reason that the ED could benefit from a formalized quality assurance program.

Decreasing Inappropriate Referrals to The Urgent Medicine Clinic

Kathryn McIntyre, Michael Peirce, Saira Zafar.

The Urgent Medicine Clinic (UMC) at Victoria Hospital is meant to serve patients with acute or subacute medical issues who require assessment within one week. Most patients are referred from the Emergency Room where they are booked directly into the UMC. Those working in the UMC felt that there were a significant number of patients referred who were not well served in the clinic. Baseline data about referrals to the UMC were collected including the proportion of inappropriate referrals and the reason such referrals were deemed inappropriate. The median proportion of inappropriate referrals per clinic was 25%. The most frequent inappropriate referrals were for patients already seeing or waiting to see another specialist for the same medical issue and patients referred for chronic, stable issues. Some patients referred required urgent subspecialty consultation and referral to the UMC was an unnecessary middle step for the patient. Based on the observed data, a referral form for the UMC has been developed with the hopes that it will decrease the rate of inappropriate referrals. The referral form suggests alternatives to the UMC for patients with chronic, stable issues and patients who are already seeing a subspecialist for the referral issue. Available urgent subspecialty clinics are listed on the form including examples of the narrow spectrum of patients who would benefit from direct referral to these clinics. The next step is to introduce the new referral form into

the Emergency Departments and then collect post intervention data on the rate of inappropriate referrals.

The Effect of Serotonergic Antidepressants on Bleeding in Orthopedic Surgeries: A Systematic Review

Kathryn McIntyre, Dr. George Dresser.

Serotonin plays a role in hemostasis via platelet activation, aggregation, and vasoconstriction. Serotonergic antidepressants (SRIs) have been associated with increased bleeding tendency in multiple observational studies including increased perioperative bleeding. The objective of this study was to systematically review the evidence regarding the association between SRIs and bleeding in patients undergoing major orthopedic surgeries. The Medline and Embase databases were searched for articles pertaining to this systematic review. Studies which compared blood loss or a bleeding related outcome in users of SRIs compared to a control group were included. After reviewing the accrued studies, it was determined that a meta-analysis would be appropriate for the outcome of risk of blood transfusion. Six studies investigating the effect of serotonergic antidepressants on bleeding in orthopedic surgeries were identified. Three used need for blood transfusion as the primary outcome. The meta-analysis for this outcome showed an association between SRI use and increased risk of blood transfusion [OR: 1.31 (95% CI: 1.17—1.46)]. Three studies investigated intraoperative estimated blood loss (EBL) as the primary outcome. Two showed that SRI users had an increase in EBL (93 mL—95 mL) compared to non-users, whereas one showed no significant difference. Based on the available evidence, there is an association between the use of SRIs and increased bleeding in orthopedic surgeries. The overall effect is small with less than 100 mL more blood loss in SRI users. The increased risk of blood transfusion may be more meaningful given the costs and potential risks associated with transfusions.

Real-world tolerability and efficacy of evolocumab among patients with a history of statin-associated muscle symptoms (SAMS)

Simone A. Mendel, MD, Tisha R. Joy, MD
FRCPC FACE.

Background: Statin-associated muscle symptoms (SAMS) are the most common cause of statin discontinuation. Randomized clinical trials of proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors demonstrate significant reductions in low-density lipoprotein cholesterol (LDL-C) levels and high tolerability among patients with prior SAMS. However, given the subjective nature of SAMS, we hypothesize that lower efficacy and higher myalgia rates would occur under open-label conditions. **Objective:** To determine the “real-world” tolerability and efficacy of the PCSK9 inhibitor, evolocumab, among patients with prior SAMS. **Methods:** In our tertiary lipidology clinic, we conducted a retrospective case series of patients with prior SAMS who required evolocumab for additional LDL-C lowering. Efficacy was defined as achievement of respective LDL-C targets. For tolerability, the percentage of patients who developed adverse events and/or discontinued therapy were documented. **Results:** Of 16 patients who met inclusion criteria, 94% were high cardiovascular risk. Three quarters had tried 4 or more statins previously. The mean LDL-C prior to evolocumab initiation was 3.71 ± 1.57 mmol/L. After a median follow-up of 5.1 (range 1-9) months, the mean LDL-C level was 1.66 ± 1.21 mmol/L. 81% of patients achieved their respective LDL-C targets. Two patients achieved LDL-C levels < 0.6 mmol/L. One patient discontinued therapy due to myalgia; another experienced neurocognitive symptoms, but resumed evolocumab after a temporary interruption, leaving overall tolerability at 94%. **Conclusions:** Evolocumab demonstrates excellent tolerability and a high rate of LDL-C target attainment among patients with prior SAMS, even under open-label conditions. Thus, evolocumab may represent a significant advance in the management of this patient population.

Improving Clinical Assessment: A Focus on the Natural Language Used by Attendings to Describe Their Trainees

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Many workplace-based assessment forms – often designed around CanMEDS competencies – fail to take into account what attending physicians can assess. The purpose of this study was to explore the naturalistic language used by attendings to describe and differentiate amongst their trainees. Constructivist grounded theory guided the design, collection and analysis. Interviews were conducted with 13 internal medicine attending physicians. During the interview, attendings were asked to describe, compare and contrast trainees they had recently worked with. Six main categories of junior trainee characteristics were identified: clinical knowledge and reasoning, level of independence, diligence, collaboration, patient/caregiver interactions, and other personal characteristics. While the categories touch on all of the CanMEDS competencies, each category represents multiple roles in ways that better match how attendings think about their trainees. Our second key finding related to how things became visible to attendings and inform their judgements. For example, case presentations were regularly used and informed attendings’ judgements about student diligence, clinical knowledge and reasoning and patient interactions. By contrast, review of clinical documents, interactions with patients and student’s own advocacy efforts on behalf of their patients either took special effort from attendings to assess or appeared to be assessed by chance. This study suggests CanMeds-based tools may not correspond well with how attendings naturally assess their students. The naturalistic ways in which attendings inform their judgments about students and the language in which they do so may assist in developing future assessment tools that provide better feedback.

Utilization of the non-selective JAK1/2 Inhibitor, Ruxolitinib, in Myelofibrosis Patients with Thrombocytopenia in the Real World: A Single Centre Retrospective Chart Review

Mount, G, Howson-Jan K, Xenocostas A, Lazo-Langner A, Lam S, Kovacs MJ, Chin-Yee I, Mangel J, Gob A, and Hsia CC.

Myelofibrosis (MF) is a myeloproliferative neoplasm characterized by anemia, splenomegaly and constitutional symptoms. Currently, there is only symptom management for the majority of these patients. Ruxolitinib is a new oral non-selective Janus Kinase (JAK)1/2 inhibitor which has been demonstrated in clinical trials to improve splenomegaly and symptoms in these patients. However, patients with platelets below $100 \times 10^9/L$ were excluded yet in clinical practice many MF patients are thrombocytopenic. Our study aimed to better characterize current physician practices in ruxolitinib-treated MF patients with thrombocytopenia, with insight into its effectiveness as well as side effects and bleeding outcomes. Thirty-six patients with MF were identified, nearly half with primary MF. Sixty-seven percent had received prior treatment, predominantly with hydroxyurea (87%). Twenty-five patients were started on ruxolitinib, the majority (52%) at 5 mg oral twice daily with titration to the recommended clinical dose of 20mg oral twice daily. All patients reported symptom improvement. Treatment suspension and reduction were noted in 1 and 11 patients, respectively. The most common side effects were hematological (anemia/thrombocytopenia) in 52% of patients. Median platelet counts and ranges at start of treatment and nadir on therapy were $192 \times 10^9/L$ (30-945) and $110 \times 10^9/L$ (12-487), respectively. Two of eight patients with thrombocytopenia at the start of treatment had bleeding events (epistaxis and ocular) which did not alter therapy and both remained on ruxolitinib at time of last follow-up. Our study demonstrates that ruxolitinib is an effective and well-tolerated treatment for MF, even in those patients with thrombocytopenia.

Participation in voluntary ultrasound courses correlates with thoracic ultrasound utilization in the emergency department.

Frank Myslik, Richard Hilsden, Kristine VanAarsen, Drew Thompson.

Background: Point of Care Ultrasound (POCUS) is becoming common place in the emergency department (ED). Its use in thoracic assessments is growing. Various courses are offered to physicians however, little is known about their impact on the frequency of subsequent POCUS use in the ED. We hypothesized that providers who have participated in these courses are more likely to apply thoracic POCUS in their practice. Methods: A locally developed thoracic ultrasound course was delivered to ED staff physicians in the spring of 2016. In January 2017, all residents in two emergency medicine programs (FRCP & CCFP-EM) as well as all practicing ED physicians were invited to participate in an anonymous online survey regarding their use of POCUS in the ED. Results A total of 68 of 96 providers responded to the survey for a response rate of 71%. Twenty-eight of 68 (41%) indicated that they had taken additional training in POCUS. Among those who did complete additional training 83% indicated that they regularly use thoracic ultrasound compared to only 57% of providers who did not take any additional courses in POCUS ($P < 0.05$). Staff emergency physicians were more likely to participate in additional training than residents, with 55% of staff indicating additional training vs 22% of FRCP residents and 10% of CCFP-EM residents ($P < 0.05$). Conclusions Providers who choose to participate in additional courses appear to have higher use and comfort with POCUS. This suggests the potential importance of continued investment in ultrasound training courses and immersive experiences at all levels.

The Effect of Mood and Cognition on the Mobility Performance of Older Adults

Anish S. Naidu, Amer M. Burhan, Emily Ionson, Alanna Black, Akshya Vasudev, Manuel Montero-Odasso.

Aging associated cognitive decline has been shown to have a negative impact on mobility, which in turn is associated with an increased risk of falls. Depression is prevalent in old age, and is associated with cognitive impairment and neurocognitive disorders like Alzheimer disease. The aim of this pilot study is to investigate the effect of depression on the interaction between cognition and mobility in older adults. We recruited 23 community-dwelling participants (age 60–85) without dementia who met the criteria for mild-moderate major depression. Their gait velocity was recorded during simple gait and dual-task gait (walking while naming animals aloud). Dual-task cost, a clinically relevant indicator of the risk of falls, is calculated as the percentage change in gait velocity between simple and dual-task gait. For comparison, 23 healthy controls and 23 mild cognitive impairment (MCI) patients, matched with respect to age, gender and comorbidities, were randomly selected from our existing research databases. The mean (\pm SD) dual-task cost of the healthy, depression and MCI groups were $2.4 \pm 11.4\%$, $11.8 \pm 9.9\%$ and $22.2 \pm 16.7\%$, respectively. One-way ANOVA followed by post-hoc Tukey HSD test revealed that all three groups were statistically different with $p < 0.05$. Our preliminary results suggest that dual-task cost is significantly larger in older adults with depression, though to a lesser degree than in those with MCI, potentially providing an explanation for the higher risk of falls described in this population. Further studies are needed to identify the underlying factors causing gait impairment in late-life depression.

Developing a formalized leadership curriculum for junior faculty and doctors: a needs-based approach.

Kristen Noges, Janet Pope.

BACKGROUND: The Future Leaders in RheumaTology (FLIRT) and Future Leaders of Western (FLOW) projects were piloted to create a formal curriculum to facilitate the development of leadership skills in junior faculty at the University of Western Ontario and in Canadian rheumatologists within the first 3 years of their career. This paper aimed to describe the design and implementation of formalized leadership curriculums for these projects and to better understand the common needs of junior faculty in developing leadership skills. **METHOD:** FLIRT was launched in 2010 and FLOW was launched in 2013. The curriculums of both pilot projects were developed through a needs assessment given to participants and participants were selected through a competitive application process. The groups met in person at two full meeting days per year, in addition to shorter, more informal interactions over each two year program. Participants were asked to evaluate the program at completion. **RESULTS:** To be added to abstract when complete. **CONCLUSION:** To be added to abstract when complete.

Access to Comprehensive Geriatric Assessment (CGA) in Lift Assist Emergency Medical Services (EMS) Call Patients

Alyson Osborne, MD, Sheri-Lynn Kane, MD.

Background: When an individual requires assistance with mobilization EMS may be called. If they do not receive treatment and are not transferred to hospital, these are termed "Lift Assist" (LA) calls. LA calls are associated with morbidity, mortality, and increased use of resources. The purpose of this study was to determine the percentage of older adults who access EMS for lift assistance that have had a CGA in the 3 months before or after the EMS call. **Methods:** A retrospective chart review was conducted using EMS call records and hospital database to identify the number of older adults who called EMS for a LA in a 3 month time period and to determine whether these individuals had a CGA in the 3 months before or after the LA call. **Results:** 227 LA calls were made by 183

individuals 65 years and older. Twelve individuals (6.5%) had a CGA in the 3 months before their call and 16 (8.7%) after the call. Fifteen (8.1%) individuals had their charts review by a Geriatric Emergency Management (GEM) nurse in the 3 months prior to the call and 22 (12%) after the call. Discussion: Only a minority of older adults who made LA calls received a CGA in the preceding 3 months or the 3 months following their call. There is a gap in service for these high risk individuals who could benefit from a CGA but are not referred. Conclusion: Strategies are required to link this vulnerable LA population with specialized geriatric services.

Impact of Comorbidity among Older Adults living in North West LHIN admitted for medical issues

Dr. Alexandra Peel, Dr. Iris Gutmanis, Dr. Trevor Bon.

Background: This study assessed the impact of comorbidity on mortality and morbidity among older adults in the North West Local Health Integration Network, where hospitalization rates for many chronic health issues exceeds that for Ontario. Methods: This retrospective cohort study examined healthcare utilization among community-dwelling older adults (aged 65 or more) who were admitted to a medical service at the Thunder Bay Regional Health Science Centre (TBRHSC) between April 1, 2004 and March 31, 2013. Survival and logistic regression were used to determine the impact of comorbidity, as measured by the Charlson Comorbidity Index, on in-hospital and 1-year mortality as well as 1-year readmission rates in the year following index admission discharge. Results: During the 10 study years, 12,033 people (47.1% male, aged 65-103 years) were admitted to TBRHSC. At index admission, 36.4% had no comorbidities while 21.2% had three or more. Odds of in-hospital mortality increased by number of comorbidities (2.5 (0 vs.1 comorbidity) vs. 3.1 (0 vs. 2) vs. 7.1 (0 vs. 3+). The hazard ratio associated with 1-year mortality increased from 1.6 (0 vs. 1) to 5.5 (0 vs. 3+). The hazard ratio associated with 1-year readmission increased from 1.2 (0 vs. 1) to 1.7 (0 vs. 3+). Conclusion: Those living with three or more comorbidities

have a very high risk of mortality. Perhaps due to care that continues to be siloed by disease categories. Older adults with multiple health issues need a comprehensive assessment that takes into account all of the issues concurrently.

CTU discharge clinic and its effect on 30-day readmission rates at London Health Science Centre

Michael Peirce, Dr Paul Lee and Dr Marko Mrkobrada.

Compared to other teaching hospitals in Ontario, LHSC ranked worst in terms of average length of stay for Medicine patients (11.1 days) and rates of unplanned readmissions (12.0%). The CTU discharge pilot project was designed to study whether or not follow-up of patients within 30 days of discharge by an internist would impact 30-day readmission and death rates. We performed a retrospective chart review of patients admitted to University Hospital between Oct 1 – Oct 31, 2016 during the CTU discharge pilot project. Of the 281 patients admitted to CTU, 21 (7%) were seen in the CTU discharge clinic. In total, 23% (66/281) of patients were readmitted or died within 30 days of discharge. Of the patients seen in the CTU discharge clinic, 33% (7/21) were readmitted or died within 30 days of discharge. There was no significant difference in readmission or death rates between patients seen in a CTU discharge clinic and those that were not ($p=0.29$) or ER visits following discharge ($p=0.10$). The LACE scores between patients seen in the CTU discharge clinic and those who were not, were significantly different ($p=0.0001$). There was no significant difference in baseline LACE characteristics except previous ER visits, which was higher in those seen in the CTU discharge clinic. However, the LACE score did underestimate readmission and death rates in patients with LACE scores less than 12. Comparing CTU discharge patients with LACE-matched patients not seen in the clinic, there was no difference in outcomes.

Does Surveillance Colonoscopy Impact Survival in Inflammatory Bowel Disease Associated Colorectal Cancer? A Systematic Review & Meta-Analysis

Sheron Perera, Andrew Warner, Rammal Almotasen, Gabriel Boldt, Hiroki Matsuoka, Brian Yan, Mike Sey, Adam Rahman, David A. Palma and Samuel Asfaha.

Background: Patients with inflammatory bowel disease (IBD) are at increased risk of developing colorectal cancer (CRC). Current guidelines recommend routine colonoscopy 8-10 years after the initial onset of disease. However, no large controlled trials have investigated the efficacy of surveillance colonoscopy and the benefit remains unproven. Materials and Methods: A systematic review was undertaken to identify studies that examined the impact of surveillance colonoscopy on overall survival of patients with IBD associated CRC. Three hundred and forty-five studies were screened by title and abstract, followed by a detailed review of twenty three studies. Effect estimates (hazard ratios [HR]) and confidence intervals (CIs) were computed, with a fixed-effects model created to estimate the effects. Cochrane's Q and I²-statistics were used to assess study heterogeneity. Additionally Dukes stage of the tumour was compared between the surveillance and non-surveillance groups using the Fisher's exact test. Results: Four relevant studies were identified, which included a total of 334 patients. Of these patients, 118 had undergone surveillance colonoscopy. Surveillance colonoscopy was associated with improved overall survival, with a HR of 0.354 (95% CI: 0.217-0.578; p<0.001). Furthermore, these studies were not found to be heterogeneous (Q = 1.727, P = 0.631, I² = 0.000). Analysis of pathology data from two of the studies demonstrated that surveillance group tumours were more likely to be diagnosed at an earlier stage (Dukes A, P < 0.001), while non-surveillance tumours were more likely to be diagnosed at a later stage (Dukes C and D, P = 0.018 and P = 0.017). Conclusion: Our study demonstrates that colonoscopy improves overall survival in patients with IBD associated CRC.

Educational Workshop on Goals of Care Discussions in Nephrology

Juliya Hemmett MD and **Elena Qirjazi MD**, Faisal Rehman MD, Valerie Schultz MD, Norman Muirhead MD.

Introduction: Studies have demonstrated a gap in nephrology training on goals of care (GOC) discussions. We addressed this deficiency by creating a GOC discussions workshop using role playing and didactic teaching. Methods: This workshop was piloted last year, and fully integrated into Western's Nephrology Fellowship curriculum this year. Participants included nephrologists, a palliative care physician, allied health professionals, standardized patients and nephrology fellows - all evenly divided into teams. After a didactic session on evidence-based approaches to discuss GOC, each nephrology fellow led a simulated family meeting, discussing either withdrawing from dialysis or conservative management in end-stage renal disease. Fellows received constructive feedback from the other team members. Participants evaluated their experience using anonymous surveys. Results: 22/24 participants completed the anonymous surveys. The workshop was ranked "very useful," "important," and "relevant" to their practice. In particular, the use of standardized patients was emphasized as a highlight. The high rankings were maintained between the two workshop iterations. Comments included: "great to do this [workshop] twice a year", and "I love small group sessions, it was realistic." Constructive feedback included providing the scenarios ahead of time and further clarifying the roles of the allied health. Importantly, nephrology staff leaders identified and addressed knowledge gaps such as what happens to patients when they stop dialysis. Conclusion: Our workshop is the first in Canada to teach GOC discussions using didactic teaching and dynamic simulations involving the main stakeholders in nephrology, and proved effective in improving current knowledge and comfort levels of care providers.

Predictors for Local Recurrence Post-Endoscopic Mucosal Resection (EMR) of Colonic Lesion with 3cm in size or more

A. Rammal, J.Gregor, .Khanna, M.Sey, N.Hussain.

Background: Colorectal cancer (CRC) is the second most common cause of death in Canada amongst all cancer deaths. Large lesions are challenging to remove endoscopically, and surgery has been the primary management technique in most centers especially if the lesion is 3 cm or more which associated with mortality and morbidity up to 5%. Endoscopic mucosal resection (EMR) is a minimally invasive technique for removal of large polyps with reduced mortality and morbidity compared to surgical intervention

Aims: To evaluate the predictors that are, increasing the recurrence rate post-EMR of colonic lesion of 3 cm in size or more Rates of recurrence and complication post- polypectomy (bleeding and perforation). Methods: Retrospective study, a chart review of 200 patients who undergo colonoscopy with EMR (piecemeal fashion) of colonic lesion of 3 cm in size or greater between January 2010 till January 2016 and had a follow-up colonoscopy between 3 to 18 month, the patient were recruited by using OHIP billing codes. Results: Overall recurrence was 42 cases (21%) (Recurrence detected between 3-6 months was 26 (13%), Recurrence detected between 6-18 months was 20 (10%). Admission secondary to intraoperative bleeding was 1 (0.5%), Bleeding within 2 weeks requiring hospitalization was 8 (4%), rate of perforation required medical treatment was 1 vs zero patient required surgical treatment. Univariate analysis for predictors of recurrence showed that rectal polyp has statistically significant recurrence rate (2.53 -1.13-5.68 -OR (95%CI) with 0.02 P-value) and the multivariate model for recurrence has proved it (2.58 (1.06-6.30)- OR (95%CI) with 0-04 P-value). Conclusion There were no statistically significant predictors of recurrence after EMR for lesions > 3cm in size except rectal location. As the recurrence rate was 21% between 3-18 month post-polypectomy similar reported in the literature, we recommend repeating the colonoscopy within this period. Earlier endoscopy may allow for earlier detection and hence smaller size of recurrence. Large colonic polyps can be

managed safely and effectively by endoscopy using EMR technic.

Real world clinical efficacy of low dose ustekinumab induction in Crohn's patients refractory to anti-TNF therapy

AIYatama, Noor, **Rofaiel R**, Chande N, Yan B, Ponich T, Gregor J..

Background: Crohn's disease (CD) is a transmural chronic inflammatory bowel disease (IBD). Interleukin (IL) inhibitors, among which is Ustekinumab, an IL-12 and IL-23 monoclonal antibody has recently been approved for the treatment of CD based on the UNITI trials. Hypothesis: To examine the clinical efficacy of standard dose subcutaneously (sc) loaded ustekinumab in patients with moderate to severe Crohn's disease who had failed at least one anti-TNF agent. Methods: 32 patients with an initial mean Harvey-Bradshaw Index (HBI) of 9.8 received 270mg subcutaneous loading dose of ustekinumab over two weeks, with 90mg maintenance doses every 8-12 weeks, followed for 6 months in this retrospective analysis study. Primary outcome: proportion of patients with HBI<3 still being administered ustekinumab at six months without the need for rescue therapy. Secondary outcomes: serious adverse effects, patients with a HBI<3 regardless of whether or not Crohn's medications were increased, and patients with any improvement in HBI. Results: At 6 months, 27/32 completed the study with 5 patients switched early to vedolizumab for side effects (3) or worsening symptoms (2). 6/32 patients (19%) achieved full remission (primary outcome), 19/32 (59%) secondary outcome (partial remission), and 7/32 (22%) were non responders. Limitation: This was a relatively small/short retrospective study with no comparator and without control for co-interventions. Conclusion: Loading doses of ustekinumab 270mg subcutaneously over a two-week period followed by maintenance doses at 8-12 week interval is well tolerated / clinically efficacious in the treatment of patients with moderate-severe CD refractory to anti-TNF therapy

Incidence of chronic macrolide therapy initiation at LHSC upon discharge, following COPD exacerbation.

Camilla Rozanski, Ragdah Arif, Michael Mitar, Alia Kashgari.

Objective: To implement a quality improvement project to improve the prescription of chronic macrolide therapy in those with moderate to severe COPD and one or more annual exacerbations. **Methods:** The Respirology Ward at London Health Sciences Centre Victoria Campus underwent a QI project whereby an oral prompt was introduced into daily morning interdisciplinary rounds by the COPD navigator upon a change in the discharge status of a patient. The charts of all patients admitted with a COPD exacerbation were retrospectively reviewed over a two-month period prior to (n=35) and following (n=?) the introduction of the oral prompt. The proportion of those on chronic macrolide therapy was then compared between the study periods. **Results:** A total of 2 (6%) were started on chronic macrolide therapy prior to the initiation of the oral prompt, while ? patients were initiated on therapy following the procedural change. Data to follow.

Preparing the Next Generation of Code Blue Leaders Through Simulation – What’s Missing?

Ayaaz K. Sachedina MD, Sarah Blissett MD, Kumar Sridhar MD, Alliya Remtulla, and Deric Morrison MD MHPE.

BACKGROUND: Despite the increasing reliance on simulation to train residents as Code Blue Leaders (CBLs), the current literature has not explored the role of Code Blue simulations to prepare residents to serve as CBLs from the learner perspective. In 2015, a formal Code Blue Simulation Program (CBSP), developed based on evidence based simulation principles, was piloted at University Hospital. We explored the

role of simulation in Code Blue training and the differences between real world and simulated Code Blues from the learner perspective. **METHODS:** Using a grounded theory approach and a purposeful sampling strategy, residents who participated in the CBSP were invited to participate in one of three focus groups. Data was collected through small group discussions guided by semi-structured interviews. The interviews were audio-recorded and transcribed. Interview transcripts were coded to assess underlying themes. **RESULTS:** Seventeen residents participated. Thematic analysis revealed that the CBSP enhanced preparedness by capturing aspects of real world codes (e.g inclusion of pre-code scenarios with awake patients, lack of readily available information) and facilitating automatization of Code Blue processes. Despite efforts to develop a high fidelity simulation, participants noted that they experienced more anxiety, observed more chaos in the environment, and encountered different communication challenges in real world codes. **CONCLUSIONS:** The CBSP enhanced resident preparedness to serve as CBLs. Learners highlighted that they valued the CBSP, however differences remain between simulated and real world codes that could be addressed to enhance the fidelity of future simulations.

Kidney Injury Molecule-1 Promotes Renal Cell Carcinoma Tumor Progression

Marie Sarabusky, Rebecca Earnshaw, Brad Shrum, Xizhong Zhang, Lakshman Gunaratnam.

Renal cell carcinoma (RCC) is the most prevalent form of kidney cancer, and >30% present with metastatic disease for which therapy is ineffective. Kidney injury molecule-1 (KIM-1) is a renal tubular epithelial cell-surface protein implicated in tissue repair after acute kidney injury (AKI). KIM-1 is expressed by most clear cell and papillary RCCs, and confers poor prognosis but the mechanism is unknown. During AKI, KIM-1 enables tubular cells to mediate phagocytic clearance of apoptotic cells, preventing release of their pro-inflammatory intracellular contents, thus inhibiting innate immune responses and mitigating tissue damage. Since release of

danger signals from dying tumor cells is critical for anti-tumor T-cell responses, we sought to determine if KIM-1 promotes RCC tumor progression by promoting phagocytic clearance of dying tumor cells. We stably transduced Renca murine RCC cells to express Kim-1. We compared phagocytic activity between Kim-1 expressing and control Renca cells using flow cytometry. We injected BALB/c mice subcutaneously with $\sim 3 \times 10^6$ Kim-1 expressing and control Renca cells ($n=10/\text{group}$). Tumor growth was measured over time. We quantified cytokine levels using RT-qPCR on RNA extracted from cancer cells and tumors. Kim-1 significantly promoted phagocytosis of apoptotic cells by RCC cells. Mean tumor growth was significantly greater in Renca cells expressing Kim-1 compared to control cells. Kim-1 expression inhibited production of several pro-inflammatory cytokines by RCC cells. We provide the first evidence that Kim-1 expression promotes RCC tumor growth in vivo. KIM-1 may influence anti-inflammatory cytokine production to promote immune evasion and therefore may serve as a therapeutic target.

(47.10%) and hypertension (50.60%) were the most common comorbidities seen with RVF ($n=85$). Upon ED arrival, 24 (28.2%) remained in RVF, 38 (44.7%) deteriorated, and 23 (27.1%) had improved. Thirty-four (40%) survived to admission, while only 18 (21.2%) survived to discharge. Patient age was statistically associated with improved rhythm on ED arrival ($p=0.013$) and survival to discharge ($p=0.015$). Conclusion: The majority of patients with prehospital RVF have a rhythm deterioration by the time care is transferred to the ED, and few survive to discharge. Younger patients are more likely to remain in RVF and survive to discharge. Further research is required to determine prehospital treatment strategies for RVF.

Outcomes associated with prehospital refractory ventricular fibrillation

Schappert, A., Davis, M., Chau, B., Leung, A., VanArsen, K..

Introduction: When ventricular fibrillation (VF) cannot be terminated, it is classified as refractory VF (RVF). There is a paucity of information regarding any associated prehospital or patient factors. The study objectives were to determine factors that may be associated with RVF, the initial ED rhythm for patients with prehospital RVF, and the incidence of survival in patients who had RVF. Methods: Ambulance Call Records (ACRs) of patients with out of hospital cardiac arrest between Mar. 1 2012 and Apr. 1 2016 were reviewed. Cases of RVF were determined by manual review of the ACR. ED and hospital records were analyzed to determine outcomes of those transported to hospital. Descriptive statistics were calculated and all variables were tested for an association with initial ED rhythm, survival to admission, and survival to discharge. Results: A history of coronary artery disease

An index case of PCP pneumonia in a patient with ITP: an important differential and difficult diagnosis in the non-HIV positive immunosuppressed population

Melissa Schorr, Seyed Hosseini.

PCP is thought of as an opportunistic infection seen in the HIV positive population. In these patients it is often an indolent infection with relatively low mortality. PCP has become more common and a significant risk for any patient who is immunosuppressed. Dr. S was a 78 year old retired surgeon with a history of CAD, dyslipidemia, OSA, CKD and hypertension. In May of 2013, he was diagnosed with ITP and was initiated on high dose steroids. In September, he was admitted to CTU with a 2 week history of diarrhea - subsequently diagnosed with C.difficile. He was initiated on fluids and antibiotics. A few days after admission he had expiratory wheeze which quickly progressed to increasing shortness of breath and oxygen requirements. With multiple xrays showing bilateral infiltrates, he was treated repeatedly with diuresis. It was only when he became profoundly septic that suspicion of an atypical respiratory infection arose. ID was consulted and bronchoscopy was arranged to rule out PCP. Transbronchial biopsy confirmed the diagnosis. Despite initiation of appropriate antibiotics, he progressed to ARDS and was found VSA in early October. PCP is not limited to HIV and transplant patients and represents an acute, fulminant

infection with high risk of ICU admission, need for mechanical ventilation and mortality. It is difficult to diagnose; radiographic findings are often confused for pulmonary congestion and BAL has low yield. There are currently no guidelines for prophylaxis in non-HIV or transplant patients; high clinical suspicion is key to early diagnosis and treatment.

Multi-dimensional assessment in idiopathic pulmonary fibrosis

Hana Serajeddini, Paola Rogliani, Marco Mura.

Background. The clinical course of idiopathic pulmonary fibrosis (IPF) is difficult to predict. Perceived dyspnea, exercise capacity, and lung physiology have all been associated with mortality outcomes in IPF, but the significance of this relationship is unclear. We sought to investigate the strength of the relationship between these variables and their independent predictive capability in determining mortality outcomes. **Methods.** Four-hundred-thirty-seven patients from 3 different centers (Western University, University of Toronto, University of Rome) with IPF were included in the study. Medical Research Council dyspnea score (MRCDS), 6-minute walk distance percent predicted (6MWD %pred) and pulmonary function tests, including calculation of the composite physiologic index (CPI), were determined at baseline. The endpoint was 18-month mortality/lung transplant (LTx). **Results.** Correlations between MRCDS, 6MWD %pred, forced vital capacity (FVC) and diffusing lung capacity for carbon monoxide (DLCO) were weak ($r < 0.5$). Collinearity, measured by variance inflation factors, was low. At the end of the observation period, 165 patients were alive, 167 had been transplanted, and 105 had died. Univariate regression analysis and c-statistics identified MRCDS (H.R.=1.89, AUC=0.74), 6MWD %pred (H.R.=0.97, AUC=0.79), FVC (H.R.=0.97, AUC=0.76), and CPI (H.R.=1.05, AUC=0.78) as significant predictors of 18-month mortality/LTx. Multivariate regression analysis retained MRCDS, 6MWD%pred and either FVC or CPI as independent predictors of outcome. **Conclusion.** Baseline dyspnea, exercise capacity and physiology are weakly correlated to each

other, translating in low collinearity among variables. MRCDS, 6MWD%pred and CPI (or FVC) provide independent prognostic information, suggesting that a multi-dimensional assessment of mortality in patients with IPF is feasible and advantageous.

Efficacy of azacytidine in Myelodysplastic Syndrome patients outside clinical trials: the LHSC Experience

Roman Shapiro, Alejandro Lazo-Langner.

Background Azacytidine is effective at prolonging survival in MDS that is int-2/high risk according to the International Prognostic Scoring System (IPSS). The revised IPSS (IPSS-R) was introduced to improve upon the IPSS. The objectives of this work are to compare the IPSS and IPSS-R in MDS patients at LHSC, and to identify a set of markers in this cohort that are predictive of azacytidine treatment response. **Methods** This is a retrospective single institution study of patients diagnosed with MDS during the period of Jan 2008 – December 2014 who were treated with azacytidine. Kaplan-Meier survival curves were constructed for the patients categorized based on IPSS and IPSS-R. Regression analysis was used to determine predictors of treatment response and time to treatment failure. **Results** Ninety-seven patients retrieved from LHSC electronic health records met criteria for inclusion in this study. The median overall survival of all patients is 7.3 months. There was no statistically significant difference between the IPSS-R intermediate, high, and very high survival curves (log-rank $p = 0.774$). The ORR for all patients treated with 5-azacytidine was 23%, with ORR of 21%, 17%, and 38% for IPSS-R intermediate, high, and very high, respectively. Factors associated with long-term response included cytogenetic response, marrow complete response, and any platelet count recovery during treatment. **Conclusions** The IPSS-R provides no improved prognostic utility in the LHSC cohort of patients as compared to the IPSS. Platelet count recovery during the first 6 cycles of treatment is a novel marker in the prediction of long-term response to azacytidine.

Mark Speechley, Dr. Kaveri Gupta, Dr. Michael Silverman.

An ICD-10 Discharge Code Based Algorithm to Identify IVDU-Related Endocarditis.

Adeel Sherazi, Laura Ball, Dora Laczko, Dr. Rommel Tirona, Dr. John McCormick, Dr. Sharon Koivu, Dr. Kaveri Gupta, Dr. Michael Silverman.

BACKGROUND: There has been a growing concern with the increasing number of infective endocarditis (IE) admissions. The rate of IE has been on an especially alarming rise in persons who inject drugs (PWID). Epidemiologic trends in PWID-associated IE are difficult to track as the ICD-10 codes used to define discharge diagnoses do not specify IV drug use (IVDU) and do not specify the components of the modified Duke's criteria which describe definite cases of IE. **OBJECTIVES:** We sought to establish a combination of ICD-10 discharge codes that would serve as diagnostic criteria to identify PWID-associated IE in patient databases. **METHODS:** We constructed two cohorts of 100 patients, ages 17-55, by sequential date of admission from 2009-2011 and 2014-2016 with a discharge diagnosis of endocarditis. We assessed the sensitivity, specificity and predictive values of 16 ICD-10 code combinations in identifying PWID-associated IE when compared to results from a retrospective chart review. **RESULTS:** A combination of endocarditis and one of HIV, HCV, drug use, or mental/behavioural disorder ICD codes yielded a sensitivity of 93% and PPV of 83% among the 2014-2016 group. The same combination had a sensitivity of 95% and PPV of 91% among the 2009-2011 group. **CONCLUSIONS:** Our ICD-10 code based algorithm accurately identifies cases of PWID-associated IE. This algorithm can be applied to patient databases to evaluate local and large-scale trends of IVDU-related cases of IE.

Endocarditis Trends at LHSC since the Delisting of OxyContin

Adeel Sherazi, Esfandiar Shojaei, Laura Ball, Brian Hallam, Dan Lizotte, Jacqueline Kueper,

BACKGROUND: OxyContin was delisted from the Ontario Drug Benefits formulary in 2012. Since 2012, the gap that OxyContin left has been filled with hydromorphone contin, which is more complex to inject and thus has more opportunities for contamination. **HYPOTHESIS:** The delisting of OxyContin in 2012 is associated with an increase in injection drug use (IDU)-related endocarditis (IE). **METHODS:** We conducted a retrospective chart review of all patients > 18 years old admitted to LHSC from 2008-2015 with a discharge diagnosis of IE. Using patients' first episode of IE, we performed a Poisson regression for IDU and non-IDU patients to estimate the rates of IE from 2008-2012 and 2013-2015, as well as the change in rate from 2012 to 2013. **RESULTS:** 413 first-time IE episodes (54% IDU patients) were analyzed. There was a 166% rise in IDU-related first episodes of IE from 2008-2015. The Poisson regression for 2012-2013 showed a jump in rate of 78% ($p = 0.04$) for first-time IE in IDU patients but a non-significant 28% ($p = 0.40$) in non-IDU patients. IDU-related IE with hydromorphone contin rose from 36.7% to 66.4% ($p < 0.05$), and with Oxycontin fell from 18.9% to 3.4% ($p < 0.05$). In cases not associated with OxyContin or hydromorphone contin, there was no significant change in IDU-related IE (17.8% before 2012 vs 23.5% after). **CONCLUSIONS:** 2012 was a landmark year with a transition from OxyContin to hydromorphone contin. Unfortunately, the change in opioid of choice has resulted in worse infectious complications and a dramatic increase in IE rates.

Applicability of the new ASE/EACVI Diastolic Function Guidelines in the population of patients with Heart Failure with Preserved Ejection Fraction

Olusegun Sheyin, Ryan Davey, Robert McKelvie, Stuart Smith, David McCarthy, Sabe De.

Background: Heart failure (HF) is the leading cause of hospitalization among patients 65 years of age and older. One-half of HF patients have Heart Failure with Preserved Ejection Fraction (HFpEF). The American Society of Echocardiography (ASE) in conjunction with the European Association of Cardiovascular Imaging (EACVI) published new diastolic function guidelines in 2016 and introduced new parameters for classifying diastolic function. Whether the new ASE/EACVI diastology guidelines will influence the classification of diastolic dysfunction in patients with HFpEF remains unknown. Aims/Objectives: 1. To see whether application of the new ASE/EACVI guidelines will influence the diastolic function classification in patients with HFpEF. 2. To see if there is an association between diastolic function class and prognosis 3. To identify markers of diastolic dysfunction which predict adverse outcome in HFpEF. Methods: This is a retrospective study of patients with HFpEF who have attended the Heart Function Clinic at St. Joseph's Hospital and who have had their left ventricular (LV) diastolic function reported on echocardiography within the past 1 year. LV diastolic function evaluation will be repeated using the 2016 ASE/EACVI guidelines for each patient included in the study. This retrospective chart review will capture data on patients over the course of one year from the date of their echocardiogram. An application has been submitted to the Institutional Review Board (IRB) for approval. Results: Pending (awaiting IRB approval). Conclusions: Pending.

Are short tapering courses of prednisone as effective and safe as long courses in patients with immune thrombocytopenia (ITP): A retrospective study

Kulraj Singh, Manika Gupta, Selay Lam, Joy Mangel, Alan Gob, Ian Chin-Yee, Chai Phua, Cyrus Hsia.

Background Immune thrombocytopenia (ITP) is an auto-immune disorder that leads to low platelets) and an increased risk of bleeding. Corticosteroid therapy with prednisone 1 mg/kg is typically the first-line therapy, however there are no clear guidelines on how rapidly to taper the

prednisone once it starts to work. Long tapering regimens have the potential for numerous side effects, leading to interest in using shorter regimens. Our retrospective study compared the effectiveness and safety of different prednisone tapering schedules: short (<8 weeks), medium (8-16 weeks) and long (>16 weeks). Methods All patients with ITP treated with prednisone at the Hematology Clinic at Victoria hospital from 2006-2016 were reviewed. The 3 different tapering schedules were compared during treatment for overall response, complete response (platelets >100x10⁹/L), partial response (platelets >30x10⁹/L), and side effects, including major and minor. Results 173 patients (95F/78M) with ITP received 236 separate courses of prednisone. Mean patient age was 58. 27% of patients received > 1 course of prednisone. Responses were seen in 89%, 84% and 92% of patients who underwent short, medium and long tapering courses of prednisone. Side effects were reported in 36%, 56% and 66% of these groups of patients respectively. Conclusions Short and medium courses of prednisone were as effective as long courses in treating patients with ITP. However, short courses had fewer side effects than medium and long courses. Short and medium courses of prednisone are just as effective and may be safer than long courses for ITP patients requiring treatment.

Does polypharmacy affect latency to first fall as medicated by Gait Impairments?

Hao Yuan Song, Dr. Manuel Montero-Odasso
Dr. Brittany Barnes.

We aim to investigate 1) the correlation between polypharmacy and gait disturbance, 2) the correlation between gait and falls, and 3) gait disturbance as mediation factors between polypharmacy and falls. Methods: For the first part of this study we performed a cross-sectional analysis on 249 geriatric patients (mean age=76. Female=62.7%) enrolled in the Brain and Gait Laboratory at Parkwood Hospital, London, Ontario who were followed for a maximum of 5 years with biannual assessments. We looked for correlation between number of medications and various gait parameters such as gait velocity, gait variability and dual-task gait cost. For the second

part of the study we investigated the relationship between polypharmacy and falls (number of falls, time to first fall, fall rates) longitudinally. We also performed a mediation analysis to investigate gait as a potential mediation variable between polypharmacy and falls. For the first part of the study we found that Increased number of medications are associated with decreased gait velocity and increased gait variability. Polypharmacy is associated with of slow gait (defined as <1m/s) during follow up with an OR of 1.2 and high gait variability. For the second part of the study we found that an increase in number of medications is associated with shortened number of month to first fall as demonstrated with a multivariable linear regression model. Further more, a mediation analysis showed that when using gait velocity a mediation factor. Gait variability was not shown to have a mediating effect. The known risk of falls in older adults taken more than 4 medications may can be mediated by a reduction of gait velocity.

Utilization of a web-based module for caregiver pain management following fractures in children: a randomized controlled trial

Robbie Sparrow, Naveen Poonai, Samina Ali, Stevi Golden-Plotnik, Tammy Wong, Amy Drendel.

Purpose Fractures are common painful conditions in childhood. Web-based platforms easily incorporate new information that is readily accessible at home. We tested the hypothesis that caregiver education on pain management at home facilitated through a novel interactive WBM was superior to video instructions and the standard of care (SOC): verbal and paper instructions. **Methods** This open-label, randomized, controlled, three-arm trial included caregivers of children with non-operative fractures presenting to the ED. The primary outcome was the gain score (pre-post intervention) on a novel 21-item questionnaire testing knowledge surrounding pain recognition and management for children with fractures. **Results** 246 participants were recruited (WBM 74; Video 88; SOC 84). There were 97 females (39.4%). The mean (SD) age was 9.7 (4.3) years

with a range of 6 months to 17 years. The SOC group had significantly lower mean (SD) gain scores: 0.3 (2.2) versus WBM: 2.3 (3.1) and Video: 2.6 (3.9) (95% CI: -3.2, -0.8, $p<0.001$ for WBM versus SOC; 95% CI: -3.4, -1.2, $p<0.001$ for Video versus SOC). There was no significant difference between WBM and Video (95% CI: -0.9, 1.5, $p=0.83$). There were no significant differences in caregiver confidence ($p=0.41$), number of absent school days ($p=0.43$), sleep-interrupted nights ($p=0.94$), or workdays missed ($p=0.95$). **Conclusion** Among caregivers of children with fractures presenting to the ED, education on pain management at home using both an interactive WBM and a video was associated with superior knowledge acquisition to verbal and paper instructions. However, there were no significant between-group differences in functional outcomes.

Identifying the role of GPSM-3 on susceptibility to kidney disease

Anette Surmanski, Dr. Brad Urquhart and Dr. Peter Chidiac.

The loss of kidney function in kidney disease typically arises from damage to glomeruli. Podocytes, which are visceral epithelial cells within glomeruli, are common targets in kidney injury. Although their physiological function is established, the role of podocytes in injury is not. Our studies focus on the role of G protein signaling modulator-3 (GPSM3), which governs G protein-coupled signaling and is selectively expressed in podocytes. Apart from established effects on G protein activation, physiological functions of GPSM3 are not well understood and its role within the glomerulus is unknown. We hypothesize that GPSM3 contributes to normal podocyte function and gene expression will be upregulated as a protective mechanism in response to glomerular damage. E11-conditionally immortalized murine podocyte cells were cultured at 37°C and treated with normal (5.5 mM) or high glucose (25 mM) medium over 48 hours. GPSM3 expression levels were measured with qPCR. Additionally, C57BL/6 mice were injected intraperitoneally with saline or streptozotocin to induce diabetes and GPSM3

mRNA was assessed by qPCR at 2- and 8-weeks post treatment. GPSM3 expression increased by 82% in high glucose treated podocytes compared to controls ($P < 0.05$). GPSM3 transcript levels were increased by 31% in 8-week but not 2-week diabetic mice compared with controls ($P < 0.05$). Understanding how GPSM3 changes under normal and pathophysiological conditions could provide insight on delineating possible mechanisms responsible for changes in podocyte signaling during injury. These findings may contribute to development of novel diagnostic techniques and development of novel approaches for treating and preventing kidney disease.

Effects of a combined educational intervention and computerized decision support on unnecessary testing in the emergency department: the case for INR & aPTT

Davy Tawadrous, Sarah Detombe, Kristine VanArsen, Drew Thompson, Terry Skoretz.

Introduction: With a shrinking healthcare budget, poor physician cost-awareness, and over-utilization of low-value tests, we designed, implemented and evaluated an educational initiative and decision support tool to reduce coagulation testing in the emergency department. **Methods:** Hospital-based prospective pre-post analysis of INR-aPTT de-bundling and implementation of an educational initiative and decision support tool in two academic hospital emergency departments. Participants include those aged 18 years or older undergoing evaluation and/or treatment during the period of August 1, 2015 to January 31, 2017. Primary outcome is coagulation testing utilization rates. **Results:** De-bundling INR-aPTT testing with implementation of our educational initiative and decision support tool resulted in significantly decreased bundled INR-aPTT testing, with significantly increased targeted testing. There was significant decrease in associated costs, realizing estimated daily and annual savings of \$474.56 and \$173,214.40, respectively. **Conclusion:** Compared to baseline practice patterns, de-bundling INR-aPTT testing resulted

in the greatest reduction of coagulation testing, with incremental benefits from implementation of an educational initiative and decision support tool. As such, we recommend institutions re-evaluate practice patterns and system design to optimize emergency department laboratory utilization.

The efficacy of PET-CT in detecting bone marrow involvement in patients with newly diagnosed lymphoma.

Kartiga Thiyagarajah, MD, Olfat Kamel-Hasan, MD, Asmaa Hawsawy, MD, David Laidley, MD, Joy Mangel, MD.

Patients diagnosed with lymphoma undergo various investigations to determine disease stage. This includes Positron Emission Tomography with Computed Tomography (PET-CT) scan and bone marrow biopsy (BMB), which has historically been considered the gold standard for detecting involvement of the bone marrow (BM) by lymphoma. Recent studies have suggested that PET-CT scans can detect BM involvement in most patients with lymphoma. The purpose of this study was to compare our local results of BMB vs. PET-CT scans for assessment of BM involvement in patients with lymphoma. We retrospectively reviewed the charts of 110 adult patients who were newly diagnosed with non-Hodgkin lymphoma (NHL, $n=102$) or Hodgkin lymphoma (HL, $n=8$) at the London Regional Cancer Program from 2013-2016, and who underwent both BMB and PET-CT for staging. For the entire cohort of patients with NHL, the sensitivity and specificity of PET-CT for diagnosing BM involvement were 78% and 86%. The accuracy was 84%. For patients with diffuse large B-cell lymphoma (DLBCL, $n=40$), the sensitivity and specificity of PET-CT were 100% and 79%. The accuracy was 83%. In this group, none of the patients with a negative PET-CT had a positive BMB. Five of the 7 patients with positive PET-CT but negative BMB had focal BM involvement on PET-CT. While limited by small sample size, our data suggests that PET-CT is particularly adept at detecting BM involvement in DLBCL and may detect focal involvement missed by BMB. This may lend support to clinicians

foregoing BMB in these patients if already imaged with PET-CT.

The Impact of Sofosbuvir-Based Therapy on Renal Function in Hepatitis C Virus Patients with Advanced Liver Disease

Benson Thomas, P. Marotta, M. Levstik, P. Adams, K. Qumosani, and B. Al-judaibi.

Background: Management of Hepatitis C virus (HCV) in chronic liver disease patients has been evolving over the past decade with the adoption of newer treatment strategies given the tolerability of these agents. HCV patients treated with Sofosbuvir-based therapy have seen hepatic recovery albeit the degree and specific patient population in which this occurs is undetermined. It can be hypothesized that renal function would improve post treatment given hepatic recovery and reduced diuretic use. The effect of Sofosbuvir-based therapy on renal function in the advanced liver disease population currently remains unclear. Aims: To assess the effect of Sofosbuvir-based therapy on renal function amongst HCV patients undergoing liver transplant assessment. Methods: Analysis of prospectively collected data of a cohort of HCV patients who have undergone liver transplant assessment at London Health Sciences Centre from January 2014 to January 2015. Patients who had commenced or completed Sofosbuvir-based therapy were selected. Patient outcomes included sustained virologic response at 12 weeks (SVR12), glomerular filtration rate (GFR) pre and post treatment, MELD-Na score, Child-Pugh score and liver transplant status were analyzed. Results: Interim analysis was performed on 44 patients. A total of 22 patients (52%), all genotype 1, had commenced Sofosbuvir-based therapy with all patients who completed therapy, 19/19 (100%), achieving SVR12. The mean MELD-Na score of these patients was 20.2 and mean Child-Pugh score was 8.4. 3/22 patients on therapy died, 1 from small bowel ischemia after completing therapy and 2 deaths prior to completion of therapy, both patients died from sepsis. 9/19 who achieved SVR12 had confirmed HCC, 3/19 have underwent orthotopic liver transplantation and were excluded from GFR evaluation. 16 patients

Pre/Post Treatment GFR were assessed. The mean GFR pre-treatment was 88.6 ml/min/1.73m² and the GFR post treatment mean was 79.5 ml/min/1.73 m², there was no significant difference between the two groups (P=0.18). None of the patients discontinued therapy. Conclusions: In this preliminary analysis, there was no clear difference in GFR post treatment with Sofosbuvir-based therapies. Sofosbuvir-based therapies were quite efficacious in this small sample size of the advanced liver disease population. Larger studies are needed to further evaluate the effect of Sofosbuvir-based therapy on renal function in patients with advanced liver disease.

Sofosbuvir-Based Therapy Leads to A Reduced for Liver Transplantation among Hepatitis C virus (HCV) patients: A Canadian Multicentre Experience

Bandar Al-judaibi, **Benson Thomas**, P. Wong, A. Benmassaoud, J. Chen, T. Hussaini, E. Yoshida, J. huac, R. Hussaini, M. Bilodeau, P. Marotta.

Background: Hepatitis C virus (HCV) infection is the most common indication for liver transplantation globally. Patients with end-stage liver disease typically were not eligible for interferon-based therapy, due to poor tolerability and deterioration of liver function. Recently, novel therapies have been proven to be effective in this population. All oral, interferon-free therapy (Sofosbuvir (SOF)-based) has been shown to have high efficacy even in decompensated cirrhosis. HCV patients treated with SOF-based therapy have experienced various degrees of hepatic recovery ranging from stabilization of liver function, to removal from liver transplant wait lists. The frequency of these occurrences in larger transplant eligible patient populations is unknown. Aims: To assess the efficacy of SOF-based therapy in HCV infected transplant eligible patients and to evaluate decompensated liver disease patients with respect to changes that occur in liver function in the short term and the resultant effect on their liver transplant status. Methods: A retrospective multicentre Canadian study of liver transplant candidates with advanced HCV cirrhosis treated with SOF-based therapy. Outcomes included sustained virologic

response (SVR), changes in MELD-Na score, Child-Pugh score and liver transplant status. Results: 96 liver transplant candidates with advance liver disease due to HCV were evaluated. 69 (71%) of patients have genotype 1, SVR was 88.3% (94% for G1, 68 % for non- G1). 49 patients were treated in the pre-assessment period and 47 patients were treated while awaiting transplantation. Of the 49 treated in the pre-assessment period, no significant difference in their average MELD-Na score (12 vs 12, p=ns) nor Child-Pugh score (7 vs 6 p=ns) occurred from baseline to SVR 12 date. However, among patients treated while wait listed for transplant, 14/47 (30%) remained active on the liver transplant list at the time of SVR12, 9/47 (19%) patients were delisted, 16/47 (34%) underwent liver transplantation. Progression of HCC lead to delisting of 1 and 8 deaths (1 after transplant) occurred. Among delisted patients, the average MELD-Na changed from 15 to 12. Conclusions: SOF-based therapy for patients progressing to liver transplantation leads to high SVR rates, short term stability in liver function, and in a sizable portion leads to delisting. These improvements may increase over time. Longer term follow up and further analysis is needed to understand the overall impact this will have on wait list deaths, number of transplants required for HCV and survival of non-HCV recipients.

Antibiotics for Induction and Maintenance of Remission in Crohn's Disease

Cassandra M Townsend, Claire E Parker, John K MacDonald, Brian G Feagan, Vipul Jairath, Reena Khanna

Background: Trials of antibiotic therapy for Crohn's disease (CD) have produced conflicting results. Objectives: We performed a systematic review and meta-analysis to determine the efficacy and safety of antibiotics for induction and maintenance of remission in CD. Methods: EMBASE, MEDLINE, Cochrane Library and Cochrane IBD Group Specialized Register were searched from inception to September 2016. Randomized controlled trials (RCTs)

comparing antibiotics to placebo or an active comparator in CD patients were considered for inclusion. Data were analyzed based on intention-to-treat. Risk ratios (RR) and corresponding 95% confidence interval (95% CI) were calculated for dichotomous outcomes. Methodological quality was assessed using the Cochrane risk of bias tool. GRADE analysis was performed. The primary outcomes were the proportion of patients who failed to achieve clinical remission and the proportion of patients who relapsed. Results: Fourteen RCTs (n = 1469 patients) were eligible. A pooled analysis of 8 placebo-controlled RCTs (801 patients) showed no significant difference in clinical remission at 6 to 10 weeks. Fifty per cent (267/535) of antibiotic treated patients failed to enter remission compared to 59% (158/266) of placebo patients (RR 0.87, 95% CI 0.75-1.01; moderate quality evidence). A pooled analysis of two placebo-controlled studies (155 patients) showed no statistically significant difference in relapse rates at 52 weeks. Forty-five per cent (37/83) of antibiotic treated patients relapsed compared to 57% (41/72) of those assigned to placebo (RR 0.87, 95% CI 0.52-1.47; low quality evidence). Conclusions: Antibiotics are ineffective for induction or maintenance of remission in Crohn's disease.

New Onset Cardiac Arrhythmia: Side Effects of Ibrutinib.

Jari Tuomi, Anargyros Xenocostas, and Douglas L. Jones.

Atrial Fibrillation (AF) is an important side effect of Ibrutinib, an irreversible inhibitor of Bruton's tyrosine kinase, used in the treatment of various B lineage lymphoproliferative disorders. We determined if a single (acute) oral dose or following a 24 hour washout period after the chronic (14 day) administration of Ibrutinib would confer susceptibility to electrical pacing-induced

atrial and ventricular arrhythmias in the mouse. We hypothesized that susceptibility to arrhythmia induction requires Ibrutinib exposure rather than being a later electrophysiological remodelling effect of the drug. One-month-old male C57BL/6 mice were blindly administered Ibrutinib (20 mg/kg) or vehicle (trappsol), by oral gavage. Intracardiac electrophysiological studies determined inducibility of AF and ventricular irritability (VI, a non-sustained response < 1 sec). A single dose of Ibrutinib increased AF inducibility (4/10 vs. 0/10, $P < 0.05$, duration 36.6 +/- 56.5 sec) and VI (5/10 vs. 0/10, $P < 0.05$). There was no difference following washout after chronic dosing for both AF (2/8 vs. 2/8, $P = 1$) and VI (2/8 vs. 1/8, $P = 0.52$). We confirmed that acute Ibrutinib increases susceptibility to atrial and non-sustained ventricular arrhythmia in the mouse. Chronic exposure does not promote persistent electrical remodelling, suggesting arrhythmia inducibility is a transient, potentially off-target, drug effect.

The Man without LDL: Solving the Genetic Conundrum Underlying a Profoundly Abetalipoproteinemic Phenotype Using Next-Generation Sequencing.

Linda R. Wang, Adam D. McIntyre, Matthew R. Ban, Henian Cao, and Robert A. Hegele.

Abetalipoproteinemia (ABL) is a rare autosomal recessive disorder in the MTTP (microsomal triglyceride transfer protein) gene, characterized by the absence of apolipoprotein B (apoB)-containing lipoproteins including LDL, VLDL, and chylomicrons. Patients present in infancy with fat malabsorption and develop severe sequelae of lipid-soluble vitamin deficiency including retinal degeneration, ataxia, acanthocytosis, and coagulopathy. Familial Hypobetalipoproteinemia (FHBL) is an autosomal codominant disorder affecting the APOB gene, whose homozygotes are virtually indistinguishable from abetalipoproteinemia, but heterozygotes benefit from half-normal levels of LDL and cardiovascular protection. We describe a patient with longstanding abetalipoproteinemic phenotype responding to empiric therapy, whose genetic sequencing revealed neither

abetalipoproteinemia nor homozygous hypobetalipoproteinemia. Rather, he had numerous heterozygous mutations involving several relevant genes, including both MTTP and APOB. By sequencing his available family members and correlating their phenotypes, we deduced that the most likely causal mutations are consistent with compound heterozygous hypobetalipoproteinemia - an extraordinarily rare entity only described once in medical literature. We review the literature on abetalipoproteinemia and hypobetalipoproteinemia, summarizing the genetic inheritance, biochemistry, clinical manifestations, diagnosis, and treatment of both conditions. We present the implications of our case on the candidate mutations for hypobetalipoproteinemia, the strengths and weaknesses of in silico predictive software compared to clinical data, and the importance of early treatment on clinical outcome.

Optimizing Scheduling of Sub-Specialty Outpatient Follow-Up for Patients Discharged from the Clinical Teaching Unit at London Health

Dr. Darren Weaver, Dr. Andrew Appleton.

Patients that are discharged from the inpatient medicine service known as the Clinical Teaching Unit (or CTU) often require follow-up from subspecialty services based at LHSC. There is significant variability in the follow-up booking process. For example, the electronic medical record, telephone, e-mail, and faxed referral sheets are all used. Different team members book the appointments, and it is unclear who is ultimately responsible for arranging follow up. This study was designed to look at who is booking follow-up, how they're booking follow-up, and the rates of successfully booked and attended appointments. We are concerned that with this non-standardized method for booking follow-up that patients are not having follow-up booked, or are missing appointments which could compromise patient care. Our goal is to study the current state of how follow-up is being booked and LHSC with a future goal of improving this process for the CTU teams at LHSC. Our methods included a chart review of the online system for patients discharged from CTU team 1

at University Hospital within LHSC, as well as an online survey of LHSC staff involved in the follow-up booking process. Our data from the chart review and survey are currently being collected, and will be available in the coming months for results and discussion.

Prevention of venous thromboembolism in pregnant patients with a history of venous thromboembolic disease: a retrospective cohort study.

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Background. Women with a history of venous thromboembolism (VTE) are at higher risk for recurrence during and after pregnancy. Optimal prophylactic strategies in these patients are unknown. **Objective.** To assess the incidence of VTE recurrence in pregnant patients with a history of VTE, and anticoagulant prophylaxis. **Methods.** We conducted a retrospective cohort study of consecutive pregnant patients with VTE history. Patients whose previous event was secondary to a transient risk factor were followed without antenatal prophylaxis. Those with a previous idiopathic event received antenatal prophylactic low-molecular-weight heparin. All patients received prophylaxis for six weeks postpartum. **Results.** We included 140 women with 198 pregnancies: 86 (127 pregnancies) with past idiopathic thrombosis and 54 (71 pregnancies) with past secondary thrombosis. In the idiopathic group, there were 7 VTE recurrences (5.5%; 95%CI: 2.69-10.94), 3 occurring postpartum. In the secondary group there was 1 recurrence (1.4%; 95%CI: 0.24-7.55) ($p=0.1$). There were 2 bleeding events (1.5% (95%CI: 0.43-5.56) in participants with previous idiopathic VTE (none in the secondary thrombosis). In the idiopathic group there were 8 fetal losses (6.3%; 95%CI: 3.22-11.94); in the secondary group there were 6 (8.4%; 95%CI: 3.9-17.24) ($p=0.5$). **Conclusions.** This retrospective cohort study demonstrated a thrombosis recurrence rate of 4% in pregnant patients with history of VTE, with a similar risk of recurrence

between those with idiopathic vs. provoked VTE. The appropriate strategy for VTE prophylaxis in pregnant patients should be guided by individual risk assessment, in keeping with current guidelines.

Associated pulmonary hypertension is an independent contributor to six-minute walk distance in chronic fibrotic interstitial pneumonias.

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Introduction: Associated pulmonary hypertension (APH) is frequently observed in fibrotic interstitial pneumonias (FIP), such as idiopathic pulmonary fibrosis (IPF). APH is associated with greater functional impairment and worse prognosis. APH may be out of proportion with the extent of FIP. Six-minute walk distance (6MWD) is widely used to assess functional capacity in pulmonary hypertension. We hypothesized that APH may be an independent contributor to exercise incapacity in FIP. **Methods:** Patients diagnosed with FIP (September 2009-January 2017) were included in the study if they underwent right heart catheterization (RHC) and six-minute walk test. Patients with connective tissue disease were excluded. APH was defined as mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg and pulmonary capillary wedge pressure ≤ 15 mmHg. The extent of fibrosis was quantified with a standard HRCT fibrosis score. **Results:** Forty-seven patients (40 with IPF, 7 with non-IPF FIP) were included. Thirty-six patients had APH. mPAP and pulmonary vascular resistance (PVR) were negatively and significantly correlated with 6MWD % pred ($r=-0.32$, $p=0.034$; $\rho=-0.40$, $p=0.007$, respectively). mPAP and PVR were significant predictors of 6MWD % pred based on stepwise regression analysis. Quantitative HRCT fibrosis score and pulmonary function tests were not significantly correlated with 6MWD % pred and were not significant predictors of 6MWD on stepwise regression. **Conclusion:** The presence of APH in FIP is associated with reduced 6MWD. This association is independent from the extent of underlying lung fibrosis. Therefore, APH has an independent impact on exercise capacity, which may be out of proportion with the extent of lung fibrosis.