University of Western Ontario
Department of Medicine

RESEARCH DAY

Thursday, May 15, 2014
Best Western Lamplighter Inn
591 Wellington Road South
London, Ontario N6C 4R3

This program has no commercial support.

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 2014
Thursday May 15, 2014
Best Western Lamplighter Inn
591 Wellington Road South

Schedule of Events			
Start	End		
8:00	8:30	**Breakfast** *(Atrium)*	**Poster Setup** *(Crystal Ballroom South)*
8:30	8:40	**Welcome & Opening Remarks** *(Crystal Ballroom North)*	
8:40	9:20	So You Want a Career in Research **Dr. James Calvin** *(Crystal Ballroom North)*	
9:20	10:00	A 20 year Journey of Clinical Research: "Cardiac Resynchronization Therapy" **Dr. Anthony Tang** *(Crystal Ballroom North)*	
10:00	11:00	**BREAK** *(Atrium)*	**Poster Presentation and Judging** *(Crystal Ballroom South)*
11:00	11:45	Global Trends in Health System Innovation **Keynote Dr. Anne Snowdon** *(Crystal Ballroom North)*	
11:45	13:45	**LUNCH** *(Atrium)*	**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)*	
15:00	15:15	**REFRESHMENT BREAK** *(Atrium)*	
15:15	16:30	**Trainee Oral Presentations** *(Crystal Ballroom North)*	
16:30	16:45	**Presentation of Awards & Final Remarks** *(Crystal Ballroom North)*	

Please ensure that you fill out the evaluation form provided in your Research Day package before you leave for the day and drop it in the box at the Registration Desk on your way out.

Poster Presentations

Poster #	Presenter	Program	Abstract Title
101	Majed Alahmadi	PGY-5	Evaluating the effect of accidental dose reduced cyclophosphamide chemotherapy in lymphoma patients
102	Saleh Alghofaili	PGY-3	Ictal Asystole
103	Faris Alhejaili	Clinical Fellow	Continuous Positive Airway Pressure (CPAP) compliance in patients with Obstructive Sleep Apnea Syndrome (OSAS)
104	Basil Al-Sabeq	PGY-2	Changes in early repolarization pattern during exercise treadmill testing do not predict symptom status in patients with long QT syndrome
105	Tom Appleton	PGY-3	Inhibition of TGFα-CCL2 signaling suppresses the progression of post-traumatic osteoarthritis
106	Alescia Azzola	PGY-2	Comparison of Five Methods for Chromogranin A Measurement in Healthy Subjects and in Patients with Neuroendocrine Neoplasms
107	Catherine Barrett	PGY-3	Risks of catecholaminergic crisis following steroid administration in patients with an adrenal mass: a literature review
108	Ali Bateman	MD Student	Work Limitations and Disability in patients with Systemic Vasculitis
109	Christine Beamish	PhD Student	Ontogeny of Ins+GLUT2- β-cell Progenitors in the Human and Mouse Pancreas
110	Erica Bernstein	PGY-2	The Effects of Implementation of Public Health Ontario's April 2013 Treatment Resistant Gonorrhea Guidelines
111	Vighnesh Bharath	PGY-2	Ocular crystal deposition leading to a diagnosis of multiple myeloma: a report of 2 cases and review of the literature
112	Vighnesh Bharath	PGY-2	Genetic polymorphisms of vein wall remodelling in the development of post-thrombotic syndrome, varicose veins, chronic venous insufficiency, and venous ulcers: a structured review
113	Michael Borrie	Faculty	Oral Hygiene in a Long Term Care Home: A Quality Improvement Project.

Poster #	Presenter	Program	Abstract Title
114	Amy Burke	MSc Student	Intervention with citrus flavonoids reverses existing metabolic disorders and modestly attenuates the progression of advanced atherosclerosis in high-fat fed Ldlr-/- mice
115	Dani Cadieux	MD Student	Time to move beyond a 'trial-and-error' approach to clinical documentation
116	Yang Cao	PGY-2	Evaluation of the Completeness of Follow-up of Echo Reports of Significant Pulmonary Hypertension in Medicine Inpatients: A Quality Assurance Study
117	David Casey	PGY-2	Genomics-guided warfarin therapy and the effect of variant CYP2C9, CYP4F2, and VKORC1 alleles on time in therapeutic INR range
118	Yuxin (Kelly) Chang	MSc Student	Dietary supplementation with olive oil to pregnant dams with type 1 diabetes reduces predisposition to type 2 diabetes in young male offspring.
119	Kuan-chin Jean Chen	PGY-3	Initial presentations and outcomes of necrotizing infections: a retrospective chart review.
120	Bainian Chen	Post-Doctoral Fellow	High fat diets induce cardiac dysfunction and fatty acids profile alterations in plasma and heart tissues of mice
121	Sanjiv Chhoker	MSc Student	Nobiletin reduces intestinal lipoprotein production in Ldlr-/- mice with diet-induced insulin resistance
122	Robert Coke	PGY-2	Proportional assist ventilation versus pressure support in patients weaning from ventilators
123	Alex Dong	PGY-1	Current management practices of acute lower abdominal/pelvic pain and vaginal bleeding in pregnant female patients using emergency department point-of-care ultrasound
124	Philip Dwek	PGY-2	Case series: 3 Cases of Suspected Podoconiosis in South Western Uganda.
125	Jaclyn Ernst	PGY-2	Playing Games with Order Set Design: The Application of 'Game Theory' to the Design Process

Poster #	Presenter	Program	Abstract Title
126	Sali Farhan	MSc Student	The application of whole-exome sequencing technology in identifying the genetic origins of unclassified familial disorders
127	Brian Feagan	Faculty	Early Combined Immunosuppression for the Management of Crohn's Disease: A Community–based Cluster Randomized Trial
128	Brian Feagan	Faculty	Responsiveness of Endoscopic Indices in the Evaluation of Ulcerative Colitis.
129	Rushi Gandhi	MD Student	Accelerated Receptor Shedding Inhibits Kidney Injury Molecule-1 (KIM-1)-mediated Efferocytosis
130	Elyse Gordon	MSc Student	Deficits in Specific Cognitive Domains Affects Gait Performance: Results from the Gait and Brain Study
131	Nihal Haque	PGY-2	Incidence and Outcomes of Post-operative Atrial Fibrillation and Supraventricular Arrhythmias - A Systematic Review and Meta-Analysis
132	Nihal Haque	PGY-2	Idiopathic hypereosinophilic syndrome presenting as generalized sweats and weight loss
133	Julie Huang	PGY-2	Decline in 6-min walk distance meters and percent predicted predicts clinical progression in pulmonary arterial hypertension
134	Ashlay Huitema	PGY-2	Diagnostic Accuracy of ST-Segment Elevation Myocardial Infarction by Various Healthcare Providers
135	Yasin Hussain	MD Student	The hypofunctional GPER P16L variant is associated with a gene-dosage related increase in plasma LDL cholesterol
136	Christine Ibrahim	PGY-2	Infrequent, low-dose regimens of rosuvastatin and their effect on the lipid profile
137	Christine Ibrahim	PGY-2	Acute on Chronic Adrenal Insufficiency—a Missed Diagnosis
138	Ola Ismail	PhD Student	KIM-1 Interacts with Gα12 and Suppresses Its Activity To Mediate Efferocytosis
139	Ibrahim Jelaidan	PGY-2	Aortic stenosis: Do we only consider the gradient in determining severity?

Poster #	Presenter	Program	Abstract Title
140	Salina Juma	PGY-2	Reasoning Tasks During Admission Case Review: A Validation Study
141	Salina Juma	PGY-2	Prevalence of Frailty in Hospitalized Patients on the Medicine Ward
142	Tayyab Khan	PGY-3	Underestimation of Fracture Risk and Osteoporosis Treatment Care Gap in Patients with Type 1 Diabetes Mellitus
143	Reena Khanna	Faculty	Agreement Among Central Readers in the Evaluation of Endoscopic Disease Activity in Crohn's Disease
144	Reena Khanna	Faculty	Patient Reported Outcome Measures Derived from the Crohn's Disease Activity Index: Correlation Between PRO2 and PRO3 Scores and CDAI-defined Clinical Thresholds
145	Lukasz Kwapisz	PGY-2	The Clinical Use of Fecal Calprotectin in the Diagnosis of Inflammatory Bowel Disease
146	Cecilia Kwok	MSc Student	Characterizing the impact of membrane vesicles produced by necroptotic tubular epithelial cells during transplantation
147	Joyce Lam	PGY-2	General Medicine Discharge Checklist Intervention To Improve Patient Discharge Safety Outcomes
148	Ngan Lam	MSc Student	Secular Trends in Cardiovascular Disease Among Kidney Transplant Recipients
149	Yves Landry	PGY-2	Patient-Prosthesis Mismatch in Valvular Heart Disease: An Evaluation of Echocardiographic Findings
150	Paul Lee	PGY-2	SNPs of GATM were not found to confer protection from statin myopathy.
151	Jason Lee	PGY-4	Bloody Sticky: A Meta-Analysis of the Risk of Venous Thromboembolism in Inflammatory Rheumatic Diseases
152	Joseph Lindsay	MSc Student	A web-based patient registry system for specialized ambulatory clinics
153	Michael Mitar	PGY-2	Procedural Correlates of Rotational Atherectomy: Analyzing the Need for Temporary Pacing

Poster #	Presenter	Program	Abstract Title
154	Michael Mitchell	PGY-2	Are Housestaff Identifying Malnourished Hospitalized Medicine Patients?
155	Sindu Mohan	PGY-2	Pulmonary Structure-function Abnormalities in Adult Congenital Emphysema
156	Manuel Montero-Odasso	Faculty	Dynapenia is associated with gait variability in community-dwelling older adults
157	Sahra Nathoo	MSc Student	Regulation of Innate Immune Response to Apoptotic and Necrotic Cells by Renal Cell Carcinoma Cells through Phagocytosis
158	Rashmi Nedadur	MD Student	Diabetes Care in Young Adults with Type 1 Diabetes after Transition to Adult Care
159	Rui Ni	PhD Student	Administration of mitochondrial targeted anti-oxidants reduces cardiac hypertrophy and improves function in diabetic mice
160	Robert Nikolov	Post-Doctoral Fellow	Examining relationships between motor impairment and cognitive sub-classification with structural & metabolic imaging in mild cognitively impaired (MCI) patients. Results from the Gait and Brain Study
161	Michael Peirce	PGY-2	Necrotizing Pneumonia: An observation of practice patterns and management changes over time.
162	Elena Qirjazi	PGY-3	Risk of Arrhythmia and Mortality among Patients Prescribed Selective Serotonin Reuptake Inhibitors (SSRIs)
163	Camilla Rozanski	PGY-2	Multi-dimensional indeces to stage idiopathic pulmonary fibrosis: a systematic review
164	Erica Rubin	PGY-2	Increasing the use of low molecular weight heparin for thromboprophylaxis: a quality improvement study
165	Joshua Samsoondar	MSc Student	The Flavonoids Naringenin and Nobiletin Stimulate the AMPKinase Pathway in Primary Mouse Hepatocytes
166	Matthew Sandre	MD Student	Psoriatic Nail Changes Are Associated With Clinical Outcomes in Psoriatic Arthritis
167	Nabha Shetty	PGY-3	Native Valve Left-Sided Infective Endocarditis in London, Ontario: A Review of the Patient Population and Outcomes

Poster #	Presenter	Program	Abstract Title
168	Nabha Shetty	PGY-3	Tricuspid Valve Infective Endocarditis in London, Ontario: A Review of the Outcomes of Surgical vs. Medical Management
169	Jenny Shu	PGY-2	A Case of Rapidly Destructive Inflammatory Arthritis of the Hip
170	Dou-Anne Siew	PGY-3	Blood pressure control in diabetic and non-diabetic renal transplant patients comparing ambulatory and office readings
171	Kulraj Singh	MD Student	A retrospective study of the predictors of clinical benefit from acetylsalicylic acid desensitization in patients with nasal polyposis and asthma
172	Victoria Smith	PGY-3	Corticosteroid use in the Treatment of Anaphylaxis in the Emergency Department
173	Swetha Sriram	PGY-2	A Systematic Review Of The Role Of Erythropoietin In The Pathophysiology Of Anemia In Elderly Patients
174	Vidya Sujana Kumar	PGY-3	Epidemiology of Infective Endocarditis in a Large Canadian Tertiary Care Centre: A Retrospective Database Study
175	Vidya Sujana Kumar	PGY-3	Infrarenal Abdominal Aortic Aneurysm Causing Common Bile Duct Obstruction
176	Shruti Tandon	PGY-5	Assessing Proposed Echo Aortic Root Measurement Guidelines: An LHSC Quality Assurance Study
177	John Teefy	MD Student	Non-invasive measurement of cardiac output in patients with aortic stenosis: Comparison of Electrical Cardiometry and Thermodilution method
178	Alison Weppler	PGY-2	The incidence of, and risk factors associated with, trastuzumab-induced cardiotoxicity in women with non-metastatic HER2-positive breast cancer
179	Jeff Yu	PGY-3	Frontline perceptions of low-value added inpatient practices on a clinical teaching unit
180	Dong Zheng	Post-Doctoral Fellow	MiR-195 represses Pim-1 expression and promotes endothelial cell apoptosis in sepsis

Poster #	Presenter	Program	Abstract Title
181	Tina Zhu	PGY-2	Effective feedback: a resident's perspective
182	Tina Zhu	PGY-2	Clinical presentation and outcome of patients with false--positive ST--segment elevation myocardial infarction
183	Ahmed Ziada	PGY-4	A Case Report of Warfarin and Carbamazepine Drug Interaction

Oral Presentations

Time	Presenter	Status	Abstract Title
2:00pm	Elie Skaff	PGY-2	Nutritional Management in Inflammatory Bowel Disease Inpatients.
2:15pm	Sarah Blissett	PGY-4	Do research findings on schema-based instruction translate to the classroom?
2:30pm	Christopher D'Sylva	PGY-2	Osteoporotic Fractures in Patients with Untreated Hyperprolactinemia vs. Those Taking Dopamine Agonists: A Systematic Review and Meta-Analysis.
2:45pm	Augene Seong	PGY-3	Comparison of cardiac enzyme testing in the emergency department before and after introduction high-sensitivity troponin testing.
3:00pm	**Refreshment Break**		
3:15pm	Ahmed Ziada	PGY-4	Management of very severe hypertriglyceridemia with and without plasma exchange.
3:30pm	Alexander Pavlosky	MSc Student	RIPK3-mediated necroptosis regulates cardiac allograft rejection.
3:45pm	Jenny Shu	PGY-2	The Impact of missing anti-citrullinated protein antibody (ACPA) serology on Outcomes in Early Rheumatoid Arthritis: Results from CATCH (Canadian Early Arthritis Cohort).
4:00pm	Arthur Lau	PhD Student	SPI-6 (Serine Protease Inhibitor-6) inhibits granzyme B mediated injury of renal tubular cells and promotes renal allograft survival.
4:15pm	Ngan Lam	MSc Student	Gout in Living Kidney Donors.

Abstract Index

Evaluating the effect of accidental dose reduced cyclophosphamide chemotherapy in lymphoma patients

Majed Alahmadi, Lazo-Langner A., Mangel J., Liu K., Dhalla A, Minuk L..

Background: An error at the drug compounder source resulted in accidental over-dilution of the chemotherapy drugs cyclophosphamide and gemcitabine utilized by several cancer centers in Ontario and New Brunswick between March 2012- March 2013. Estimated dilution was 10%. 1202 cancer patients were affected overall, including 177 hematology patients at LRCP. We evaluated the effect of cyclophosphamide under-dosing on patients with diffuse large B cell lymphoma (DLBCL), the largest subset of patients affected.
Methods: All DLBCL patients at LRCP who received diluted cyclophosphamide during at least one cycle of chemotherapy were reviewed. Data was collected on baseline characteristics, prognostic risk categories, response rates, disease progression and death.
Results: 77 patients (39M/37F) with a median age of 66 (31-91) received a total of 431 cycles of chemotherapy, 343(79%) of which contained diluted cyclophosphamide. 53 patients (68.8%) had advanced stage disease. IPI risk scores were good (6.5%), intermediate (35.1%) and poor (58.1%). Cyclophosphamide was given as part of combination chemotherapy. Regimens included R-CHOP (51), mini-R-CHOP (20), R-CVP (2), other (4). Overall response rate at completion of chemotherapy was 84% (38% complete, 46% partial). At a median follow up of 229 days, there were 7 progressions and 8 deaths.
Conclusion: Response rates in our affected cohort are similar to those reported in the literature. This suggests that a minor dose reduction in 1 drug in multi-agent chemotherapy may be inconsequential in terms of disease response and risk of relapse. This study is currently ongoing, including reviewing a matched cohort of historical controls, and longitudinal follow up of the affected cohort.

Ictal Asystole

Saleh Alghofaili, G. Farag, D. Massel.

Ictal asystole (IA) is a rare complication of epileptic seizures that frequently goes unnoticed by non-neurologists. Both acute and long-term management is multidisciplinary with cardiology involvement essential. Here we present the case of a 51-year-old man presenting with a sudden fall caused by ictal asystole triggered by previously undiagnosed cavernomas, a very rare cause of IA. This case illustrates the features of IA and highlights that controversy still exists with regards to the pathogenesis of IA and the use of pacing in the management of these patients.

Continuous Positive Airway Pressure (CPAP) compliance in patients with Obstructive Sleep Apnea Syndrome (OSAS)

Faris Alhejaili, Charles George.

Abstract: Despite the efficacy of CPAP in treating OSAS, adherence to therapy has been variable. Previous studies have shown variable compliance rate between 40-60 % of nights. No single factor consistently predicts compliance. In this study, we entertained the question of compliance and its relation to different CPAP providers. Methods: Patients who started on CPAP therapy between Jan-Dec 2011 and had a minimum of 3 months compliance data were included. Baseline characteristics includes age, body mass index (BMI), baseline apnea-hypopnea index (AHI) (PSG) and AHI on CPAP were analyzed. Compliance information includes total hours used, percentage of days used and average hours used per night. Results: 500 patients included (M 351, F 149; age 57±12, yrs; BMI 35 ± 10; AHI 49 ± 33). CPAP usage > 4 hours/night was seen in 86% of patients. The average usage/ night was 6 hours and 49 minutes. There was no significant difference in compliance between different CPAP providers or

CPAP machine models. Neither apnea severity nor gender influenced compliance. Conclusion: CPAP compliance was not affected by patient characteristics, CPAP providers or type of CPAP machine. However, we found that our patients have significantly higher compliance rate than previously reported in the literature. This observation may reflect our model of care which involves patient education throughout their clinic visit and the presence of a dedicated respiratory therapist involved in the out-patient follow-up care of patients with OSAS on CPAP therapy.

Changes in early repolarization pattern during exercise treadmill testing do not predict symptom status in patients with long QT syndrome

Basil Al-Sabeq, Zachary Laksman, Allan C. Skanes, Peter Leong-Sit, Jaimie Manlucu, Anthony S.L. Tang, Raymond Yee, Lorne J. Gula, Andrew D. Krahn, George J. Klein.

Background: Early repolarization (ER) is a common electrocardiographic pattern that has been associated with cardiac symptoms in patients with long QT syndrome (LQTS). Changes in ER with exercise or in recovery may help further risk stratify this population. Methods: We identified patients with genotype positive and genotype negative (Schwartz score ≥3.5) LQTS followed in the London inherited arrhythmia clinic who underwent ECG treadmill testing. Symptom status was recorded as any history of cardiac syncope or sudden cardiac death. ER was defined as QRS slurring/notching associated with ≥1mm J-point elevation in 2 or more contiguous leads. Change in ER pattern was recorded quantitatively on treadmill tests using the following time points; at rest, peak exercise, and 4 minutes into recovery. Results: 124 patients (mean age 42 ± 19.4, 69 female) were identified with 115 genotype positive and 9 genotype negative LQTS. 30 patients (26%) had a history of symptoms. Exercise stress ECGs were available in 117 (94%) patients. Fifty-four (46%) had ER at rest, 28 patients (52%) demonstrated persistent ER throughout the exercise test, and 26 patients (48%) demonstrated diminishing ER pattern with exercise. Of the 28 patients demonstrating persistent ER pattern, 9 patients (32%) had a history of symptoms, while of those patients demonstrating diminishing ER pattern (26 patients) only 6 (23%) had a history of symptoms. This difference did not meet statistical significance ($p = 0.457$). Only one patient developed ER in recovery. Conclusions: In patients with LQTS, ER changes in exercise stress testing were not predictive of symptom status.

Inhibition of TGFα-CCL2 signaling suppresses the progression of post-traumatic osteoarthritis

Tom Appleton, Usmani, SE, Pest, MA, Pitelka, V, Ulici, V, Welch, ID, Hill, TL, Mort, JS and Beier, F.

Objectives: Despite the high prevalence of osteoarthritis and its large societal impact, no disease-modifying treatments are available. Increased expression of Transforming Growth Factor alpha (TGFα) in osteoarthritic cartilage of rats and humans has been shown, but its functional role in disease progression in vivo is unknown. We aimed to demonstrate that TGFα promotes cartilage degradation using two animal models of post-traumatic osteoarthritis. Methods: Primary rat chondrocytes and articular cartilage explants were treated with TGFα and inhibitors of MEK1/2, p38, PI3K, ROCK and CCL2 signaling to investigate the effects of TGFα on cartilage degradation and CCL2 expression. An established rat model of post-traumatic osteoarthritis was used to administer pharmacologic inhibitors of TGFα and CCL2 signaling in vivo for up to 10 weeks. To confirm pharmacological data through a genetic approach, we induced post-traumatic osteoarthritis in Tgfa knockout and heterozygous mice via surgical destabilization of the medial meniscus (DMM). Results: TGFα and CCL2

(chemokine (C-C motif) ligand 2) were co-temporally upregulated in the rat model of post-traumatic osteoarthritis. TGFα induced expression of CCL2 in vitro. Pharmacological inhibition of the receptors for TGFα or CCL2 markedly slowed cartilage degradation in vivo. Tgfa knockout mice showed reduced cartilage degeneration 7 and 14 weeks after DMM surgery and reduced expression and activity of MMP13. Conclusions: We present a novel TGFα-CCL2 signaling axis that promotes cartilage degradation in post-traumatic osteoarthritis. Inhibition of the TGFα-CCL2 pathway by pharmacological or genetic means slows osteoarthritis progression in vivo, identifying a promising target for treatment in humans.

Comparison of Five Methods for Chromogranin A Measurement in Healthy Subjects and in Patients with Neuroendocrine Neoplasms

Alescia Linda Azzola, MD, PGY2 Internal Medicine, Kristin K Clemens, MD, FRCPC, LHSC - University Hospital, University of Western Ontario, London, ON, Canada, Hala H Mosli, MD, FRCP(c), ABIM, ABEM, Dept of Medicine, King AbdulAziz University, Jeddah, Saudi Arabia, Alan Dennis, PhD, FCACB, MBA, London Laboratory Services Group, London, ON, Canada, Walter Kocha, MD, FRCPC, London Regional Cancer Program, London Health Sciences Centre, London, ON, Canada and Stan Van Uum, MD, PhD, FRCPC, Endocrinology and Metabolism, Western University, London, ON, Canada.

Background: Accurate measurement and interpretation of Chromogranin A (CGA) is important for the care of neuroendocrine neoplasms(NEN). Information on reference ranges of CGA assays and effects of collection mediums is limited. This study aims to determine the reference range of CGA across assays, and assess its utility in NEN patients with active and inactive disease. Methods: This cross-sectional study collected serum and plasma samples in 61 healthy subjects and 116 NEN patients, 57 having active disease. All were analyzed in a single laboratory using CGA ELISA assays from CisBio, Alpco, Dako , RIA from CisBio and chemiluminescent method from Invitron. Reference ranges were determined with bootstrap non-parametric procedure and Passing-Bablok non-parametric regression. Results: Reference ranges were calculated for CGAs specified by assay and medium with considerable variation found between plasma and serum. Ranges varied significantly from those in package inserts. CGAs were significantly higher in NENs compared with healthy controls throughout assays($P<0.001$), being even higher with active disease($P<0.05$). ROC curve analysis revealed no strong cut off points for active disease(Sensitivity 41-68%, specificity 50-72%). DAKO was superior when differentiating healthy subjects vs. NEN and disease states(AUC 0.823, 0.641). Conclusions: CGA reference ranges in healthy subjects differ from package references and must be established separately for serum and plasma. This information is critical for correct interpretation of CGA results. High CGAs are characteristic of NENs, varying with level of disease activity. ROC curve analysis suggests its utility as a prognostic marker rather than a screening tool.

Risks of catecholaminergic crisis following steroid administration in patients with an adrenal mass: a literature review

Catherine Barrett, MD, Stan Van Uum MD, PhD, FRCPC and Jacques W.M. Lenders MD, PhD, FRCP.

Background: Administration of exogenous corticosteroids for diagnostic or therapeutic purposes has been reported to carry an increased risk of a catecholaminergic crisis (CC) in patients harbouring a Pheochromocytoma. Objective: To assess the characteristics of

patients with catecholamine-producing tumors that were reported to have suffered from CC after administration of a steroid, CRH or cosyntropin. Methods: Pubmed was searched using combinations of the following terms: pheochromocytoma, adrenal incidentaloma, dexamethasone suppression test (DST), glucocorticoid, hypertensive crisis, CRH and cosyntropin. From all published reports (1962-2013) we retrieved information on medical history, presenting symptoms, steroid administration, location and size of adrenal mass, biochemical phenotype and outcome. Results: We identified 22 cases. Incidentalomas: Three patients with an incidentaloma were reported to suffer from a CC after a high dose DST (fatal in one patient). Adrenal diameter was > 4 cm in all and density was > 28 HU in two. Biochemical tests were falsely normal in 2 patients. There are no reports of a CC in incidentaloma patients undergoing a low dose DST (1 mg). Steroid treatment: In 15 patients, therapeutic steroid doses were administered orally, parenterally, intramuscularly or intra-articular for a variety of clinical indications. Three patients died. There were pre-existent symptoms compatible with pheochromocytoma in 5 patients. CRH and cosyntropin: CC occurred in 1 patient following CRH administration and in 3 patients following cosyntropin. All cases were fatal. Conclusions: In patients with a large adrenal incidentaloma (>4 cm), biochemical testing for pheochromocytoma should be carried out before doing a high dose DST.

Work Limitations and Disability in patients with Systemic Vasculitis

Ali Bateman, Sherry Rohekar, Lillian Barra.

Objectives: Systemic Vasculitis (SV) commonly causes long-term organ damage, including chronic dyspnea, kidney impairment, pain, vision/hearing loss, cognitive impairment, nerve and joint damage, which can impact function. The objective of this study is to assess work limitations and disability in SV. Methods: Ongoing single-centre prospective cohort of SV. Inclusion: diagnosis of SV by a Rheumatologist; age >18yrs and <65yrs. Work-disabled was defined as not working, early retirement or reduced hours at work due to SV. Participants completed the Work Limitations Questionnaire (WLQ). Other work-related measures were self-reported via questionnaire. The Birmingham Vasculitis Scale (BVAS), Vasculitis Damage Index (VDI) and Health Assessment Questionnaire (HAQ) were assessed at the time WLQ was completed. Pain was measured using a visual analogue scale. Results: 47 subjects met inclusion criteria: 28% were work disabled at enrollment. 60% were eligible to complete WLQ: mean age 50yrs (18-62yrs), 70% female, disease duration 4yrs (0.4-18yrs), mean BVAS was 2.44±1.47, VDI was 2.96±2.03 and pain score was 3.11±2.93. After being diagnosed with SV, 46% of subjects reported income decline due to SV (mean decline of 22%). The WLQ score significantly correlated with HAQ and pain scores (Pearson coefficients 0.34 and 0.49, respectively). Loss of work productivity in SV determined by the WLQ score was 17%, which is higher than in Rheumatoid Arthritis patients (6%) and Spondyloarthritis patients (8%) from the same centre. Conclusions: Work disability and loss of work productivity are frequent in patients with systemic vasculitis and are associated with pain and functional impairment

Ontogeny of Ins+GLUT2- β-cell Progenitors in the Human and Mouse Pancreas

Christine Beamish, Brenda J Strutt, Sofia Mehta, Yuzhen Tong, Subrata Chakrabarti, Manami Hara, Michael Millis, Piotr Witkowski, and David J Hill.

The presence and location of pancreatic β-cell progenitors that could be exploited for the reversal of diabetes is controversial. A rare subpopulation of Insulin+Glucose transporter-2-(Ins+GLUT2-) cells has been identified as multipotent pancreatic progenitors in both adult

mouse and human islets. We have shown a significantly higher population of Ins+GLUT2- cells in extra-islet β-cell aggregates (BCA, ≤5 β-cells) of neonatal mouse pancreas compared to islets. Here, we sought to identify the presence of these progenitor cells throughout life in both mouse and human, and how their abundance changes with age. Mouse pancreata were assessed between postnatal P7 and 18months, and human pancreas between 22weeks gestation and >80years. Sections were analyzed by immunohistochemistry for cells expressing insulin and GLUT2. In mice, the number of Ins+GLUT2- cells decreased after P7, whilst the proportion of BCA decreased during the first month of life. A significant increase in Ins+GLUT2- cells occurred in BCA but not islets between P9 and P21 (22.5±2.1 vs 9.9±1.3%, P21 vs P28), but decreased thereafter. Human Ins+GLUT2- cells showed a similar distribution and ontogeny, being more abundant in BCA than islets at all ages, and decreasing with age (Ins+GLUT2- cells 5.0±1.0 vs 2.5±0.1%, <1 yr vs adult). The proportion of BCA was higher in human pancreas than in mouse at all ages examined. These data suggest that Ins+GLUT2- cells are primarily located within BCA throughout life in both species, and may represent a source of β-cell plasticity.

The Effects of Implementation of Public Health Ontario's April 2013 Treatment Resistant Gonorrhea Guidelines

Erica Bernstein, Doug Sider, Michael Whelan, Brenda Lee, Vanessa Allen.

Introduction: The Public Health Agency of Canada (PHAC) guidelines do not reflect global and local resistance patterns of gonorrhea (GC) as described by the World Health Organization (WHO) and a recent Canadian study. In an effort to address this discrepancy Public Health Ontario (PHO) released new guidelines to reflect current resistance patterns in April 2013 that differ from current PHAC guidelines. This study addresses the impact that the PHO guidelines made. Methods: All reported cases of GC from Integrated Public Health Information System (IPHIS) data were identified over a 3 month period, prior to and then after release of PHO April, 2013 GC guidelines. Information on treatment, lab confirmation technique, type of specimen used, health unit and gender were extracted from the database using non-probability purposeful sampling and trends were identified before and after dissemination of PHO guidelines. Results: Ceftriaxone use increased by 84%. Cefixime use decreased by 50%. Laboratory testing by culture increased by 3%, testing by NAAT decreased by 2% and testing by microscopy increased by 18%. Specimens collected of discharge decreased by 1% and by urine increased by 4%. Conclusion: Ceftriaxone use increased after the implementation of the PHO guidelines and Cefixime use decreased. The only change in lab techniques or culture specimens observed was an increase in microscopy. PHO guidelines were successfully implemented for treatment.

Ocular crystal deposition leading to a diagnosis of multiple myeloma: a report of 2 cases and review of the literature

Vighnesh Bharath, Cyrus C. Hsia, Leonard Minuk, Rookaya Mather, Bruce D. Nichols.

Corneal crystal deposition due to multiple myeloma is a rare ocular manifestation caused by elevated immunoglobulin levels in the eye. It presents with decreased visual acuity and crystalline deposits in the corneal epithelium or stroma. We describe here two cases of myeloma crystal deposition in the eye, one of which involved crystal deposition in a Laser-Assisted in situ Keratomileusis (LASIK) interface, and one that demonstrated rapid and complete response of corneal crystals with induction chemotherapy (to our knowledge, the first such cases in the literature). We also present a brief review of the literature. A 50-year-old woman presented with decreased vision and crystal deposition in her LASIK

interface. This led to a diagnosis of IgG multiple myeloma and treatment with melphalan and prednisone improved her vision to 20/20, but did not completely resolve the corneal crystals. Similarly, a 53-year-old woman presented with foggy vision and dense ocular crystalline deposits. Work-up revealed smoldering myeloma, and the patient was managed conservatively until she developed end-organ damage including anemia and lytic bone lesions. Systemic therapy was initiated, and the crystal deposits resolved completely. With these cases, we hope that clinicians will recognize these unusual ocular manifestations, and consider myeloma in the differential diagnosis. Further research is warranted, but in light of the observed response to therapy and the significant patient burden associated with vision loss, it may be prudent to consider systemic therapy for myeloma-associated ocular disease (though this is not the current convention), potentially with bortezomib.

Genetic polymorphisms of vein wall remodelling in the development of post-thrombotic syndrome, varicose veins, chronic venous insufficiency, and venous ulcers: a structured review

Vighnesh Bharath, Susan R Kahn, Alejandro Lazo-Langner.

Post-thrombotic syndrome is a significant chronic complication of deep venous thrombosis that develops in up to 50% of patients despite appropriate anticoagulation. It manifests as chronic venous disease including venous insufficiency, varicose veins, lipodermatosclerosis, and ultimately venous ulceration. Some evidence suggests a genetic predisposition to chronic venous disease and perhaps post-thrombotic syndrome due to gene polymorphisms associated mainly with vein wall remodelling. We conducted a structured literature review to identify and characterize these culprit genes and polymorphisms. Some important candidate genes/proteins include: the matrix metalloproteinases (involved in extracellular matrix degradation), vascular endothelial growth factors (involved in angiogenesis and vessel wall integrity), FOXC2 (associated with vascular development), and various types of collagen (related to vein wall strength). In this review, we present the current evidence around these and other gene polymorphisms as contributors to chronic venous disease, and attempt to uncover a potential link to post-thrombotic syndrome. Additional studies are required to examine these genetic associations further, especially given the burden of venous disease worldwide and the ongoing potential for novel therapeutic targets.

Do research findings on schema-based instruction translate to the classroom?

Sarah Blissett, Mark Goldszmidt, Bryan Dias, Matthew Sibbald.

Background: A schema is a diagnostic algorithm that separates similar diagnoses through clinically relevant, discriminating features. Schema-based instruction is associated with improved performance and reduced cognitive load in research conditions. Classroom settings may have increased cognitive load because of increased distractions, larger group sizes, and decreased internal motivation, which may limit generalization of education research studies. It is unclear whether schema-based instruction in a large classroom setting will maintain its beneficial effects on cognitive load optimization and performance. Methods: One hundred and one first year medical students at Western University were randomized to receive a traditional lecture (n=48) or a schema-based lecture (n=53) using cardiac auscultation as a model. Students completed 4 written questions to test performance and a cognitive load assessment at the end of the lecture. Results: Schema-based instruction was associated with increased performance on written questions (64 vs 44%, $p<0.001$) and reduced intrinsic cognitive load (mean difference=15%, $p<0.001$). There was no significant difference in reported

extraneous (p=0.36) or germane (p=0.42) cognitive load. Discussion: The reduced intrinsic cognitive load can explain the observed increase in performance. Similar reported extraneous load assessments were expected, as both experimental conditions would be subject to the same sources of extraneous load (e.g. distractions from internet or classmates). The reduced intrinsic load, similar extraneous load and improved performance replicate the findings of schema-based instruction in a research setting. Conclusions: In this study, the benefits of schema-based instruction were maintained in a classroom environment.

Oral Hygiene in a Long Term Care Home: A Quality Improvement Project.

Jackie Borrie , RDH, Jane Mastrandrea, RN, Sue Sweeney, RN, Sharon Beck, RN, Michael Borrie, MB,ChB.

RELEVANCE: Older adults are retaining their teeth. However comorbidities, poor oral hygiene attitudes and practices in Long Term Care (LTC) increase the risk of oral disease and aspiration pneumonia. Oral care was identified as an issue in the family survey at McCormick Home and the senior management requested assistance from the Regional Geriatric Program. METHODOLOGY: A quality improvement pilot project was conceived and included the following steps; The RNAO gap analysis on oral care was completed. A knowledge, attitudes and behaviour survey was completed by the Personal Support Workers (PSWs). One of the 5 units receptive to the project was selected and the lead RN provided with extra time. PSW champions on each shift viewed the 12 youtube videos on oral hygiene/care. A new daily oral care chart was placed in each resident's bathroom. Baseline and 3 month oral assessments were completed by the project Registered Dental hygienist (RDH). RESULTS: Participants 30, dentate 17, full dentures 9, partial 4. Overall outcomes: Improved 12; Unchanged 8; worsened 3; incomplete 1; Limited access 2; deceased 4 (all dentate). Unit Changes in attitudes, practice and behaviour: PSWs recognize the importance of good oral care; PSWs are more confident in delivering oral care and residents are less resistive to oral care. Changes in Policy: Families are made aware of available contract dental services for the home; Home oral care policy rewritten; Rollout of new policy, procedures and education to the other 4 units.

Intervention with citrus flavonoids reverses existing metabolic disorders and modestly attenuates the progression of advanced atherosclerosis in high-fat fed Ldlr-/- mice

Amy C. Burke, Brian G. Sutherland, Cynthia G. Sawyez, Dawn E. Telford, Joseph Umoh, Maria Drangova and Murray W. Huff.

Previous studies demonstrated that addition of the citrus flavonoids naringenin or nobiletin to a high-fat diet prevented the development of many disorders linked to the metabolic syndrome. In the present study, we assessed the ability of intervention with naringenin or nobiletin to reverse pre-established obesity, insulin resistance, hepatic steatosis, dyslipidemia and attenuate atherogenesis. Ldlr-/- mice were fed chow or a high-fat, cholesterol-containing (HFHC) diet for 12 weeks. For an additional 12 weeks, the HFHC-fed mice: (1) continued on the HFHC diet or were transferred to (2) HFHC + 3% naringenin, or (3) HFHC + 0.3% nobiletin. Following rapid weight gain during HFHC-induction, intervention with naringenin or nobiletin stimulated weight loss, while maintaining caloric intake. Micro-CT imaging revealed flavonoid intervention reversed both subcutaneous and visceral adipose tissue accumulation by 40-60%. At 12 weeks, the HFHC-fed mice were hyperinsulinemic (6-fold). Flavonoid intervention normalized plasma insulin and improved insulin sensitivity. The HFHC diet increased cholesterol within VLDL (10-fold) and LDL (6-fold), which was reduced (~50%) by naringenin or nobiletin intervention. HFHC-

induction significantly increased hepatic steatosis. Flavonoid intervention reduced hepatic cholesterol (>50%) and triglyceride (~20%) via increased Pgc1a and Cpt1a expression and reduced Srebp1c expression. HFHC-induction increased atherosclerotic lesion area (13-fold), which was further increased (2.5-fold) at 24 weeks. Flavonoid intervention modestly retarded lesion size progression (16-20%) and reduced lesional necrotic area (~25%), suggesting improved lesion morphology. These studies demonstrate in mice that intervention with naringenin or nobiletin reverses existing obesity, dyslipidemia, hepatic steatosis and insulin resistance, and modestly attenuates the progression of advanced atherosclerosis.

Time to move beyond a 'trial-and-error' approach to clinical documentation

Dani Cadieux, Natasha Aziz, Lisa Faden, Mark Goldszmidt.

Background: As an integral member of the healthcare team, junior trainees (junior residents and medical students) play an important role in follow-up care on the Internal medicine inpatient clinical teaching unit (CTU). While the role of documentation in this setting has been shown to be pivotal in supporting patient care, little is known about how trainees approach this task. Methods: Constructivist grounded theory was used to guide the collection and analysis of data regarding junior trainee documentation practices. We observed 17 junior trainees on the CTU at an academic center while they provided and documented follow-up care. Data sources included field notes, field interviews, and de-identified patient charts. Results: Trainees described learning to document as a trial-and-error practice, lacking guidance. Review of their notes and observation of their practices showed wide variation which, at the extremes, could be grouped into two categories: 1) a strategic approach where they used their existing knowledge of the patient and their sense of documentation purpose to guide information gathering and documentation format, and 2) an emergent approach in which they performed a generic encounter, gathered data as questions arose during documentation and documented with minimal anticipation of readership. The data also revealed a range of strategies that trainees used to handle uncertainty and to address the challenge of being both learner and care provider. Conclusions: Given the importance of documentation in supporting collective care of patients, it is imperative that new strategies be developed for training and entrusting junior trainees with this essential role.

Evaluation of the Completeness of Follow-up of Echo Reports of Significant Pulmonary Hypertension in Medicine Inpatients: A Quality Assurance Study

Dr. Yang Cao, Dr. Sanjay Mehta, Dr. Seychelle Yohanna.

Background: Pulmonary hypertension (PH) is a rare but serious disease that is often difficult to diagnose. Chronic thromboembolic pulmonary hypertension (CTEPH) is an important cause of PH and is potentially curable. Echocardiography is a preliminary test that can suggest a diagnosis of PH and this study will review the echocardiograms of patients admitted to Medicine with findings suggestive of PH and determine further investigations and follow-ups undertaken. Methods: All echo reports done for LHSC medicine and medicine subspecialty inpatients from January 1, 2013 to December 31, 2013 were included. In patients with echocardiographic evidence of PH (high RVSP, RV hypertrophy, RV failure), demographic and clinical data from the patient's chart was collected, including age, race, gender, reason for admission, reason for echo, medications, underlying medical conditions, and risk factors for CTEPH. These charts were analyzed to determine whether residents/staff are appropriately recognizing the importance of new diagnosis PH, and investigating for the possibility of CTEPH using further imaging (V/Q

scan, spiral CT angiogram) and/or referral to PH specialists. In patients without adequate investigation or follow-up, their family doctor will be contacted with a suggestion for further evaluation. Results: Results to follow. Discussion: PH is a disease with significant morbidity and mortality, and CTEPH is a potentially curable cause of PH. It would be beneficial to improve awareness of the disease, and decrease the amount of time to diagnosis and management. Awareness and further evaluation of PH on echo is an important step in achieving this.

Genomics-guided warfarin therapy and the effect of variant CYP2C9, CYP4F2, and VKORC1 alleles on time in therapeutic INR range

Dr. David Casey, Dr George Dresser Dr. Uta Schwartz.

INTRODUCTION: Warfarin is a commonly used anticoagulant but dose response is affected by well-characterized genetic variations in hepatic metabolic enzymes cytochrome P450 (CYP) 2C9 and 4F2, and the pharmacological target of warfarin, vitamin K epoxide reductase complex 1 (VKORC1). A recent Meta-analysis showing variants of VKORC1 and CYP 2C9 require lower warfarin dose and variant 4F2 alleles confer significantly higher dose requirements (1) contrasts a previous study showing significantly decreased bleeding events with variant CYP4F2 alleles but no change with variant CYP2C9 or VKORC1 alleles (2). To our knowledge, this association between allele variants and bleeding events has never been studied in genomics-guided warfarin therapy. We sought to determine local trends in time in therapeutic INR range 2-3 (TTR) in patients receiving genomics-guided therapy. METHODS: Using the PG-WF database, this retrospective chart review was performed in stable outpatients with previously determined CYP2C9, CYP4F2, and VKORC1 genotype. TTR was assessed using Rosendaal linear interpolation methods. RESULTS: We identified 56 patients with complete genomic data and available TTR. We found no association of variant CYP2C9, VKORC1, or CYP4F2 alleles and impairment in TTR. Analyses of these variant alleles for other factors affecting TTR, including drug burden and therapeutic turbulence, will be presented. DISCUSSION: The lack of association with variant CYP2C9, VKORC1, CYP4F2 alleles and impairment in TTR suggests that genomics-guided warfarin therapy negates the detrimental impact of variant alleles. Our preliminary data suggests an inverse trend versus what is previously reported and supports our hypothesis that genomics-guided warfarin therapy favours variant alleles.

Dietary supplementation with olive oil to pregnant dams with type 1 diabetes reduces predisposition to type 2 diabetes in young male offspring.

Yuxin Chang, Alicia Jawerbaum and Edith Arany.

Maternal diabetes impairs fetal and placental development increasing the risks of miscarriage and malformations and the predisposition to metabolic and cardiovascular disorders later in life. Previously we showed that dietary supplementation with 6% olive oil (enriched with 34% oleic acid) given to diabetic mothers increased the numbers of term births and decreased neonatal malformations and stillbirth by reducing intrauterine oxidative stress. Although these benefits were seen at birth, it is still unclear how this may affect the overall predisposition to disease later in life. Our aim was to elucidate the effect of this supplementation on fetal and neonatal pancreatic development and its impacts in early adulthood. Diabetes was induced by STZ in females early in life. Control and diabetic mothers were separated and fed with rat chow or with the addition of olive oil. Body and pancreatic weights were recorded as well as fasting glycemia. Dual immunohistochemistry was performed to detect α and β cells in islets at

day 2 and 4 months postnatal. Morphometric analysis was carried out to study islet area, its distribution by size and density. β-cells mass, α and β area and ratio was also analyzed. Our preliminary results showed that olive oil supplementation had a restorative effect on islet and beta cell area at 4 months compared to the offspring of diabetic mother fed with the standard diet as well as fasting glycaemia. These findings addressed the importance of the quality of the diet in mothers with type 1 diabetes prevent disease on their offspring.

Initial presentations and outcomes of necrotizing infections: a retrospective chart review.

Kuan-Chin Chen, Klingel M, McLeod SL, Ng V.

Objective: To determine the clinical features at presentation of patients diagnosed with necrotizing fasciitis and the in-hospital outcomes. Methods: Retrospective review of adult patients with a discharge diagnosis of necrotizing fasciitis at LHSC (annual census 125,000) over a 5-year period (April 2008 to March 2013). Results: 60 patients were included. Mean (SD) age was 53.7 (17.8) years, 60% were male and the median (IQR) hospital length of stay was 17.1 (7.8, 33.5) days. Common co-morbidities at presentation included immunocompromise (58.3%), diabetes mellitus (41.7%), vascular disease(45.0%) and obesity (24.6%). Initial presentations included swelling (91.7%), erythema (86.7%), bullae (28.3%), petechiae (8.3%), and bruising (45.0%). 59 (98.3%) patients received antibiotics, of which 69.5% were ordered by the ED. Median (IQR) time to antibiotic administration was 3.5 hours (1.9, 7.5). 50 (83.3%) underwent surgery, with a median (IQR) time from initial presentation to surgery of 15.5 hours (7.8, 74.9). In-hospital mortality amongst those who had surgical intervention was 14.0%, compared to in-hospital mortality of 60.0% for those who did not receive surgical intervention (Δ 46%, 95% CI 14.8 – 70.2%). Conclusions: This study suggests that diabetes mellitus, immunocompromise, and obesity are common co-morbidities of necrotizing fasciitis, and that survival is higher amongst patients who receive surgical treatment. Patients presenting to the ED meeting this clinical picture warrant a high degree of suspicion.

High fat diets induce cardiac dysfunction and fatty acids profile alterations in plasma and heart tissues of mice

Bainian Chen, Dong Zheng, Rui Ni, Mark Bernards, Tianqing Peng.

Studies have revealed that diets rich in saturated fatty acids are related to metabolic disorders and cardiovascular diseases. The present study aimed to investigate the effects of high fat diets on heart function and fatty acids profile in mice. Adult mice were fed with control high fat diet (CHD), high palm oil diet (HPD), high beef tallow diet (HBD), high cocoa butter diet (HCD) or high milk fat diet (HMD) for 6 months. There were no changes of body weight, heart weight and blood glucose in HPD, HBD and HCD groups compared with CHD. However, HMD increased the body weight of mice. No difference of blood pressure was observed in all of the high fat diets groups. HPD decreased insulin sensitivity in mice. A trend of insulin resistance was also observed in both HBD and HCD groups. Echocardiography demonstrated systolic and diastolic dysfunction in all of fat diets groups compared with CHD. The content of palmitic acid in plasma (PL) and phospholipids fraction of heart tissues (PH) of HPD group increased dramatically compared with CHD group. All of the high fat diets increased the levels of stearic acid and arachidonic acid in PH. Additionally, both HPD and HCD significantly augmented the concentration of total saturated fatty acids in PH. In summary, this study for the first time shows that HPD, HBD, HCD and HMD induce myocardial dysfunction. Differential changes of

fatty acid profile are observed in these high fat diets groups.

obiletin reduces intestinal lipoprotein production in Ldlr-/- mice with diet-induced insulin resistance

Sanjiv S. Chhoker, Brian G. Sutherland, Dawn E. Telford and Murray W. Huff.

Insulin resistant subjects display excessive postprandial lipemia (PPL), defined by overproduction of intestinal triglyceride (TG)-rich, apoB48-containing chylomicrons (CM) which contribute significantly to atherogenesis. However, the underlying mechanisms remain poorly understood. In mice, the flavonoid nobiletin prevents diet-induced obesity, dyslipidemia, insulin resistance, and VLDL overproduction. In the present study, we sought to characterize the aberrant PPL response in mice with diet-induced insulin resistance and determine if treatment with nobiletin can correct this abnormal response. Ldlr-/- mice were fed a high-fat, cholesterol-containing (HFHC) diet (42% fat, 0.2% cholesterol), a HFHC diet plus 0.3% w/w nobiletin or chow. Compared to chow, HFHC-fed mice displayed elevated TG (3-fold) within intestinal tissue following a 6 hour fast, which was completely normalized by nobiletin. Fasting-refeeding studies revealed impaired FoxO1 phosphorylation, increased mTOR phosphorylation and elevated Srebp1c mRNA in the jejunum of HFHC-fed mice, indicating intestinal insulin resistance. These parameters were normalized by nobiletin. Intestinal CM production was determined by injection of mice with poloxamer-407 to inhibit plasma TG-rich lipoprotein lipolysis followed by a gavage containing olive oil and 3H-triolein. Although plasma TG was higher at baseline in HFHC-fed mice, no difference in secretion rates of TG mass or TG radioactivity was observed compared to nobiletin-treated or chow-fed mice. However, secretion of apoB48 was elevated by 20% in HFHC-fed mice, whereas nobiletin decreased apoB48 secretion to levels observed in chow-fed mice. These results indicate that nobiletin prevents intestinal TG accumulation and apoB48 overproduction induced by a HFHC diet, in part, through correction of intestinal insulin resistance.

Proportional assist ventilation versus pressure support in patients weaning from ventilators

Robert Coke, Brooke Read, Mohammad Nikoo, Tracey C. Bentall, Delores Tack, Fran Priestap, Karen J. Bosma.

For patients undergoing mechanical ventilation (MV), asynchrony may occur if the ventilator-delivered breaths are not timed with the patient's spontaneous respiratory efforts. The Asynchrony Index (AI) denotes the percentage of breaths which are asynchronous. , An AI>10 considered high and is associated with prolonged duration of MV. Proportional Assist Ventilation, (PAV+), is a spontaneous breathing mode that provides assistance to the patient in proportion to the patient's effort. This study examined whether patients experience less asynchrony using a PAV+ weaning algorithm compared to conventional Pressure Support Ventilation (PSV) weaning algorithm. METHODS: Mechanically ventilated adults meeting eligibility criteria were assigned to either a PAV+ (n=34) or PSV (n=30) weaning algorithm. Using ICU-lab (KleisTek, Italy), patients had their ventilator tracings of flow and airway opening pressure recorded and analyzed at baseline (pre-intervention), high, and low ventilator settings. RESULTS: At baseline, 14 patients (7 in each group) had AI>10. No patient had an AI>10 on high or low ventilator settings on PAV+, whereas 1 patient on PSV had AI>10 on high settings and 1at low settings. On both high and low wean settings, there was no significant difference in AI between PAV+ and PSV groups, with respective medians of 1.34 (0, 9.47), and 1.66 (0.212, 15.4) on PAV+, vs. 1.63 (0, 24) and 0.805 (0. 10.8) on PSV (p=NS) INTERPRETATION: Both the PAV+ and PSV weaning protocols showed

comparable reductions in ventilator asynchrony from baseline. Either protocol could be used to decrease AI compared to non-protocolized weaning.

Current management practices of acute lower abdominal/pelvic pain and vaginal bleeding in pregnant female patients using emergency department point-of-care ultrasound

Dong, A.X., Roebotham, R., McLeod, S.L., Thompson, D..

Pregnant women presenting to the emergency department (ED) with abdominal/pelvic pain are at risk for conditions where delayed diagnosis may lead to significant morbidity. Recently, point-of-care ultrasound (POCUS) has played an increasing role in evaluating abdominal/pelvic pain in women during their 1st trimester in the ED. Although the literature illustrates the benefits of POCUS, many patients have negative/indeterminate studies. The literature describing the management of these patients is limited, and strategies likely differ between physicians. This study will describe the current use of POCUS in 1st trimester patients presenting to the ED with abdominal/pelvic pain, vaginal bleeding, and/or syncope/pre-syncope. Through a retrospective study, we will identify practice patterns and trends in the use of POCUS in the ED over one year. A random selection of charts will be chosen based on chief complaint. Patients greater than 20 weeks gestation will be excluded. Charts will be cross-matched with Q-path (an electronic database of POCUS in the ED), to determine whether POCUS was performed, the modality, and the physician interpretation. Demographics, past medical history, vital signs, physical exam, management plan (consultative imaging, referral to gynecology or the early-pregnancy assessment unit, follow up with family physician), diagnosis, and treatment will be recorded. Results will be presented at RRD 2015. This study will help clarify the optimal process to investigate and manage adult pregnant patients in their 1st trimester presenting to the ED. This process could be further used as a platform to intervene and educate physicians, improve patient care, and optimize resource use.

Osteoporotic Fractures in Patients with Untreated Hyperprolactinemia vs. Those Taking Dopamine Agonists: A Systematic Review and Meta-Analysis

Christopher D'Sylva MD, Tayyab Khan MD, MSc, Stan Van Uum MD, PhD, Lisa-Ann Fraser MD, MSc.

Hyperprolactinemia has been associated with increased bone resorption and low bone mineral density. Historically attributed to prolactin-induced hypogonadism, recent studies have identified increased fracture rates independent of gonadal function. To further assess the impact of hyperprolactinemia on bone health, we performed a systematic review to identify studies assessing fracture risk in patients with untreated hyperprolactinemia compared to those treated with dopamine agonists, with fracture as an outcome. Two authors independently performed title and abstract searches, full-text searches, data abstraction, and quality assessment using the Newcastle-Ottawa Scale. A summary odds ratio (OR) was calculated using a random effects model. A total of 197 articles were identified, with 2 studies meeting full inclusion criteria. Both were high quality cross-sectional studies examining cabergoline use (or non-use) in patients with prolactin-secreting adenomas, with vertebral fractures as the primary outcome. For women, vertebral fractures were identified in 46% of untreated patients, vs. 20% of patients on cabergoline (OR: 0.29, 95% CI: 0.1-0.78). For men, the results were 67% in untreated, vs. 26% in treated patients (OR: 0.18, 95% CI: 0.03-0.94), with no difference between eugonadal and hypogonadal men (p = 0.8). This gave a summary measure odds ratio of 0.25 (CI: 0.11-0.59), I2 = 0%. In the limited studies available,

fracture prevalence was increased in patients with untreated hyperprolactinemia compared to those on treatment, independent of gonadal function. Further studies need to clarify if post-menopausal women, or high-risk men, with no other indication for a dopamine agonist, should receive treatment to decrease fracture risk.

Case series: 3 Cases of Suspected Podoconiosis in South Western Uganda.

Philip Dwek, Meghan Wafer, Ling Yuan Kong, Romina Pace, Bill Cherniak, Micahel Silverman.

INTRODUCTION: Podoconiosis, or non-filarial elephantiasis, is a tropical disease resulting in debilitating bilateral asymmetrical lymphedema of the feet and legs due to irritant soil in red volcanic clay. It is estimated that the prevalence of podoconiosis in Ethiopia is 3.4% and up to 7.4% in central Ethiopia. To date, it has been observed in Eastern Uganda, Mt. Elgon area, but there have been no reported cases in south western Uganda or any other parts of Uganda. This paper describes 3 cases of suspected podoconiosis in south western Uganda. METHODS: Health camps were set up in south western Uganda in 2013 and 2014, individuals with suspected podoconiosis had their blood drawn to assess for eosinophilia and to look for microfilariae to rule out filariasis. Individuals were also interviewed in regards to occupation, shoe wearing, and stigma associated with lymphedma. RESULTS: A total of 3 suspected cases were found, two were male and 1 female. All were farmers and had limited shoe use. Two out of three of the cases had felt stigmatized in their community. CONCLUSION: Podoconiosis is a neglected tropical disease with high potential for elimination as it is easily preventable if shoes are consistently worn. We report 3 suspected cases, more likely exist. Unfortunately, shoe wearing is not always affordable in Uganda, we hope that with more awareness, funds can be put towards supplying at risk individuals with proper foot ware as the economic burden of such a debilitating disease has bee shown to be great.

Playing Games with Order Set Design: The Application of 'Game Theory' to the Design Process

Jaclyn Ernst, Shanil Narayan.

BACKGROUND Narrowing the gap between available medical knowledge and clinical practice remains an ongoing issue in healthcare. Order sets have emerged to facilitate the use of best practice guidelines. However, the creation and implementation of order sets poses many challenges. Many of these challenges relate to our current economic climate, which is defined by limited fiscal and human resources. We introduce an order set process built on the economic principles of game theory. Game theory is a theoretical framework for analyzing how individuals work together. It is used here to guide the structure of our proposed order set process by elucidating provider relationships needed to maximize patient and physician outcomes in a hospital setting with limited resources. METHODS Through literature review and discussion with the Huron Perth Health Care Alliance Order Set Committee, potential bottlenecks in the Order Set Process were identified. Using a framework outlined in “The Art of Designing Markets” by Alvin Roth, 2012 Nobel Prize winner in Economics, we organized and designed the critical elements to workflow in an order set process. CONCLUSIONS A focus on the creation of novel therapies without appreciation for the translation of this knowledge into practice, limits their potential. By applying the elements of game theory to the order set design process, we have proposed a structured approach to translating best practice guidelines into clinical practice. We identified individuals’ patterns of behaviour as they worked together in the order set process, and structured their relationships to foster synergy and diminish deconstructive behaviour.

The application of whole-exome sequencing technology in identifying the genetic origins of unclassified familial disorders

Sali M. K. Farhan, Lisa M. Murphy, Ericka Scott, Jennifer Fu, Grace Wang, Jian Wang, John F. Robinson, Victoria M. Siu, C. Anthony Rupar, Asuri N. Prasad, FORGE Canada Consortium, and Robert A. Hegele.

Next-generation sequencing (NGS) has revolutionized Mendelian genomic studies. NGS allows for rapid detection of genetic variants present within genomes at a nucleotide resolution. The current cost of sequencing a human genome is ~$7,500, a relatively low cost when compared to previous large-scale genome sequencing projects. Recently, whole-exome sequencing, an alternative and more affordable sequencing approach that allows for variant calling within the protein-coding regions of the genome has helped discover hundreds of disease-causing mutations. The value of NGS technology in complex disorders remains uncertain however as such diseases tend to be genetically heterogeneous and are often affected by the patient's environment. We are investigating the genetic aetiology of eight rare paediatric-onset diseases. Their clinical presentation varies in severity, symptoms and tissues affected. I propose to apply our scientific approach, known as the 'disease-causality toolkit', which employs NGS, in silico analyses, population screening and functional studies to fully characterize monogenic disorders in addition to a potentially complex genetic disorder, familial amyotrophic lateral sclerosis (ALS). While each disorder is distinct, the process used to identify the causative gene is the same for each. By applying our approach, we are thus able to rapidly and fully characterize the molecular basis of each genetic disorder. Defining the genetic basis of the disorders in all objectives will be important for the individual families as we can implement presymptomatic testing and carrier screening. Furthermore, because of the importance of ALS, any insights into new genetic markers may have broader implications for diagnosis and treatment.

Early Combined Immunosuppression for the Management of Crohn's Disease: A Community–based Cluster Randomized Trial

Reena Khanna MD, Barrett G. Levesque, Brian Bressler, Guangyong Zou, Larry Stitt, Gordon R Greenberg, Remo Panaccione, Alain Bitton, Pierre Paré, Severine Vermeire, Geert D'Haens, Donald MacIntosh, William J. Sandborn, Margaret K Vandervoort, Joan C Morris, **Brian G Feagan**.

INTRODUCTION: Conventional management (CM) of Crohn's disease (CD) consists of sequential corticosteroids, antimetabolites, and tumor necrosis factor (TNF)-antagonists. Recent evidence indicates that early combined immunosuppression (ECI) with a TNF-antagonist and antimetabolite may be more effective than CM. We compared the effectiveness of ECI (Figure 1) to CM in community gastroenterology practices. METHODS: In this cluster randomization trial practices in Canada (n=34) or Belgium (n=5) were randomly assigned in a 1:1 ratio to ECI or CM. Up to 60 consecutive adult patients with documented CD in each practice were evaluated for 24-months. The primary outcome was the proportion of patients in remission (Harvey-Bradshaw Score (HBS) ≤4 in the absence of steroids) at 12-months, evaluated at the practice level. Secondary measures were the rates of complications, hospitalizations, and surgeries over the entire follow-up period, based on patient-level analyses. RESULTS: Twenty-one centers (1084 patients) were assigned to ECI and 18 (898 patients) to CM. Mean (SD) remission rates in the ECI and CM groups were .66 (.14) and .62 (.17) at 12-months (P = .648). Highly significant and clinically important differences in the rates of complications, surgeries, and the combined outcome of hospitalizations, complications, and surgeries were observed in favor of ECI over 24-months.

The 24-month actuarial estimates for the combined outcome were 27.7% and 35.1% in the ECI and CM groups, respectively. CONCLUSION: Community-based data suggest that 1) symptom-based conventional approach to CD management may not be optimal and 2) ECI may be more effective in preventing CD-related complications.

Responsiveness of Endoscopic Indices in the Evaluation of Ulcerative Colitis.

Barrett G Levesque MD, Edward V Loftus, Remo Panaccionne, John W McDonald, Gert Van Assche, Guangyong Zou, Larry Stitt, Reena Khanna, William J Sandborn, Geert D'Haens, Margaret K Vandervoort, **Brian G. Feagan**.

Background: Central endoscopic evaluation of patients is a reliable process that decreases enrollment bias and placebo rates in trials. However the responsiveness of the current endoscopic indices (EI) in ulcerative colitis (UC) has not been fully evaluated. Methods: Data from a randomized placebo controlled trial conducted in patients with mildly-to-moderately active UC, was used to assess the responsiveness of the Modified Mayo Clinic Endoscopic Score (MMCS), Modified Baron Score (MBS), and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) at weeks 0 and 6 or 10. Four central readers individually evaluated 121 videos obtained in clinically changed and unchanged patients. Clinical change was defined as ≥2-point alteration in the modified UCDAI bleeding or stool frequency subscales. Responsiveness for each index was quantified by Cohen's effect size, Guyatt's responsiveness measure, and area under the receiver-operating characteristic (ROC) curves. Results: Among 121 patients, 29 were clinically unchanged and 92 were changed. Between weeks 0 and 6 or 10, the effect sizes and Guyatt's responsiveness statistics (95% confidence intervals [CIs]) based on mean scores for the MMCS, MBS, and UCEIS were 0.49 (0.28, 0.71), 0.49 (0.28, 0.71), and 0.58 (0.36, 0.81) and 0.32 (0.11, 0.53), 0.33 (0.12, 0.54), and 0.47 (0.25, 0.69), respectively. The corresponding estimates (95% CI) for the areas under the ROC curves were 0.66 (0.55, 0.78), 0.65 (0.54, 0.77), and 0.68 (0.58, 0.79).Conclusion: Although the UCEIS had greater numerical values, the MMCS, MBS, and UCEIS displayed similar, small-to-moderate, responsiveness for the assessment of UC disease activity.

Accelerated Receptor Shedding Inhibits Kidney Injury Molecule-1 (KIM-1)-mediated Efferocytosis

Rushi Gandhi, James Yi, Jihyen Ha, Hang Shi, Ola Ismail, Sahra Nathoo, Joseph V. Bonventre, Xizhong Zhang, Marie Sarabusky and Lakshman Gunaratnam.

Efficient clearance of apoptotic cells (efferocytosis) prevents inflammation and permits repair following tissue injury. Kidney injury molecule-1 (KIM-1) is a receptor for phosphatidylserine, an "eat me" signal exposed on the surface of apoptotic cells that marks them for phagocytic clearance. KIM-1 is upregulated on proximal tubule epithelial cells (PTECs) during ischemic acute kidney injury (AKI), enabling efferocytosis by surviving PTECs. KIM-1 is spontaneously cleaved at its ectodomain region to generate a soluble fragment that serves a sensitive and specific biomarker for AKI, but the biological relevance of KIM-1 shedding is unknown. Here, we sought to determine how KIM-1 shedding might regulate efferocytosis. Using cells that endogenously and exogenously express KIM-1 we found that hydrogen peroxide-mediated oxidative injury or phorbol-12-myristate-13-acetate (PMA) treatment accelerated KIM-1 shedding in a dose-dependent manner. KIM-1 shedding was also accelerated when apoptotic cells were added. Accelerated shedding or the presence of excess soluble KIM-1 in the extracellular milieu significantly inhibited efferocytosis. We also identified that tumor necrosis factor alpha-converting enzyme (TACE or ADAM17)

mediates both the spontaneous and PMA-accelerated shedding of KIM-1. While accelerated shedding inhibited efferocytosis, we found that spontaneous KIM-1 cleavage does not affect the phagocytic efficiency of PTECs. Our results suggest that KIM-1 shedding is accelerated by worsening cellular injury and excess soluble KIM-1 competitively inhibits efferocytosis. These findings may be important in AKI when there is severe cellular injury.

Deficits in Specific Cognitive Domains Affects Gait Performance: Results from the Gait and Brain Study

Elyse Gordon, Susan Hunter, Mark Speechley, Manuel Montero-Odasso.

Background: Gait as an automatic motor task, requiring minimal cognitive processes is too simplistic. It is well established that at least one cognitive domain, executive function(EF), plays an important role controlling gait. However, the role of additional cognitive domains remains unknown. Individuals with Mild Cognitive Impairment(MCI) are at greater risk for falls, mobility decline and cognitive deterioration, representing an ideal population to explore this relationship. Our aim is to identify associations between deficits in specific cognitive domains and gait variability(GV), an accepted marker of gait control and stability. Methods: Older adults with MCI were cognitively assessed for EF (Trail Making A&B), attention (Digit Span), language (Boston Naming), working (Letter Number Sequencing) and episodic memory (Rey Auditory Verbal Learning). Gait was evaluated under usual gait(UG) and dual-tasking(DT) conditions using an electronic walkway (GaitRITE®). Gait variability was evaluated using the co-efficient of variation of five gait parameters: stride time, stride length, step length, step width and double support time. Results: Sixty-four MCI participants (Mean age: 76.0±6.7 and 57% Males) were included. Multi-variable linear regression analysis (adjusted for confounders) indicated that under both walking conditions EF, attention, working memory and episodic memory were significantly associated with GV ($p<0.05$). DT gait revealed a significant association with the language domain ($p<0.05$) not seen under usual gait. Conclusion: Deficits in cognitive domains beyond EF, including working and episodic memory, are associated with GV. These associations suggest gait control shares similar neural brain circuits as memory and language.

Incidence and Outcomes of Post-operative Atrial Fibrillation and Supraventricular Arrhythmias - A Systematic Review and Meta-Analysis

Nihal Haque BHSc MD, Tahir Kanji BHSc MD, Marko Mrkobrada MD FRCPC.

It is uncertain whether post-operative new onset atrial fibrillation (POAF) and supraventricular arrhythmias (POSA) have long-term consequences for patients. With 200 million non-cardiac surgeries being performed worldwide per year, this translates into a large number of potential consequences such as stroke, MI and death. We performed a systematic review in order to ascertain the incidence of POAF and POSA in non-thoracic surgeries. We also sought to examine the association with stroke, MI and mortality. We identified 24 studies which found POAF in 11,317 out of 391,534 patients for an overall incidence of 2.9%. Pooled data from three studies showed that in-hospital mortality was not significantly increased in POAF patients (unadjusted OR 1.75, CI 0.98-3.1). However, another study did show an increased risk of death when adjusting for other prognostic factors (adjusted OR 1.68, CI 1.52-1.86). In-hospital MI rate was significantly increased in POAF after pooling data from two studies (unadjusted OR 3.68, CI 1.41-9.66). We also identified 6 studies which found POSA in 501 out of 6206 patients for an overall incidence of 8.1%. In-hospital mortality was statistically increased after pooling data from two studies (unadjusted OR 7.36, CI 4.65-11.65). In-hospital

MI rate was statistically increased in one study (RR 4.2, CI 2.7-6.6). No studies reported on the incidence of stroke. In conclusion, data on the outcomes of POAF and POSA remain sparse. We suggest a prospective study which aims to comprehensively assess the short and long term consequences of POAF and POSA.

Idiopathic hypereosinophilic syndrome presenting as generalized sweats and weight loss

Nihal Haque BHSc MD, George Dresser MD PhD FRCPC.

A 54 year old man presented with generalized sweats and a forty pound weight loss. He was previously found to have cervical and mediastinal lymphadenopathy on CT imaging. Previous axillary and bone marrow biopsies were negative for malignancy. An excisional biopsy of a cervical lymph confirmed the absence of malignancy. On day 5 of admission, the patient developed acute bronchospasm requiring steroids. CT imaging of the chest showed subpleural ground-glass opacities and interlobular septal thickening suggestive of eosinophilic pneumonia. His most recent differential showed a serum eosinophil count of 2.1x109 cells/L. His previous records revealed a serum eosinophil count of 9.9x109 cells/L two months ago. His previous bone marrow biopsy had shown 5-10% eosinophils, and a previous axillary core biopsy revealed eosinophilia. His workup was negative for viral causes. His cANCA, pANCA, complements 3 and 4 levels were normal. His total Immunoglobulin E was elevated (11,780 kU/L) 3 months ago but he had no signs or symptoms of parasitic infection. A detailed medication history revealed that he was started on Meloxicam three days prior to the bronchospastic episode. However, his eosinophil count was high prior to the start of this medication. Given the patient's serum eosinophilia, end organ damage (lungs) and exclusion of other factors, he was diagnosed with idiopathic hypereosinophilic syndrome. He was initially treated with high dose prednisone and is currently on a maintenance dose of the same. His constitutional symptoms have improved with this course of treatment.

Decline in 6-min walk distance meters and percent predicted predicts clinical progression in pulmonary arterial hypertension

Julie Huang, John T. Granton, Sanjay Mehta, Marco Mura.

Background: Six-minute walk distance (6MWD) is commonly used to assess pulmonary arterial hypertension (PAH). The role of 6MWD in predicting outcome in PAH is controversial. We sought to investigate whether longitudinal changes of 6MWD (meters) and percent predicted (%pred) predict progression of PAH. Methods: Ninety-six patients with group I PAH or group IV chronic thromboembolic PAH were retrospectively assessed. Average pulmonary artery pressure was 50 mmHg. Average follow-up was 38 months after diagnosis. 6MWD %pred was calculated using Canadian (%pred CAN) or American (%pred US) reference equations. Six-month changes in 6MWD (∆6MWD) were recorded. Progression was defined as either: development of right heart failure, hospital admission for PAH-related issues, referral for lung transplantation, or initiation of intravenous prostanoids. Optimal 6-month differences in 6MWD to detect progression were defined with receiver operating characteristics (ROC) analysis. Results: Progression rate was 55%. Progressors and non-progressors showed significant differences in ∆6MWD meters and %pred. A clinically significant 6-month decline of 6MWD was defined as ≥20 meters or ≥6 %pred. Cox proportional hazard, ROC and Kaplan-Meier analysis consistently showed a slight superiority of 6MWD %pred US as predictor of progression. A ≥6% decline in 6MWD %pred US predicted progression with high specificity but low sensitivity. Conclusions: Early decline in 6MWD

in the first 6 months after diagnosis predicts future progression of PAH with high specificity, which is further enhanced by the use of %pred. However, given the poor sensitivity, decline in 6MWD should be used together with other clinical tools to properly assess PAH progression.

Diagnostic Accuracy of ST-Segment Elevation Myocardial Infarction by Various Healthcare Providers

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Study Objective: Electrocardiograms (ECGs) are still our most effective way to identify ST elevation myocardial infarctions (STEMI). This study aimed to compare the accuracy of ECG interpretation for the diagnosis of STEMI, by different groups of healthcare professionals involved in the STEMI program at London Health Sciences Center (LHSC).
Methods: Each participant interpreted an ECG package and was asked to identify STEMI and indicate appropriate initiation of the Coronary Catheterization Lab (CCL). Participants were also asked to provide information regarding their experience and confidence with ECG interpretation.
Results: A total of 64 participants completed the study package across a population of Paramedics and various clinician groups associated with the STEMI program at LHSC. Cardiologists out-performed all other clinical groups, aside from Emergency Physicians (Mean 81%, p<0.001). False positive diagnoses were more likely made by Paramedics but only significantly different (p<0.01) when compared to Cardiologists. There was a positive correlation between increased exposure to ECGs and accurate STEMI diagnosis (r= 0.482, p<0.001). A threshold of >20 ECGs read per week showed a statistically significant (P<0.001) improvement in accuracy. Self-reported confidence also correlated with positively with accuracy (r= 0.402, p= <0.001).
Conclusions: Experience and exposure to ECG interpretation remains an important influence on accuracy of ECG diagnosis, STEMI recognition and CCL activation. Cardiologists remain the most accurate diagnosticians, and are the least likely to falsely activate the CCL. Weekly exposure of >20 ECGs may improve diagnostic accuracy regardless of underlying experience and training.

The hypofunctional GPER P16L variant is associated with a gene-dosage related increase in plasma LDL cholesterol

Yasin Hussain, Qingming Ding, Jozef Chorazyczewski, Matthew R. Ban, Adam D. McIntyre, Rob Gros, Rob Hegele, Ross D. Feldman.

Intro: Estrogen deficiency is linked with dyslipidemia, especially in postmenopausal women. GPER, a recently recognized GPCR is activated by estrogens. We recently identified a common hypofunctional missense variant of GPER, namely P16L (allele frequency ~ 20%). We studied its association with plasma LDL cholesterol levels. Further, we studied GPER's role in regulating LDL receptor expression. Methods: Our discovery cohort was a genetically isolated population of Northern European descent (n=415), our validation cohort consisted of 505 healthy subjects from London, Ontario. Genomic DNA was extracted from whole blood and genotyped for GPER using a dedicated TaqMan assay. GPER's regulatory role on LDL receptor expression was examined using GPER agonist, G1. Results: In the discovery cohort, the GPER P16L genetic variant was associated with a significant gene-dosage increase in mean+SD LDL cholesterol (CC [homozygous wild type] =3.18±0.84; CT [heterozygote] =3.25±0.80; and TT [homozygous variant] =4.25±0.87 mmol/L, p<0.05). In the validation cohort, the GPER P16L genetic variant was associated with a

similar significant gene-dosage increase in mean±SD LDL cholesterol (CC =2.16±0.67; CT [heterozygote] =2.29±0.67; TT =2.40±0.84 mmol/L, p<0.05). In HepG2 cells expressing GPER, G1 mediated a concentration-dependent increase in LDL receptor expression. Pre-treating the cells with the GPER antagonist G15 attenuated G1's effect on LDL receptor upregulation. GPER downregulation via infection with a shGPER construct attenuated G1 mediated LDL receptor upregulation. Conclusion: GPER activation upregulates LDL receptor expression. Further, carrying the hypofunctional P16L GPER, increases plasma LDL cholesterol in humans.

Infrequent, low-dose regimens of rosuvastatin and their effect on the lipid profile

Christine Ibrahim, MD, Matthew R Ban, BSc, and Robert A Hegele, MD.

Background: While statins reduces cardiovascular (CV) morbidity and mortality, a significant proportion of patients cannot tolerate them, particularly at high doses. Some patients take low daily or non-daily doses to attain some benefit while reducing the potential for adverse events. Rosuvastatin has the longest half-life of available statins; a recent study showed a statistically significant benefit using rosuvastatin only 3 times a week (~30 mg/week). However, some patients still cannot tolerate this regimen and require even less frequent dosing. Methods: This retrospective study included 21 eligible patients who received rosuvastatin < 3 times per week (mean frequency 1.7 doses/week, mean dose 11.7 mg/week). We assessed clinical risk and lipid profile at baseline and after at least three months of therapy. Results: The mean age was 66.4 years and body mass index was 28.9 kg/m2. 19.5% (n=4) had type 2 diabetes mellitus, 38.1% (n=8) were smokers, 42.9% (n=9) had hypertension and 23.8% (n=5) had cardiac disease. Initially, 42.9% (n=9) were taking other lipid-lowering medications, and 52.4% (n=11) continued concomitant medications or were started on additional therapy. On low-dose rosuvastatin, LDL-C was reduced by 1.43 + 0.83 mmol/L or 31.5% (P <0.001). A subgroup analysis found no difference in LDL-C response according to concomitant use of other lipid-lowering medications. Conclusions: In those with statin intolerance, low doses of rosuvastatin significantly improved LDL-C, which is of importance in a population with increased CV risk. Clinicians should consider non-daily statin dosing in those who cannot tolerate daily or alternating day statins.

Acute on Chronic Adrenal Insufficiency—a Missed Diagnosis

Christine Ibrahim, MD, Stan Van Uum, MD, PhD.

A 19-year-old woman was admitted to hospital with nausea, vomiting, urinary tract infection and severe hypotension, necessitating a 5-day stay in the intensive care. A few weeks later she was readmitted to hospital with a respiratory infection. Laboratory investigations found a sodium of 130 (reference range 135-145), potassium 6.1 (3.5-5), serum cortisol immeasurably low at <11 (120-384) nmol/L, and an ACTH of >278 (0.0-10.1) pmol/L, leading to a diagnosis of acute adrenal insufficiency crisis, specifically Addison's disease. She was started on hydrocortisone and fludrocortisone. Her detailed history suggested that her adrenal insufficiency had developed much earlier in that she had a 3-4 year history of non-intentional, 40-pound weight loss, progressive weakness, fatigability, darkening of her skin, and episodes of orthostatic presyncope. In-between the episodes of being unwell, she was fine, but when she did become ill, she deteriorated quite rapidly. In retrospect her clinical picture was almost textbook for someone having an adrenal crisis, however, given the rarity of this disease, it is often misdiagnosed until patients arrive in critical conditions. This case study will go through the clinical, biochemical, diagnostic, and therapeutic features of acute and chronic adrenal insufficiency. It will also touch on a novel

tool – measurement of hair cortisol, as provided by the patient in this case, to determine cortisol levels and indicate deficiency.

KIM-1 Interacts with Gα12 and Suppresses Its Activity To Mediate Efferocytosis

Ola Ismail, Xizhong Zhang and Lakshman Gunaratnam.

The phagocytic clearance of apoptotic cells (efferocytosis) serves to attenuate inflammation and enable tissue repair following injury. Kidney injury molecule-1 (KIM-1) is phagocytic receptor that is upregulated on renal proximal tubular epithelial cells (PTECs) following acute kidney injury. It specifically recognizes phosphatidylserine displayed on the surface of apoptotic cells. The signalling mechanism by which KIM-1 uptakes apoptotic cells is not known. Previously, we identified the Gα12 as a novel KIM-1-interacting protein in PTECs using co-immunoprecipitation and mass spectrometry. We hypothesized that KIM-1 interacts with Gα12 to mediate efferocytosis. First, we established that Gα12 interacts with the cytosolic domain of KIM-1 via co-immunoprecipitation. We also observed the co-localization of KIM-1 with GFP-tagged Gα12. Using an active Gα12 pull-down assay, we determined that Gα12 activity is significantly reduced in KIM-1-expressing PTECs upon exposure to apoptotic cells. To determine the role of Gα12 activity, we overexpressed a constitutively active mutant of Gα12 in KIM-1-expressing PTECs and found a significant decrease in their phagocytic efficiency. Conversely, we found an increase in phagocytosis when Gα12 expression was silenced using siRNA. In addition, we observed that KIM-1 inhibited Gα12 activation loaded with non-hydrolyzable GTP in the absence of apoptotic cells. The latter was also confirmed using PTECs isolated from wild type and Kim-1 knock-out mice. Taken together, our experiments suggest that KIM-1 interacts with and inhibits Gα12 activation to mediate efferocytosis.

Aortic stenosis: Do we only consider the gradient in determining severity?

Ibrahim Jelaidan, Yves Landry, Mandy Jeffery, Michael Chu, David McCarty.

Background: Aortic stenosis (AS) patients with severe disease and low gradients despite normal ejection fraction (LVEF) have recently been described, are frequently mischaracterized as moderately diseased, and are at high risk of adverse outcomes. We explored the prevalence, characteristics and outcomes of these patients in London. Method: Echocardiograms from patients with severe AS (aortic valve area, AVA<1.0 cm2/) and normal LVEF over a five year period (09/2008–08/2013) were included. For each patient, flow was determined by stroke volume index (SVI) as low (LF, SVI<35 ml/m2) or normal (NF, remainder). Mean trans-aortic gradient was low (LG, <40 mmHg) or high . Standard demographic and echocardiographic parameters were evaluated. Patients undergoing subsequent aortic valve replacement (AVR) were identified from cardiac surgical and echo lab databases. Results: 983/6079 AS studies met inclusion criteria (47% males, mean age 75 (+/-13) years). LFLGAS prevalence was 29% (n=285). Other patients were NFHGAS (267), NFLGAS (267), LFHGAS (164). Compared to patients with HG, LFLGAS patients were more likely to be female (44% vs. 36%), older (77 vs. 73 years), with larger AVA (0.8 vs. 0.6 cm2), and less LV hypertrophy (p<0.001 for all). During a mean follow up of 34 (17) months, 43 LFLGAS patients (15%) proceeded to AVR, compared to 207/431 (48%) HG patients (p<0.001). 44/267 (16%) NFLGAS patients underwent AVR. Conclusions: A substantial subset of AS patients have LFLGAS, with characteristics similar to those reported by other centres. Despite severe AS, fewer patients proceed to AVR compared to HG AS patients.

Reasoning Tasks During Admission Case Review: A Validation Study

Mark Goldszmidt, **Salina Juma**.

BACKGROUND: In a prior study, we identified a unified list of 24 reasoning tasks that physicians may engage in during clinical encounters. The purpose of this study was to further validate these and explore how they are used during admission case review. METHODS: We used a constant comparative approach to analyze the clinical records and transcripts of 38 real admission case review conversations between junior trainees, senior residents and their faculty supervisors. The analysis focused on three areas: Identifying performed and missed tasks; identifying new tasks; exploring relationships between tasks. RESULTS: Junior trainees and their supervisors engaged in a mean of 16.6 (SD=1.5; Min=13, Max=19) reasoning tasks per case review. Twenty-two of the 24 tasks were observed in at least one of the reviews; no new tasks were identified. Several tasks were observed to consistently cluster together. The predominant reasoning tasks related to establishing the diagnosis (48% of coded tasks). The tasks most frequently omitted were establishing goals of care, exploring the psychosocial impact of illness, and considering the impact of comorbid illness on management. DISCUSSION: During case review, multiple reasoning tasks are addressed. However, rather than reflecting discrete tasks, many cluster in complex relationships with each other. While there is an appropriate emphasis on diagnosis, other relevant tasks are frequently left unaddressed. This study provides further validity evidence to support our unified list of reasoning tasks. For clinical teachers and trainees, our findings may support professional development efforts intended to improve admission case review.

Prevalence of Frailty in Hospitalized Patients on the Medicine Ward

Salina Juma, Mary-Margaret Taabazuing, Manuel Montero-Odasso.

BACKGROUND: Frailty in the hospital setting predicts important outcomes including length of stay, incidence of delirium, and mortality. Our objective was to assess the prevalence of frailty on the Acute Care of the Elderly (ACE) service at LHSC Victoria Hospital in comparison to other Medicine teams. METHODS: Data was collected on a subset of patients from the Move-On Project, which aimed at increasing mobilization in patients over 65 admitted to the CTU teams, ACE (n=33), Blue (n=16), and Gold (n=17) between May- June 2013. Palliative patients were excluded. Age, gender, comorbidities, medications, and length of stay were collected. The Clinical Frailty Score, assessed by a Geriatrician, ranged from 1 to 9 (more frail). RESULTS: In this sample, ACE medicine had higher frailty scores than non-ACE teams on average (5.5, SD 1.49 vs. 4.97, SD 1.76), but this was not statistically significant (p=0.167) The mean age on ACE was 83.5, SD 1.03 while the mean age on non-ACE was 78.5, SD 1.78 (p=0.019). When adjusted for age, the mean frailty score on ACE was 5.4 vs. 5.1 on non-ACE. The mean length of stay on ACE was also longer at 9.5 (SD 8.8) compared to 6.6 (SD 6.4) days (p= 0.192). DISCUSSION: ACE patients were frailer and experienced longer length of stay when compared to other Medicine patients of the same age. Differences were not statistically significant likely due to the limited sample size. Recognizing frailty in hospitalized patients can help clinicians better implement strategies to avoid complications related to frailty.

Underestimation of Fracture Risk and Osteoporosis Treatment Care Gap in Patients with Type 1 Diabetes Mellitus

Tayyab S. Khan, M.D., M.A.Sc., Tamara Spaic M.D., M.Sc., Lisa-Ann Fraser M.D. M.Sc..

Current osteoporosis guidelines suggest using the WHO fracture risk assessment tool (FRAX) to identify those in need of treatment. Individuals with type 1 diabetes (DM1) have a 6-fold increased risk of sustaining a hip fracture compared to the general population. FRAX incorporates DM1 status into its calculation, but fracture validation studies within the DM1 population are lacking. We studied bone health in patients with DM1 being followed by Endocrinologists at SJHC. Patients completed a bone health questionnaire which was used to up-date their electronic medical record (EMR). De-identified data was then extracted for all DM1 patients over age 40, and fracture risk was calculated using FRAX. 201 individuals were identified, with mean age of 53.9 years (40-82), of which 40 (19.9%) had experienced at least one fragility fracture. Despite this, only 25 patients (12.4%) were identified as "high risk" for fracture by their calculated FRAX score, and 19 (9.5%) were in the "moderate risk" FRAX category. Despite current osteoporosis guidelines to treat all high risk patients, and to consider treatment of moderate risk patients, only 24% of the FRAX-identified "high risk" patients, and 11% of the "moderate risk" patients were on osteoporosis therapy. Our results reveal that FRAX underestimates fracture risk in individuals with DM1, suggesting that alternate assessment tools may be needed in these patients. This study also demonstrates a care gap for osteoporosis treatment in patients with DM1, highlighting the need to include bone fragility in diabetes care guidelines and to educate clinicians about fracture prevention therapies.

Agreement Among Central Readers in the Evaluation of Endoscopic Disease Activity in Crohn's Disease

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BACKGROUND: The Crohn's Disease Endoscopic Index of Severity (CDEIS) and the Simple Endoscopic Score for Crohn's Disease (SES-CD) are commonly used to assess Crohn's disease (CD) activity; however neither instrument has been fully validated. We assessed intra- and inter-rater agreement and identified items responsible for disagreement between these measures. METHODS: Video recordings of colonoscopies obtained from 50 patients with CD who participated in an induction trial of a biologic therapy were randomly reviewed, in triplicate, by 4 central readers. Inter-class correlation coefficients (ICCs) for inter- and intra-rater agreement were calculated for CDEIS, SES-CD, and a global assessment of endoscopic lesion severity (GELS). Subsequently readers participated in a Delphi process that identified common sources of disagreement. RESULTS: Intra-observer ICCS for CDEIS, SES-CD and GELS (95% CIs) were 0.89 (0.86 to 0.93), 0.91 (0.87 to 0.94), and 0.81 (0.75 to 0.86), respectively. Corresponding inter-rater ICCs were 0.71 (0.61 to 0.79), 0.83 (0.75 to 0.89), and 0.62 (0.52 to 0.73). Correlation between CDEIS and VAS was 0.75, between the SES-CD and VAS 0.74, and between CDEIS and SES-CD 0.92. The most common source of disagreement was interpretation of superficial ulceration, definition of disease site at ileocolonic anastomosis, assessment of anorectal lesions, and grading severity of stenosis. The correlation coefficients with GELS were nearly identical for the original and modified indices, which excluded stenosis. CONCLUSION: Central reading of CDEIS and SES-CD had "substantial" to "almost perfect" intra- and inter-rater agreement, however the responsiveness of these instruments has yet to be determined.

Patient Reported Outcome Measures Derived from the Crohn's Disease Activity Index: Correlation Between PRO2 and PRO3 Scores and CDAI-defined Clinical Thresholds

Reena Khanna MD, Geert D'Haens, Brian G. Feagan, William J Sandborn, Margaret K

Vandervoort, Guangyong Zou, Robert L. Rolleri, Enoch Bortey, Barrett G Levesque..

BACKGROUND: The Crohn's Disease Activity Index based on symptoms, signs, and laboratory tests. The US FDA has indicated that patient reported outcomes (PROs) should be used as an outcome measure in trials for Crohn's disease (CD). As no validated PROs exist for CD, we investigated whether the CDAI diary card items could be adapted for this purpose. METHODS: Development consisted of two phases. In Phase I data from an RCT of rifaximin therapy were used to identify cut-points that yielded optimum sensitivity and specificity for identification of CDAI-defined remission. Two (pain, stool frequency) and 3-item (pain, stool frequency, well-being) PROs were generated. In Phase II these instruments were assessed using data from NACSGI, a RCT of methotrexate (MTX) induction therapy. PRO2 and PRO3 scores that correspond to CDAI-defined thresholds and change scores were determined by regressing CDAI on PRO2 and PRO3 using data from a MTX induction trial. RESULTS: Optimal cut points were mean daily stool frequency ≤1.5, mean daily abdominal pain score ≤1, and mean daily general well-being score of ≤1. Effect estimates were similar using PRO2, PRO3, or the original CDAI-based outcomes. PRO2 and PRO3 values corresponding to CDAI scores of 150, 220, and 450 points were 8, 14, and 34 and 13, 22, and 53 respectively and the corresponding values for CDAI changes of 50, 70, and 100 points, were 2, 5, and 8 and 5, 9, and 14 respectively. CONCLUSIONS: PROs derived from CDAI diary cards may be appropriate for use in CD trials.

The Clinical Use of Fecal Calprotectin in the Diagnosis of Inflammatory Bowel Disease

Lukasz Kwapisz, Mosli M, Chande N, Yan B, Beaton M, Barnett W, Bax K , Ponich T, Howard J, Lannigan R, and Gregor J..

BACKGROUND: With growing numbers of patients with inflammatory bowel disease (IBD), it is important to find new ways to detect disease activity other than with endoscopy procedures. The aim of this study is to correlate fecal calprotectin (FC), a stool inflammatory marker, with endoscopic evidence of inflammation in patients undergoing colonoscopy or flexible sigmoidoscopy for suspected IBD or for patients with established IBD to assess disease activity. METHODS: Interim analysis has been gathered on 60 patients who either had established IBD with flare-like symptoms or suspected new IBD and provided high range FC samples within 4 weeks of their scheduled endoscopic assessment. RESULTS: 31 females and 29 males were included with a mean age of 40 years. Among these patients, 30 had a pre-existing diagnosis of IBD and 30 had signs or symptoms suggestive of IBD. Using two different cut-off points for FC compared to endoscopic findings the following results were calculated: a cut-off point of 100 µg/g showed sensitivity of 95%, negative predictive value of 94%, specificity of 59% and positive predictive value of 60%; a cut-off point of 200 µg/g showed sensitivity of 79%, negative predictive value of 85%, specificity of 78% and positive predictive value of 71%. CONCLUSIONS: FC is a useful test as an initial screening tool for patients with active inflammation in the ileum or colon with a cut-off point of 100 ug/g providing higher sensitivity and negative predictive value and 200 ug/g providing higher specificity and positive predictive value.

Characterizing the impact of membrane vesicles produced by necroptotic tubular epithelial cells during transplantation

Cecilia Kwok, Arthur Lau, Alexander Pavlosky, Anthony Jevnikar, Zhuxu Zhang.

Necroptosis, regulated necrosis that is dependent on receptor-interacting protein kinase 1 and 3 (RIPK1, RIPK3), has been newly

identified as a form of programmed cell death that can greatly impact graft survival. During death, cells release nanometer size membrane vesicles (MVs) that induce inflammatory response. Whether necroptotic tubular epithelial cells (TECs) will release MVs and elicit inflammatory responses has not been evaluated. In this study, we have found that TNF-α induced necroptosis in TECs. Differential ultracentrifugation and flow cytometry were used to isolate and analyze MVs for extraction, quantification, RNA and DNA analysis. TNF-α-induced necroptosis in TECs was confirmed by death assay (0.366±0.177 fold change vs. untreated; $p<0.001$). Immunoblot for high-mobility group box 1 (HMGB1) confirmed necroptotic death. Total protein release was enhanced following necroptosis (1.48±0.09ug/uL) compared with apoptosis (1.06±0.02ug/uL; $p<0.05$). In conclusion, we have found that TEC undergo necroptosis after TNF-α treatment in presence of caspase inhibition, which resulted in more cDAMP and cell content release than apoptotic death. Further studies will focus on proteomic analysis of MV content and examine their proinflammatory functions in transplantation.

General Medicine Discharge Checklist Intervention To Improve Patient Discharge Safety Outcomes

Joyce Lam, Marko Mrkobrada, Andrew Smaggus.

Background: This quality improvement study implemented a discharge checklist in a tertiary centre general medicine inpatient ward to study its effect on the primary outcome, a composite of 30 day mortality, readmissions to hospital, and emergency department visits. Methods: The study compared the primary outcome between a pre-intervention (2 weeks, n=88 patients) and intervention (3 weeks, n=135 patients) period. The pre-intervention period involved gathering data on: number of discharge summaries dictated within 24 hours post-discharge; number of discharge summaries verified within 72 hours post-discharge; time from discharge to discharge summary verification; number of patients whose family physician received phone call notification within 24 hours pre-discharge; number of patients with follow up family physician appointments booked within 7, 8-14, 15-30 days or not booked. The intervention period involved implementation of a discharge checklist composed of the aforementioned variables. Results: The intervention was associated with a decrease in the composite primary outcome from 42.05% to 28.89% ($p=0.042$). 30 day emergency department visits decreased from 22.73 to 8.15% ($p=0.002$). It also correlated with an increase in discharge summaries dictated within 24 hours from 81.82% to 91.11%% ($p=0.04$), patients whose family physician was notified by phone call from 10.81% to 42.71% ($p<0.00001$), and patients with a family physician appointment booked within 7 days of discharge from 28.38 to 41.67%. ($p=0.043$). Conclusions: The implementation of a discharge checklist on a general medicine ward was associated with favourable patient outcomes of decreased emergency department visits and improved markers of outpatient follow up with family physicians.

Secular Trends in Cardiovascular Disease Among Kidney Transplant Recipients

Ngan N. Lam, K. L. Naylor, S. Z. Shariff, E. McArthur, G. A. Knoll, S. J. Kim, A. X. Garg.

Background: Cardiovascular death remains the number one cause of mortality in kidney transplant recipients. Cardiovascular events alone are associated with significant morbidity. Methods: We conducted a retrospective cohort study using Ontario's linked healthcare databases to follow all first-time kidney-only transplant recipients between 1994 to 2009. Our primary outcome was a composite of death or first major cardiovascular event defined as one

of myocardial infarction, coronary angioplasty, coronary bypass surgery, or stroke within three years of the transplant date. Results: There were 4954 first-time kidney-only transplant recipients during the study period, of which 63% were male. The median age steadily increased from 43 years (interquartile range [IQR] 33-54) in 1994 to 53 years (IQR 42-62) in 2009 as did the proportion of recipients aged 65 years old older (3.8% in 1994 to 20.4% in 2009). There was also an increase in the proportion of recipients with coronary artery disease (23.7% in 1994 to 37.7% in 2009) and diabetes (19.2% in 1994 to 29.9% in 2009). A total of 444 recipients (9.0%, 95% confidence interval 0.082 to 0.098; 3.15 events per 100 person-years) died or experienced a major cardiovascular event within three years of transplantation with no significant change over time (P=0.59). Conclusion: Despite transplant centres accepting recipients who are older with more co-morbidities, the three-year incidence of death or major cardiovascular event has remained stable from 1994 to 2009. These results are reassuring for transplant programs.

Gout in Living Kidney Donors

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Background: In the general population, a high serum uric acid concentration is an independent risk factor for gout. We studied the risk of gout in living kidney donors, as the serum concentration of uric acid rises in donors after nephrectomy. Methods: We conducted a retrospective cohort study of living kidney donors (n=1988) matched to non-donors selected from the healthiest segment of the general population (n=19,880). Donations occurred between 1992-2010 in the province of Ontario, Canada and individuals were followed through provincial healthcare databases until March 2013. The outcomes were the time to a diagnosis of gout and receipt of medications typically used to treat gout (allopurinol or colchicine). The median follow-up was 8.4 years (maximum 20.8 years). Results: Donors compared to non-donors were more likely to be diagnosed with gout (67/1988 [3.4%] vs. 390/19,880 [2.0%]; 3.5 vs. 2.1 events per 1000 person-years; hazard ratio 1.6; 95% confidence interval [CI], 1.2 to 2.1; P<0.001). Similarly, donors compared to non-donors were more likely to receive a prescription for allopurinol or colchicine (3.8% vs. 1.3%; odds ratio 3.2; 95% CI, 1.5 to 6.7; P=0.002). Results were consistent in multiple additional analyses. Estimates of the lifetime cumulative probability of gout were highest in individuals who underwent nephrectomy at a younger age. Conclusions: Donating a kidney increases an individual's long-term risk of gout. While this information should not deter living donor kidney transplantation, it can be shared with potential donors and their recipients as part of the informed consent process.

Patient-Prosthesis Mismatch in Valvular Heart Disease: An Evaluation of Echocardiographic Findings

Yves Landry, Ibrahim Jelaidan, Mandy Jeffery, Michael Chu, David McCarty.

Background: Guidelines for reporting echocardiographic studies in prosthetic heart valve patients have recently been published. Undersized prostheses relative to body size (patient-prosthesis mismatch, PPM) may result in higher transprosthetic gradients and adverse patient outcomes. We examined reporting trends in patients with prosthetic valves, focusing on PPM. Method: Patients with prosthetic aortic (AVR) and mitral (MVR) valves undergoing echocardiography between 09/2003-08/2013 were included. PPM was defined as effective orifice area (EOA)/body surface area (BSA). Demographic and echocardiographic parameters were evaluated. Results: 8901 studies from 3378 patients were included (61% male; age 68 (+/-13) years). Studies (mean 2.6) were performed in patients with AVR (6290, 71%) MVR (1904, 21%) or both (707, 8%). PPM

was present in 44% of AVR studies (severe in 3%) and 7% of MVR studies. Patients with AVR PPM were older at surgery (71 vs. 63 years) and follow-up (73 vs. 65 years), heavier (87 vs. 81kg), larger BSA (1.98 vs. 1.91kg/m2), smaller LV dimensions (47 vs. 49mm), LVOT (19 vs. 20mm) and aortic roots (30 vs. 32mm), with higher transprosthetic gradients (34 vs. 26mmHg) and lower DVI (0.41 vs. 0.44) than patients without PPM ($p<0.001$ for all). PPM was more common in females (46% vs. 41%, $p=0.002$), with bioprosthetic AVR (55% vs. 9%, $p<0.001$), concurrent CABG (52% vs. 39%, $p<0.001$) or without aortic root enlargement (46% vs. 33%, $p<0.001$). Conclusions: PPM in AVR patients is frequent. Our data identify subsets with higher PPM prevalence and reveal impaired cardiac performance in these groups.

SPI-6 (Serine Protease Inhibitor-6) inhibits granzyme B mediated injury of renal tubular cells and promotes renal allograft survival

Arthur Lau, Kelvin Shek, Alex Pavlosky, Ziqin Yin, Xuyan Huang, Aaron Haig, Weihua Liu, Bhagi Singh, Zhuxu Zhang, Anthony M. Jevnikar.

Background: Protease inhibitor 9 (PI-9) is an intracellular serpin that specifically inhibits granzyme B, a cytotoxic protease found in the cytosolic granules of cytotoxic T and NK cells. Enhanced cortical expression of PI-9 has been observed in kidney allografts with subclinical rejection, suggesting tubular epithelial cell (TEC) expression of this protein may have a protective role and attenuate overt allograft rejection. Methods/Results: We demonstrate TEC express SPI-6 protein, the murine homolog of PI-9, basally with a modest increase following cytokine exposure. TEC expression of SPI-6 blocks granzyme B mediated death as TEC from SPI-6 null kidneys have increased susceptibility to cytotoxic CD8+ cells in vitro. We then tested the role of SPI-6 in a mouse kidney transplant model using SPI-6 null or wild type donor kidneys (H-2b) into nephrectomized recipients (H-2d). SPI-6 null kidney recipients had reduced renal function at day 8 post-transplant compared to controls (creatinine: 113+23 vs. 28+3 □mol/L, n=5, $P<0.01$) consistent with greater tubular injury and extensive mononuclear cell infiltration. Finally, loss of donor kidney SPI-6 shortened graft survival time (20+19 vs. 66+33 days, n=8-10, $P<0.001$). Conclusions: Our data shows for the first time that resistance of kidney TEC to cytotoxic T cell, granzyme B induced death is mediated by expression of SPI-6. We suggest SPI-6 is an important endogenous mechanism to prevent rejection injury from perforin/granzyme B effectors and enhanced PI-9/SPI-6 expression by TEC may provide protection from diverse forms of inflammatory kidney injury and promote long term allograft survival.

SNPs of GATM were not found to confer protection from statin myopathy.

Paul Lee, Adam McIntyre, Matthew Ban, Rob Hegele.

OBJECTIVE: Three single-nucleotide polymorphisms (SNP) in the glycine amidinotransferase (GATM) gene were recently found to be associated with a reduced risk of statin myopathy. The purpose of our study was to verify GATM's role in reducing risk of statin myopathy. METHODS: We identified subjects with statin myopathy - defined as patients who had symptoms of muscle weakness or pain while on a statin. A matched control population was identified. The incidence of different haplotypes of 3 SNPs (rs9806699, rs1346268, rs1719247) of the GATM gene in both the statin-intolerant and control population was then determined. Significance of deviation from Hardy-Weinberg equilibrium for statin-intolerant group compared to control was calculated. Analysis was repeated in a subgroup with elevated creatine kinase (CK) of greater than five times upper-limit of normal (5xULN). RESULTS: The statin intolerant group composed of 181 subjects versus 192 in the control group. 27 patients with a CK greater than

5xULN were identified for subgroup analysis. Demographics were similar between all groups. Statins used were different in the statin-intolerant groups versus control (chi-square < 0.0001). No difference was noted between statin-intolerant group or subgroup versus control with regards to incidence of SNP haplotypes. CONCLUSIONS: SNPs of GATM were not found to be associated with statin intolerance in our lipid clinic population. Our study was limited by small sample sizes. Our findings contradict data from other recent trials which used predominantly simvastatin. One possible explanation is that GATM-mediated protection from statin intolerance is limited to simvastatin.

Bloody Sticky: A Meta-Analysis of the Risk of Venous Thromboembolism in Inflammatory Rheumatic Diseases

Jason J Lee, Janet E Pope.

Objectives: We performed a meta-analysis investigating the risk of developing deep vein thrombosis and/or pulmonary embolisms in patients with inflammatory arthritis, vasculitis, and connective tissue diseases. Methods: PubMed, Embase, Cochrane Databases, and Medline were searched identifying full text English publications in adults related to rheumatologic inflammatory diseases and VTE. Data regarding rates of DVTs and PEs were extracted. Using random effects models, pooled estimates for VTE in individual and pooled diseases compared with matched populations where possible. Studies were excluded if VTEs were in the setting of pregnancy, postoperative outcomes or solely antiphospholipid antibody syndrome. Results: Most of the 3,929 studies were excluded due to lack of rate or incidence of VTE. Twenty studies remained for analysis. Eight studies of RA identified 5,273,942 patients and 891,530,181 controls with a cumulative incidence of 2.18% (95% CI: 1.82–2.54%) and an odds ratio of 2.23 (95% CI: 2.02–2.47) compared to age and sex, matched population. Six studies included 36,582 SLE patients with a cumulative incidence of 8.24% (95% CI: 6.27–10.22%); three Sjogren's syndrome studies (N=16,180) demonstrated a VTE cumulative incidence of 2.62% (95% CI: 2.15–3.10%); four studies of inflammatory myositis (N=8,245) yielded a VTE cumulative incidence of 4.03% (95% CI: 2.38–5.67%), SSc and ANCA vasculitis rates (3 studies each) were 3.82% and 8.51% respectively. Conclusions: Inflammatory rheumatologic diseases studied were all associated with high rates of VTEs, nearly three times higher than the general population.

A web-based patient registry system for specialized ambulatory clinics

Joseph Lindsay, Michael Borrie.

BACKGROUND: Current electronic medical record systems are not tailored to the workflow of a specialized geriatric clinic. Systems that can be adapted to meet the needs of a geriatric clinic rarely allow the collected data to be analyzed for research purposes. Many software solutions are not practical and lack usability due to small buttons, fonts, complex menu systems and challenging user interfaces. METHODS: After an extensive analysis of the clinical and research work/data-flow, an initial dataset was identified. Workflow was further analyzed to determine the functional requirements for the system. The system development utilized web-based programming technologies in order to allow the system to be used on any modern web-enabled computer or tablet. Usability testing/evaluation was conducted throughout development to ensure that system users were included in the process. RESULTS: The system is able to digitally capture tests such as the SMMSE, GDS, IADL/ADLs, Cornell, Zarit Burden Interview and many more. The "alpha" version has been developed as a modular web-based system, operating on all tested web-capable computer and tablet devices. Interviewed users reported positive feedback in user testing and

indicated that the system could be integrated into clinic workflow. CONCLUSION: The use of an electronic system, which meets both the needs and workflows of clinicians and clinical researchers, can have several benefits. We anticipate this system will decrease dictation time, the need for transcription and eliminate repetitive data entry. It will facilitate clinical research by allowing for the entire clinical cohort to be analyzed longitudinally.

Procedural Correlates of Rotational Atherectomy: Analyzing the Need for Temporary Pacing

Michael Mitar, Shemer Ratner, Shahar Lavi.

Background: Rotational atherectomy (RA) during PCI is commonly associated with embolization of calcific particles resulting in conduction abnormalities. As a result, temporary pacing is often employed. It is unknown whether temporary pacing should be routinely used. Methods: We retrospectively analyzed 138 patients undergoing RA at our institution between January 2011 and September 2013 for the presence of heart block or pacemaker activation. Results: 42 (31.3%) patients experienced heart block (n=16) or pacemaker activation (n=26). There was no difference between those who experienced heart block or temporary pacing, and those who did not in terms of gender, age or cardiac risk factors. Burr size (1.58±0.21 vs. 1.54±0.19, p=0.29), max RPM (189024±16109 vs. 186054±11288, p=0.22), number of runs per burr (3.45±2.5 vs. 3.29±2.3, p=0.72) and maximum run duration (26.4±10.4 vs. 25.2±12.3, p=0.57) were also similar. Heart block or temporary pacing occurred in 29 patients undergoing RA to the RCA (69%, p<0.001). One patient (2%, p<0.01) with RA to the LM and 2 patients (5%, p<0.001) with RA to the LAD experienced heart block or temporary pacing. Average duration of pacemaker activation was 19s (95%CI 13-25s), while average duration of heart block was 16s (95%CI 6-26s). Seven patients (44%) experienced heart block greater than 10s, while 3 (19%) experienced systole. Conclusion: Heart block or temporary pacing were more commonly associated with RCA lesions. Consideration should be made for prophylactic pacemaker insertion only when RA is performed to the RCA.

Are Housestaff Identifying Malnourished Hospitalized Medicine Patients?

Michael Mitchell, Donald R Duerksen, Adam Rahman.

Background: Malnutrition is common and under recognized in hospital. The purpose of this study is to determine the prevalence of malnutrition in medical wards in a tertiary teaching hospital and to determine whether medical housestaff are assessing for malnutrition. We also aim to determine the knowledgebase of housestaff in performing nutritional assessments. Methods: The nutritional status of medicine patients admitted to the internal medicine service at a teaching hospital was assessed using the Subjective Global Assessment screening tool at University Hospital in London, Ontario. Patients' charts were reviewed to determine if housestaff performed nutritional assessments or identified malnutrition-related parameters. Housestaff then completed a survey to determine knowledge in performing nutritional assessments. Results: There were 74 patients assessed, and 42 (57%) were found to be malnourished. Documentation of nutritional assessment occurred in 3 patients (4%). Of the 42 patients found to be malnourished, only 8 (19%) had a request for dietician consult. Survey of housestaff indicated a lack of knowledge in the area of malnutrition, despite them identifying it as an important aspect to clinical care. Conclusion: Our study demonstrates that malnutrition remains prevalent and under recognized by medical housestaff in a tertiary care hospital. Medical housestaff lack sufficient training in the area of nutritional assessment; a majority of cases are not identified despite the recognition of its importance. Medical schools and training programs must place greater emphasis of

providing qualified physician nutrition specialists to implement effective nutrition instruction and the need to implement system-wide nutritional risk screening.

Pulmonary Structure-function Abnormalities in Adult Congenital Emphysema

Sindu Mohan, D.Pike, W.Ma, J.F.Lewis and G.Parraga.

Introduction: Congenital Lobar Emphysema (CLE) is a rare bronchopulmonary anomaly characterized by localized hyperinflation with the majority diagnosed in the neonatal period. Recently, there are increasing reports of adulhood diagnoses of CLE often with normal pulmonary function tests. There is limited understanding of the in vivo airway morphology, parenchymal microstructure and ventilation abnormalities in CLE. Hypothesis: Structure-function imaging of ventilation defects and airway morphology may help explain the etiology and severity of symptoms in patients with CLE. Methods: After written consent was obtained, we evaluated clinical, hyperpolarized helium-3 magnetic resonance imaging (3He MRI) and x-ray computed tomography (CT) airway measurements in a 20 year old with newly diagnosed and symptomatic CLE. Results: Lung function tests demonstrated mild airflow limitation with high airways resistance and normal diffusion capacity. Localized emphysema was present in the superior aspect of the left upper lobe (LUL) and CT-derived airway tree showed an abnormally thin-walled and wide-lumen atretic bronchus serving the apico-posterior segment of the emphysematous lobe. The parenchymal microstructure was distorted in the emphysematous region with elevated outer and inner radii of the acinar ducts and elevated acinar duct sleeve depth. Finally, the LUL had a high percent area of 3He ventilation defects with a heterogenous pattern of signal filling inwards from the edges of the emphysematous region suggesting collateral ventilation. Conclusion: Quantitative thoracic imaging provides a way to non-invasively and regionally evaluate the critical structure-function relationships in an adult case of CLE that was not evident using clinical spirometry or diffusing capacity breathing tests.

Dynapenia is associated with gait variability in community-dwelling older adults

Manuel Montero-Odasso, Anam Islam, Tim Doherty.

The loss of muscle mass, sarcopenia, in older adults is an important marker of frailty due to the association with mobility decline, falls, fractures, and mortality. However, dynapenia, the loss of muscle strength, has been shown to manifest earlier than sarcopenia and is more consistently associated with disability and mortality. It is unknown whether dynapenia is associated with early gait disturbances, specifically gait variability. Gait variability is a measure of gait regulation, and high gait variability has been proposed as an early marker of mobility decline and a predictor of falls. Our aim was to determine if dynapenia in community older adults is associated with poorer gait performance, specifically high gait variability. In 235 community-dwelling older adults (age ≥75) muscle weakness was assessed by measuring the average grip strength in the dominant hand using a handheld dynamometer. Gait variables were assessed under “usual” and “fast” pace conditions using an electronic walkway. Relative risk analysis evaluated the association of muscle weakness to each of the gait parameters. Older male adults in the lowest quartile of grip strength (≤22.17) had higher risk of slow gait velocity [RR (95%CI)= 2.54 (1.10- 5.84)] and increased stride time variability [RR (95%CI)= 2.08 (0.86- 5.00)], then those in the highest quartile of grip strength (>32.75). Our findings have interesting clinical implications because muscle strength assessments can be used in the clinic as an early screening tool to detect those with high gait instability, risk of falls, and mobility decline.

Regulation of Innate Immune Response to Apoptotic and Necrotic Cells by Renal Cell Carcinoma Cells through Phagocytosis

Nathoo, S, Zhong, Y. and Gunaratnam, L.,

The phagocytic clearance of apoptotic cells is essential for maintaining immune tissue homeostasis. Uncleared apoptotic cells can undergo secondary necrosis releasing endogenous danger associated molecular pattern (DAMP) molecules such as high mobility group box protein 1 (HMGB1) into the extracellular milieu, triggering the innate immune system. While most chemotherapeutic agents kill tumor cells via apoptosis, some cause the release of HMGB1 from dying cancer cells that facilitates dendritic cell maturation required for antigen presentation and cytotoxic T-cell activation known as immunogenic cell death. Kidney Injury Molecule -1 (KIM-1) is a receptor for the apoptotic “eat me” signal phosphatidylserine, shown to confer on epithelial cells the ability to clear apoptotic and necrotic cells during kidney injury. KIM-1 is overexpressed in various human tumours including renal clear cell carcinoma (RCC), though the significance of this on tumour progression is unknown. Using siRNA-mediated knockdown, we reveal that KIM-1 enables RCC cells to become semi-professional phagocytes for apoptotic and necrotic cells. The rapid clearance of apoptotic and necrotic cells by RCC cells was associated with a decrease in the passive leakage of HMGB1 from dying cells, attributable to KIM-1 expression. Finally, we show that conditioned medium from RCC cells that were fed apoptotic cells activated dendritic cells to lesser degree compared to the conditioned medium taken from RCC cells treated with siRNA targeting KIM-1. This suggests that the KIM-1 expression by cancer cells may allow them to evade immunogenic cell death and potentially explain why RCC tumours are highly resistant to chemotherapy.

Diabetes Care in Young Adults with Type 1 Diabetes after Transition to Adult Care

Rashmi Nedadur, Dr. Cheril Clarson, Selam Mequanint, Tracy Robinson, Dr. Tamara Spaic.

Transition from pediatric to adult diabetes care is a period of vulnerability with increased risk for interruption in care and adverse health outcomes. A population-based cohort study was conducted from 2002-2012 using local electronic medical records (Web DR). The goal was to determine the impact of transition on glycemic control and diabetes-related complications. Data from 148 subjects (47.3 % male), age 16-20 years with type 1 diabetes were collected. The majority (n=89, 60.1%) of subjects were on insulin pump therapy or multiple daily injections (n=58, 39.2 %). Mean A1C values during the 2 years prior to and post transition were 8.7 ± 1.7 % and 8.9 ± 1.8 % (p=0.33). Mean diastolic blood pressure increased from 67.3 ± 6.3 to 72.6 ± 7.9 mmHg (p<0.001) following transition but there was no change in systolic blood pressure. . Mean LDL cholesterol values did not change during transition Screening for microalbuminuria and dyslipidemia two years following transition were completed in 47 (31.8%) and 36 (24.3%) participants. Prior to transition there were 4 (2.7 %) participants with nephropathy,1 (0.7%) with dyslipidemia. Following transition, there were 8 (5.4%) patients with nephropathy, 7 (4.7%) with dyslipidemia, 4 (2.7%) with retinopathy, 4 (2.7%) with neuropathy, and 3 (2.0%) with hypertension. We documented a trend toward deteriorating glycemic control and increasing diabetes-related complications following transition from pediatric to adult diabetes care. Interpretation of these results is limited by the low uptake of complication screening. Strategies to optimize complications screening in those ‘at risk’ should be explored.

Administration of mitochondrial targeted anti-oxidants reduces cardiac hypertrophy and improves function in diabetic mice

Rui Ni, Dong Zheng,Tianqing Peng.

Introduction: Reactive oxygen species (ROS) production and consequent oxidative stress have been implicated in diabetic cardiomyopathy. Mitochondria are considered as one of main sources of ROS in cardiomyocytes. However, it has never been reported whether selective inhibition of mitochondrial ROS reduces cardiomyopathy in diabetes. This study investigated the therapeutic effects of mitochondria-targeted antioxidants on diabetic cardiomyopathy in both type-1 and type-2 diabetic mice. Methods and Results: Type-1 diabetes was induced in mice with multiple injections with streptozotocin (STZ, 50 mg/kg/day for 5 days). The diabetic mice received SS31 (mitochondria-targeted antioxidant peptide, 2mg/kg/day, i.p.) or mito-TEMPO (0.7 mg/kg/day, i.p.). A peptide SS20, which lacks antioxidant properties, served as a control for SS31. Two months after treatment with mitochondria-targeted antioxidants, myocardial function was assessed by echocardiography. Cardiac hypertrophy and mitochondrial ROS generation were determined thereafter. Injection with STZ significantly increased mitochondrial ROS production in mouse hearts. Administration with SS31 or mito-TEMPO significantly attenuated myocardial dysfunction and reduced myocardial hypertrophy as determined by decreased cardiomyocyte size and a reduction in hypertrophic gene expression (ANP and beta-MHC) in type-1 diabetic mice. In type-2 diabetic db/db mice, mitochondrial ROS generation was also increased in the heart compared with control db/+/- mice. Injection with mito-TEMPO for 30 days (0.7 mg/kg/day, i.p.) improved myocardial function in db/db mice. Conclusions: Administration of mitochondrial targeted anti-oxidants reduces cardiac hypertrophy and improves function in both type-1 and type-2 diabetic mice. Thus, selective inhibition of mitochondrial ROS generation may represent an effective therapy for diabetic cardiomyopathy.

Examining relationships between motor impairment and cognitive sub-classification with structural & metabolic imaging in mild cognitively impaired (MCI) patients. Results from the Gait and Brain Study

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The ability to assess the risk of transition between mild cognitive impairment (MCI) to dementia (such as Alzheimer's Disease) is a goal of the Gait and Brain Study. By longitudinally tracking biometric data (such as motor-signature of gait), cognitive testing, and structural and metabolic brain data (through use of magnetic resonance imaging (MRI)) we hope to determine who will progress to dementia. Sixty participants with MCI were classified into amnestic and non-amnestic groups based on current criteria. Motor function was evaluated assessing their gait performance using an electronic walkway. The role of cognition on their gait performance was evaluated using the dual task paradigm: walking while talking. Brain 3Tesla MRI was performed in each participant. The goal of this project is to investigate the relationships between cognition and gait by analyzing underlying structural and metabolic imaging data for various task conditions. Our preliminary results show significant differences between cognitive groups and task dependent volumetric correlations to motor signature which begins to uncover underlying brain anatomy and metabolism that link gait and MCI.

RIPK3-mediated necroptosis regulates cardiac allograft rejection

Pavlosky A, Lau A, Su Y Lian D, Huang X, Yin Z, Haig A, Jevnikar AM*, Zhang Z-X*.

Cell death results in tissue damage and ultimately donor graft rejection. Cell death can occur as an active molecular process through apoptotic, necrotic and newly identified Receptor Interacting Protein 1 and 3 kinase (RIPK1/3) mediated necroptotic pathways. Necroptosis leads to the release of inflammatory molecules which can activate host immune cells. This pathway has yet to be studied in heart transplantation. We have found that necroptosis was induced in murine cardiac microvascular endothelial cell (MVEC) under anti-apoptotic condition following TNFα treatment. Necroptotic cell death and release of the danger molecule high mobility group box 1 (HMGB1) were inhibited by the RIPK1 inhibiting molecule necrostatin-1 and by genetic deletion of RIPK3. In addition, tissue necrosis, release of HMGB1 and graft cell infiltrate were attenuated in RIPK3 null heart allografts following transplantation. Finally, a brief sirolimus treatment markedly prolonged RIPK3 null cardiac allograft survival in allogeneic BALB/c recipients as compared to wildtype C57BL/6 donor grafts (95+5.8 vs. 24+2.6 days, $P<0.05$). This study has demonstrated that RIPK1/3 contributes to MVEC death and cardiac allograft survival through necroptotic death and the release of danger molecules. Our results suggest that targeting RIPK-mediated necroptosis may be an important therapeutic strategy in transplantation.

Necrotizing Pneumonia: An observation of practice patterns and management changes over time.

Michael Peirce, Jade Coyne, Fran Priestap, Karen Bosma.

Rationale: Necrotizing lung infections are a rare, but severe and life-threatening complication of community-acquired pneumonia. Data on optimal management in the modern era is limited to case reports and case series' dating from 1975 to the present. The goal of this project was to examine local ICU practice patterns and determine if management or outcomes of necrotizing pneumonia have changed over time. Methods: A retrospective, observational study of patients admitted to the LHSC MSICU or CCTC from January 1, 2003 to December 31, 2013 was completed by chart review. Patients were screened for inclusion if they had an admitting diagnosis of pneumonia and/or had undergone bronchoscopy or computed tomography (CT) scan of the thorax (N=1267). Of these 1267 patients, we identified 49 cases for review and examined time intervals 2003-06, 2007-10 and 2011-13. Results: Using the Cochrane-Armitage trend test, our data shows improved survival over the 11-year study period ($p=0.02$). The number of CT scans increased over time ($p=0.03$) but there were no significant changes in the numbers of operating room visits or thoracic surgery consults. Chest x-rays showed features concerning for necrotizing pneumonia in 11 (22%) of 49 patients whereas CT was diagnostic in the 46 (100%) patients who had a CT. There was no significant difference in the incidence of necrotizing pneumonia over time. Conclusion: Our preliminary data suggests an increase in survival and the number of CT scans over time whereas management otherwise has not significantly changed in terms of thoracic surgery consults and operating room visits.

Risk of Arrhythmia and Mortality among Patients Prescribed Selective Serotonin Reuptake Inhibitors (SSRIs)

Elena Qirjazi, Amit Garg; Stephanie Dixon, Danielle Nash; Matthew Oliver, Akshya Vasudev, Ron Wald, Matthew Weir;.

Certain Selective Seratonin Receptor Antagonists (SSRIs) have been implicated as

triggers of ventricular arrhythmia through their effect in prolonging the QTc segment. This has resulted in FDA warnings against using higher doses of citalopram and escitalopram. This retrospective population-based cohort study aims to characterize the 90-day risk of ventricular arrhythmia from citalopram and escitalopram, versus sertraline and paroxetine (which have limited effects on the QTc). The study population consists of individuals from Ontario, Canada, who received a new out-patient prescription for the four study drugs between April 1st 2002 and Dec 31st 2012. The primary outcome is ventricular arrhythmia. Secondary outcomes are mortality, and the composite of ventricular arrhythmia and mortality. Adults from the exposed group (receiving citalopram and escitalopram) are matched one-to-one, to those in the unexposed group (receiving sertraline and paroxetine) based on demographics, index year, residential status, comorbidities (particularly coronary artery disease - CAD, congestive heart failure - CHF, and renal disease), medications, baseline healthcare use, medication dose (high/low), and type of prescriber; thus controlling for statistically significant confounding factors. Preliminary data indicate an overall event rate of ventricular arrhythmia in the order of 0.1%, increasing to 0.2 and 0.3 % respectively for individuals with CAD and CHF. The final analysis is still pending, but we expect that it will help define the clinical significance of ventricular arrhythmias in this group of medications.

Multi-dimensional indeces to stage idiopathic pulmonary fibrosis: a systematic review

Camilla Rozanski, Marco Mura.

Idiopathic pulmonary fibrosis (IPF) has the highest mortality rate among all interstitial lung diseases, with a mean survival time of 2 to 3 years from the time of diagnosis. Prognosis is difficult to determine, due to the recognized heterogeneous progression of the disease, as well as lack of a well recognized staging system. This in turn raises challenges when considering therapeutic options for IPF patients, such as lung transplantation, versus a more conservative approach. Multiple independent factors have been identified as prognostic indicators in IPF, and a number of studies have proposed multi-dimensional indices that combine several parameters in order to achieve a more accurate delineation of disease progression. In this systematic review, the Medline database was used to identify studies in the area of multi-dimensional staging of IPF. We analysed and critically appraised previously proposed prognostic scoring systems. Our aim is to encourage research developments in this area to help identify an optimal multi-dimensional staging system for IPF. Key words: idiopathic pulmonary fibrosis, multi-dimensional, staging, prognosis, survival, scoring system.

Increasing the use of low molecular weight heparin for thromboprophylaxis: a quality improvement study

Erica Rubin, Alan Gob, Andrew Smaggus.

BACKGROUND: Low-molecular-weight heparins (LMWH) and unfractionated heparin (UFH) are approved for DVT prophylaxis in medical inpatients. LMWH is associated with a ten-fold decreased rate of heparin-induced thrombocytopenia (HIT), and is considered the preferred agent at our centre. Our objective was to document to what extent UFH is still being prescribed to medical inpatients for DVT prophylaxis, and explore the reasons for its use. METHODS: A single day, cross-sectional audit of all 74 patients admitted to the medicine service was conducted. Patient charts were examined for medical factors influencing DVT prophylaxis prescriptions, and documentation explaining the choice of agent prescribed. RESULTS: Dalteparin was prescribed to 45% of patients, UFH to 19%, and no DVT prophylaxis was prescribed to 36%, usually due to bleeding or the need for anticoagulation. Of the patients initially prescribed UFH, 100% had a creatinine

over 160mL/min on admission. Of the patients initially prescribed dalteparin, three (11%) had a creatinine over 135mL/min. Of these three, two were switched to UFH within two days of admission. In two cases, patients were switched from dalteparin to UFH for renal insufficiency due to a suggestion by the pharmacist. CONCLUSIONS: UFH prophylaxis is prescribed to a large percentage of inpatients, and the primary reason for it being prescribed is renal insufficiency. Both residents and pharmacists appear to prefer UFH in renal insufficiency, despite the fact that dalteparin can be safely prescribed in this population. Phase 2 of the study will implement educational interventions to increase the use of dalteparin for DVT prophylaxis.

The Flavonoids Naringenin and Nobiletin Stimulate the AMPKinase Pathway in Primary Mouse Hepatocytes

Joshua Peter Samsoondar, Joshua P. Samsoondar, Lazar A. Bojic, Brian G. Sutherland, Gregory R. Steinberg, Cynthia G. Sawyez, Jane Y. Edwards, Dawn E. Telford and Murray W. Huff.

Dyslipidemia associated with insulin resistance and obesity are core features of the metabolic syndrome and type 2 diabetes, which contribute significantly to atherosclerosis. In mouse models of diet-induced metabolic dysregulation, the citrus flavonoids naringenin and nobiletin prevent obesity, hepatic steatosis, apoB100 overproduction, dyslipidemia, insulin resistance and atherosclerosis. To elucidate the mechanism of action in liver we assessed flavonoid-induced activation of AMP-activated protein kinase (AMPK), the major regulator of cellular energy homeostasis, in primary mouse hepatocytes. Stimulated AMPK activity promotes catabolic, ATP-generating processes such as fatty acid (FA) oxidation while inhibiting anabolic processes such as FA synthesis. In primary C57BL/6 (WT) hepatocytes, naringenin and nobiletin increased phosphorylation (P) of AMPK and its downstream target acetyl-CoA carboxylase (ACC) in a time- and dose-dependent manner. Phosphorylation of ACC by AMPK inhibits the formation of malonyl-CoA reducing substrate for FA synthesis while relieving inhibition of mitochondrial FA oxidation by malonyl-CoA. Under insulin resistant conditions stimulated by high glucose media, reduced pAMPK and pACC were reversed by flavonoid treatment in WT hepatocytes, whereas these effects were lost in Ampkβ1-/- hepatocytes. Sterol receptor element binding protein-1c, which stimulates lipogenesis, was also phosphorylated (inhibited) by flavonoid-induced AMPK activation. In chow-fed mice, i.p. injection of nobiletin following a fasting-refeeding protocol, depressed the respiratory exchange ratio indicative of a switch to FA oxidation. Freeze-clamped liver samples from these mice showed marked induction of pAMPK and pACC. These results suggest that naringenin and nobiletin attenuate hepatic steatosis and metabolic dysregulation, in part, through activation of hepatic AMPK.

Psoriatic Nail Changes Are Associated With Clinical Outcomes in Psoriatic Arthritis

Matthew Sandre, Dr. Sherry Rohekar, Dr. Lyn Guenther.

Objective: To characterize relationships between specific nail changes, psoriasis, and joint involvement in psoriatic arthritis patients. Methods: 188 subjects meeting CASPAR criteria had joint counts, axial measurements and physician global assessment of disease activity (MDGA) recorded by their rheumatologist. Fingernails were assessed, and photographs taken for dermatologist review. Results: 52.4% were male, mean age 53.8 years (SD+12.5), mean psoriasis and PsA duration 20.4 and 12.5 years respectively. 85.7% ever had skin disease, 89.9% peripheral arthritis and 12.7% axial arthritis. The mean tender joint count (TJC) was 2.5 (SD+4.8), swollen joint count (SJC) 2.0 (SD+3.7), Schober's 4.4cm (SD+1.5), occiput-to-wall 0.7cm (SD+2.3), chest expansion 4.1cm (SD+1.5) and MDGA 2.3 (SD+2.3). 91.5% had

>1 nail change (matrix 78.7%, bed 73.9%). Nail matrix changes included pitting (59.0%)>leukonychia (42.0%)>rough onychorrhexis (23.9%). Nail bed changes included splinter hemorrhages (55.9%)>onycholysis (51.6%)>oil spots (27.7%). Higher SJCs were associated with distal interphalangeal (DIP)/periungual psoriasis (p=0.001), more splinter hemorrhages (p=0.006) and any nail bed change (p=0.03). Higher TJCs were associated with rough onychorrhexis (p<0.001), DIP/periungual psoriasis (p=0.03), red spots in the lunula (p=0.001), crumbling (p=0.046), and any matrix (p=0.03), and bed change (p=0.03). Any nail change was associated with a higher Schober's measurement (p=0.01). Mean MDGA was higher with any nail matrix (p=0.03) or bed change (p=0.002). Conclusion: DIP/periungual psoriasis, splinter hemorrhages, rough onychorrhexis and red spots in the lunula were associated with higher joint counts, and nail matrix and bed changes with higher MDGA.

Comparison of cardiac enzyme testing in the emergency department before and after introduction high-sensitivity troponin testing

Augene Seong, Michelle Klingel Shelley McLeod Karl Theakston Munsif Bhimani.

Introduction: The purpose of this study was to compare the use of cardiac enzyme testing in the ED before and after introduction of the new hs-TnT assay. Methods: TnT and HsTnT data was retrieved for all visits to one of two academic tertiary care EDs during two separate one-year periods; before and 6 months after introduction of hs-TnT testing. Frequency of tests ordered, frequency of positive tests, time between repeat tests, and ED length of stay were compared between the two groups. Results: During the first study period, there were 111,206 ED visits for which 16.7% had an initial TnT ordered. During the second study period there were 111,769 ED visits and 17.4% had an initial hs-TnT ordered. The proportion of these initial tests that were positive increased from 9.2% to 10.8%. Of those patients who had an initial test done, 16.4% went on to have repeat testing with the TnT system, while 29.2% had repeat testing in the hs-TnT period. Of those patients who had repeat testing, positive repeat tests increased from 5.6% to 8. 3%. After implementation of hsTnt, the median time between initial and repeat tests decreased by 57 minutes. For those patients discharged home after repeat testing, the median ED length of stay decreased by 30 minutes. Conclusions: This study suggests that hs-TnT has reduced the time for repeat testing as well as length of stay for patients discharged after repeat testing. However, it has also increased the frequency of repeat testing.

Native Valve Left-Sided Infective Endocarditis in London, Ontario: A Review of the Patient Population and Outcomes

Nabha Shetty, Dr Marko Mrkobrada, Dr Sharon Baker, Dr Dave Nagpal.

Infective endocarditis (IE) is a serious condition with management challenges when it comes to the need for and timing of valve surgery. We conducted a retrospective review of native valve left-sided IE treated at London Health Sciences Centre between 2008 and 2011. We described the patient population and assessed two year outcomes in those that received surgery versus those that didn't, with a special interest in the intravenous drug use (IVDU) population. We also looked at outcomes based on timing of surgery. In total there were 93 patients of whom 48 received surgery. Non-surgical patients had a greater mean age compared to surgical patients (52 vs. 60, p=0.048). The non-surgical group had more hepatitis-C and hypertension. The surgical group had more congenital heart disease (p<0.05). Death in the non-surgical group was 58% versus 17% in the surgical group. A larger proportion of patients died during

their initial hospitalization in the non-surgical group compared to the surgical group (38% vs. 2%). Disease free survival was 33% for the non-surgical group and 77% for the surgical group. The IVDU subgroup had similar outcomes. We divided surgery into three subsets of timing: within 7 days, greater than 7 days/within 30 days, and greater than 30 days from admission. Death for each group was 11%, 0% and 30% respectively. Our results suggest early, non-emergent surgery may be beneficial in left-sided IE. Surgical cases had greater disease free survival at two years. Additional trials would aid in evaluation of the benefit of surgery.

Tricuspid Valve Infective Endocarditis in London, Ontario: A Review of the Outcomes of Surgical vs. Medical Management

Nabha Shetty, Dr Marko Mrkobrada, Dr Sharon Baker, Dr Dave Nagpal.

Tricuspid valve endocarditis is often a complication of intravenous drug use (IVDU). While guidelines for medical management are established, the benefit of surgery in this condition is unclear. We did a retrospective study of isolated native tricuspid valve endocarditis treated at London Health Sciences Centre between 2008 and 2011. We described the patient population and assessed two year outcomes in those that received surgery versus those that did not. We also looked at outcomes based on timing of surgery. There were 38 patients in total of whom 7 received valve surgery; 5 repairs, 2 replacements. All patients had a history of IVDU. Baseline characteristics were equal in both groups. Death was 43% in the surgical group versus 26% in the non-surgical group. In those that received surgery within 30 days of admission, death was 33% versus 50% in those who had surgery after 30 days from admission. No patients received emergent surgery (within 7 days of admission). The surgical group had 29% disease free survival at two years, versus 52% in the non-surgical group. Survival with complications was 29% in the surgical group and 23% in the non-surgical group. Morbidity was mainly related to ongoing IVDU. We concluded that in isolated native tricuspid valve endocarditis there was a trend towards increased mortality with surgery compared to non-surgical patients. Given the small number of cases and retrospective nature of this study, further clinical trials in this area would be beneficial to draw definitive conclusions.

A Case of Rapidly Destructive Inflammatory Arthritis of the Hip

Jenny Shu, Ian Ross, Bret Wehrli, Richard W. McCalden, Lillian Barra.

Rapidly destructive coxarthrosis (RDC) is a rare syndrome that involves aggressive hip joint destruction within 6-12 months of symptom onset with no single diagnostic laboratory, pathological, or radiographic finding. We report an original case of RDC as an initial presentation of seronegative rheumatoid arthritis (RA) in a 57-year-old Caucasian woman presenting with 6 months of progressive right groin pain and no preceding trauma or chronic steroid use. Over 5 months, she was unable to ambulate and plain films showed complete resorption of the right femoral head and erosion of the acetabulum. There were inflammatory features seen on computed tomography (CT) and magnetic resonance imaging (MRI). She required a right total hip arthroplasty, but arthritis in other joints showed improvement with triple disease modifying anti-rheumatic drugs (DMARD) therapy and almost complete remission with the addition of Adalimumab. We contrast our case of RDC as an initial presentation of RA to 8 RDC case reports of patients with established RA. Furthermore, this case highlights the importance of obtaining serial imaging to evaluate a patient with persistent hip symptoms and rapid functional deterioration.

The Impact of missing anti-citrullinated protein antibody (ACPA) serology on Outcomes in Early Rheumatoid Arthritis: Results from CATCH (Canadian Early Arthritis Cohort)

Jenny Shu, V.P. Bykerk, G. Boire, B. Haraoui, C. Hitchon, C. Thorne, D. Tin, E.C. Keystone, and Janet E. Pope for CATCH Investigators.

Anti-citrullinated protein antibody (ACPA) is a serum biomarker that is as sensitive as, but more specific than the rheumatoid factor (RF) and detected earlier in rheumatoid arthritis (RA). Although ACPAs are part of the American College of Rheumatology RA classification criteria, ACPA testing is not routinely paid for / accessible in all jurisdictions. The impact of missing ACPA in early inflammatory arthritis patients was studied to determine if failure to perform ACPA testing could cause a gap in care. 2191 patients recruited to CATCH were allocated to 3 groups: 1. seropositive (rheumatoid factor positive (RF+) and/or ACPA+), 2. seronegative (RF- /ACPA-) and 3. missing ACPA (RF negative [RF-]). Adjustments were made using regression analyses for age, sex, symptom duration, and smoking status if $p<0.1$ from Pearson's Chi-squared or Analysis of variance (ANOVA) tests. More seropositive patients fulfilled 2010 ACR/EULAR RA criteria. At 3 months, group 3 was treated with less DMARDs and methotrexate, but there were no significant differences in DAS28, HAQ-DI, proportion receiving corticosteroids, or physician/patient global assessments. Hence, patients with missing ACPAs were less likely to fulfill RA criteria and were treated differently with fewer medications. There may be a care gap in the unknown ACPA group who were RF negative, but there were no significant differences in outcomes such as DAS28, 3 month change in DAS28, or HAQ-DI despite less treatment. Hence, further study is needed regarding the cost-effectiveness of ensuring ACPA testing is available for patients with new onset inflammatory arthritis.

Blood pressure control in diabetic and non-diabetic renal transplant patients comparing ambulatory and office readings

Dou-Anne Siew, Norman Muirhead, Mary-Jeanne Edgar.

There has been ongoing debate about the contribution of hypertension to renal allograft survival and overall patient morbidity in the renal transplant population. Hypertension in the renal transplant patient is complex, and is likely an interplay between rejection, anti-rejection medications, a patient's comorbidities and their native renal disease. Nonetheless, blood pressure control whatever the cause has been shown to be crucial to improving patient and graft survival. Numerous studies have noted that hypertension has been associated with a higher incidence of early rejection. One study showed a higher rate of allograft failure of 30% for each 10mmHg elevation in systolic blood pressure. Studies examining ambulatory blood pressure in renal transplant patients are few, and report significant differences between office and ambulatory blood pressure readings. Our cohort study examined retrospective data, and ambulatory blood pressure data collected from Nephrology transplant clinic patients at LHSC. Approximately 100 non-diabetic and 50 diabetic patients were analyzed, with 19 non-diabetic and 10 diabetic patients taking part in the ambulatory blood pressure segment of the study. We anticipate differences between the two groups in antihypertensive medication, achieved blood pressure control, clinic compared with ambulatory blood pressure readings. This cohort retrospective study aims to illustrate differences in anti-hypertensive management and control between diabetic and non-diabetic transplant patients. (DATA PENDING)

A retrospective study of the predictors of clinical benefit from acetylsalicylic acid

desensitization in patients with nasal polyposis and asthma

Kulraj Singh, Christine Ibrahim, Gina Tsai, David Huang, Jorge Mazza and William D Moote.

Background: Aspirin-exacerbated respiratory disease (AERD), also known as Samter's triad, is a clinical syndrome that consists of aspirin (ASA) intolerance, chronic rhinosinusitis with nasal polyposis, and intrinsic bronchial asthma. ASA challenge is the gold standard for diagnosis1, although 'silent desensitization' has been reported in patients on chronic therapy with montelukast.1 Little is known about the practice of ASA challenge and desensitization in Canada, which may have accounted for its omission as a viable therapeutic option in the latest Canadian clinical practice guidelines for acute and chronic rhinosinusitis. Methods: This retrospective study included 111 patients who underwent ASA desensitization in the Allergy and Immunology clinic at St. Joseph's Healthcare (SJHC) in London, Ontario. The mean age was 50.7 years, and 58 (52.5%) were male. 64 (61%) patients claimed prior significant reactions to ASA and features consistent with AERD. Results: 81 (73%) patients stated symptom improvement after achieving maintenance dosing on the desensitization protocol. Of this population, 24 (21.6%) improved in all 3 areas of AERD (sense of taste/smell, upper respiratory symptoms and lower respiratory symptoms). 29 (26.1%) had adverse effects, most often gastrointestinal upset, but no severe adverse effects were seen. Conclusion: ASA desensitization improves AERD symptoms and allows patients to better tolerate ASA and non-steroidal anti-inflammatories (NSAIDs), which is of particular benefit in the pain and cardiovascular population. There should be further studies conducted in Canada as well as consideration of this procedure under the next clinical practice guidelines.

Nutritional Management in Inflammatory Bowel Disease Inpatients

Elie Skaff, Nilesh Chande.

The goal of this quality improvement study was to examine the nutritional management of patients with CD or UC admitted with disease flares at University Hospital (UH) and Victoria Hospital (VH) of London Health Sciences Centre. Methods: All inpatients admitted with either CD or UC flare in the 2011-2012 calendar years were identified. Charts were reviewed and comparisons were made between UH patients who are in a Gastroenterology Ward under a gastroenterologist, and VH patients who are in a Medicine Clinical Teaching Unit Ward under a non-gastroenterologist most of the time. Results: 115 patients met inclusion criteria. 76 patients were at UH with 48.7% having CD, and 39 patients were at VH with 56.4% having CD. There was no evidence of a difference between sites and/or between diseases adjusting for the other. 41.7% of patients received a dietitian consult, 21.7% of patients were placed on restricted diets for no valid reason. Mean length of stays (LOS) were 6.9 and 4.9 days for CD patients at UH and VH, respectively, and 7.7 and 6.6 days for UC patients at UH and VH, respectively. LOS were longer at both UH and VH sites when dietitians were consulted. Conclusions: There was no evidence of a difference between sites (UH and VH) and/or between diseases (CD and UC) adjusting for the other. Proper nutritional management of CD and UC could contribute to decreased LOS of inpatients, but other factors not taken into account in this study can also significantly play a role.

Corticosteroid use in the Treatment of Anaphylaxis in the Emergency Department

Victoria Smith, Michelle Klingel, Shelley McLeod, Eman Loubani.

INTRODUCTION: Emergency department (ED) treatment of a acute anaphylaxis should consider the possibility of biphasic reactions, which can develop within 72 hours of the initial reaction. Although corticosteroids have been suggested for prevention of biphasic anaphylaxis, there is no clear consensus regarding their use. The objective of this study was to determine the proportion of patients treated with corticosteroids after presenting to the ED with acute anaphylaxis, and the proportion having a biphasic reaction within 72 hours of their initial ED visit. METHODS: This was a retrospective chart review of all patients presenting to one of two tertiary care EDs with a discharge diagnosis of anaphylaxis or anaphylactic shock from April 2012-March 2013. Patient data were recorded by trained research personnel. RESULTS: Of the 140 patient encounters included, 118 (84.3%) had epinephrine administered either pre-hospital or in-hospital. 127 (90.7%) patients received corticosteroids in the ED. Of these, 40 (31.5%) were given orally and 87 (68.5%) were given intravenously. Median (IQR) time to steroid administration was 36.5 min (19, 57). 5 (3.6%) patients were admitted. No in-hospital patient deaths occurred. Biphasic reactions occurred in 6 (4.3%) patients, all of whom were given corticosteroids during the initial ED presentation. CONCLUSIONS: Despite the paucity of evidence supporting their use in the prevention of biphasic anaphylactic reactions, corticosteroids were used by the majority of clinicians in the treatment of anaphylaxis in the ED. Future studies should assess the use of corticosteroids to prevent biphasic reactions in anaphylaxis.

A Systematic Review Of The Role Of Erythropoietin In The Pathophysiology Of Anemia In Elderly Patients

Swetha Sriram MD, Anargyros Xenocostas, MD, FRCPC and Alejandro Lazo-Langner, MD, MSc.

Introduction: Anemia has a significant impact on morbidity and mortality in the elderly, but identifying the etiology can be challenging. Postulated mechanisms of anemia of unknown etiology (AUE) include a blunted response to erythropoietin (EPO) or inadequate EPO production in response to anemia. We conducted a systematic review of observational studies to explore the relationship between EPO levels and anemia of unknown etiology. Methods: We searched Medline, EMBASE, Web of Science, Biosis Previews, and Dissertations and Theses using the MeSH subject headings erythropoietin, anemia, elderly and diagnosis. Additional articles were identified by searching the meeting abstracts of the European Hematology Association and the American Society of Hematology. Studies needed to report data on EPO levels in elderly individuals diagnosed with AUE for inclusion. Results: The search identified 4277 relevant citations, of which 31 studies were reviewed in full. 7 cohort studies were included in the final review. In general, studies found: 1) lower EPO levels in AUE compared to other forms of anemia; 2) no correlation between EPO levels and the severity of anemia; and 3) EPO levels in AUE that are generally higher than in non-anemic patients. Conclusion: Our findings suggest that EPO levels are generally elevated in elderly individuals with AUE, but remain inappropriately low when compared to anemia of other etiologies. This suggests either a relative EPO deficiency, an abnormal EPO response, or an abnormal erythroid cell response to EPO. Further research is required to elucidate the mechanisms involved and the value of pharmacological interventions.

Epidemiology of Infective Endocarditis in a Large Canadian Tertiary Care Centre: A Retrospective Database Study

Dr. Vidya Sujana Kumar, Dr. Sameer Elsayed.

INTRODUCTION: Infective endocarditis (IE) is a common problem seen in clinical practice worldwide. The epidemiology of IE varies from centre to centre and has evolved over the course of time. To our knowledge, there are very few published studies on the epidemiology of IE in Canada. As such, the aim of our study was to assess various epidemiological and microbiological trends related to IE at London Health Sciences Centre (LHSC). METHODS: A 6-year retrospective electronic and hard copy medical chart-based study was performed on patients admitted to LHSC from January 1, 2007 to December 31, 2012. Inclusion criteria included a clinical diagnosis of infective endocarditis, age greater than or equal to 16 years, and address of residence within Southwestern Ontario. RESULTS: A total of 194 patients met the study criteria. Of these, 85 (43.8%) had a history of IV drug use (IVDU). A total of 172 (88.7%) cases of IE involved native heart valves. In patients with native valve IE, 91 (46.9%) had no known history of IVDU. Prosthetic valve infection occurred in 22 (11.3%) cases. Staphylococcus aureus was the causative organism in 106 (54.6%) cases and was associated with higher mortality rates. Viridans group streptococcus accounted for 46 (23.7%) cases, while non-viridans group streptococci was associated with 11 (5.7%) cases. CONCLUSION: Infective endocarditis is a serious healthcare concern at LHSC, with Staphylococcus aureus accounting for over half of cases. Further work needs to be done to characterize long-term outcomes in this population.

Infrarenal Abdominal Aortic Aneurysm Causing Common Bile Duct Obstruction

Dr. Vidya Sujana Kumar, 1) Dr. Abdullah Alnasser, PGY5 in Gastroenterology 2) Dr. Roya Etemad-Rezai, Department of Medical Imaging 3) Dr. Karim Qumosani, Department of Gastroenterology, faculty supervisor.

Biliary obstruction is commonly caused by obstructive stones, pancreatic cancer, cholangiocarcinoma, or hepatic cholestasis. Here we present a rare case of biliary obstruction in an 85 year old male, secondary to a large infrarenal abdominal aortic aneurysm compressing the common bile duct. Eight similar case reports exist in the literature. This is a very rare cause of biliary obstruction, but should be carefully considered in a patient with a known abdominal aneurysm after other causes of biliary stasis have been excluded. Our patient opted against operative intervention, and is still being followed by a vascular surgeon for progression of his symptoms.

Assessing Proposed Echo Aortic Root Measurement Guidelines: An LHSC Quality Assurance Study

Shruti Tandon M.D., A.J. McInnis, David McCarty M.D..

Background: Aortic root dilation is strongly associated with the presence and progression of aortic insufficiency and the occurrence of aortic dissection. It is recommended this standard measurement be reported on all transthoracic echocardiograms (TTE). Current guidelines define normal aortic root diameters for 3 age subgroups based on body surface area. A recent study reported strong independent associations of aortic root size with age, body size and gender, and based on these variables, proposed normal ranges. We explored the effect of reclassifying aortic root dimensions using the proposed system and hypothesized this would reduce the prevalence of patients classified as dilated. Methods: We included TTE studies in patients ≥15 years old, over 39 months. The presence of conditions associated with aortic root dilation was determined for all patients including aortic regurgitation, hypertrophy and abnormal geometry. Data are expressed as mean or percentages, with appropriate statistical tests used to attribute significance for differences observed between continuous or categorical data. Results: 59912 studies from LHSC/SJHC were screened for inclusion and

27376 studies analyzed after applying exclusion criteria. Using the current criteria, 3.1% of our population was dilated. Using the proposed BSA classification, this reduced to 2.2%. Patients reclassified as normal were younger, lower in weight and less likely to have LV pathology. 7.1% of our population was dilated according to the echocardiographer. Males, increased height and increased LV volume were amongst parameters associated with over reporting. Conclusion: The proposed classification system reduced the prevalence of dilation and identified disease more appropriately.

Non-invasive measurement of cardiac output in patients with aortic stenosis: Comparison of Electrical Cardiometry and Thermodilution method

John Teefy, Kourosh Karimi, Bayan Malakouti, Priya Varghese, Amin Zagzoog, Patrick Teefy and Kambiz Norozi.

Aim: The purpose of this study was to evaluate the agreement of cardiac output (CO) measurements obtained by non-invasive Electrical Cardiometry (EC, COEC), and those derived from the “gold standard” measured by the Thermodilution (COTD) during catheter investigation in 52 adults with aortic valve stenosis. Methods: Simultaneous measurements of CO, obtained by means of COEC and COTD, were compared, so far in twenty-one patients (10 female, 11 male), mean ages 74 years (SD=9), undergoing diagnostic right and left heart catheterization. For non-invasive measurements of COEC, which is a variation of impedance cardiography, standard surface electrodes were applied to the left side of the neck and the left side of the thorax at the level of the xiphoid process. COTD was determined during the heart catheterization. Results: A good correlation (r = 0.72) was found between COEC and COTD (p=0.0005). The bias between the two methods (COEC – COTD) was -1.1 L·min-1.According to the Bland and Altman method, the upper and lower limits of agreement, defined as mean difference ± 2SD, were +1.2 L·min-1 and -2.8 L·min-1, respectively. Conclusions: Although Electrical Cardiometry compared to Thermodilution in these twenty-one patients underestimates the cardiac output, COEC demonstrates acceptable agreement with data derived from COTD in adults with aortic stenosis. In the first glance it seems that EC can be applied for continuous non-invasive beat-to-beat estimation of CO. Further data will be acquired to establish more robust analysis of data.

The incidence of, and risk factors associated with, trastuzumab-induced cardiotoxicity in women with non-metastatic HER2-positive breast cancer

Dr. Alison Weppler, Dr. Bryan Dias.

BACKGROUND Trastuzumab confers a significant survival benefit in HER2-positive breast cancer, decreasing both locoregional and distant recurrence and increasing overall survival. However, trastuzumab-induced cardiotoxicity (TIC) has emerged as a significant, but still incompletely understood, source of morbidity for patients. To date, there is conflicting data on the factors that place women at increased risk of TIC. OBJECTIVE To retrospectively quantify the incidence of TIC at the LRCP and to identify risk or protective factors associated with TIC. METHODS Retrospective chart review using an institutional database, which identified women with non-metastatic breast cancer who started trastuzumab between January 1, 2011 and December 31, 2012. OUTCOME Primary outcome was TIC, defined as LVEF<50% or an absolute decline in LVEF ≥15% from baseline. Secondary outcomes were the ORs associated with the potential risk and protective factors. RESULTS Among 127 patients, there were 20 cases of TIC (15.7%, 95% CI 10.5-23.5%) and 6 cases of symptomatic heart failure (4.7%, 95% CI 2.2%-10.3%). Treatment was altered in half of the cases of TIC, with trastuzumab stopping

after an average of nine cycles. None of the classic cardiac risk factors or other potential risk factors (age>60, prior radiation, anthracycline exposure) were associated with a statistically significant increased risk of TIC. Similarly, use of cardiac medications did not decrease the risk of TIC. CONCLUSION TIC is a relatively common, though generally asymptomatic, morbidity associated with trastuzumab. Unfortunately, it remains difficult to risk stratify women, and therefore frequent surveillance with cardiac imaging is required.

Frontline perceptions of low-value added inpatient practices on a clinical teaching unit

Jeff Yu, Marko Mrkobrada.

BACKGROUND: Urinary catheterization and daily “routine” blood work are two commonly performed inpatient activities that may not add value to overall care, and thought to be poorly recognized by resident physicians. This study aims to compare resident perceptions to actual practice. METHOD: 50 internal medicine residents were surveyed regarding perceptions on urinary catheter management and daily routine blood work. 164 charts of general medicine inpatients were retrospectively reviewed. RESULTS: 79.2% of residents believed in prompt removal of urinary catheters, while only 16.0% would assess this daily. The majority of residents overestimated the catheter utilization rate at 41-60 (52.0%) or 61-80 (28.0%) per 100 patient-days; actual rate 39.6. Most residents (46.0%) felt that only 21-40% of patients had catheters removed by admission day three, and 41-60% by day five; actual practice 67.9% and 78.6%, respectively. 72.3% of responders believed daily routine blood work is somewhat important; 21.3% thought very important. Most residents estimated the blood work utilization rate at 61-80 (53.1%) or 81-100 (42.9%) per 100 patient-days; actual rate 100.6. All responders believed 81-100% of patients had routine blood work for the first three admission days; actual practice 81.1%. However, residents overestimated this for day five at 61-80% (34.7%) or 81-100% (63.3%); actual practice 33.1%. CONCLUSION: Residents agreed, though overestimated, that urinary catheters are overused and not promptly removed. Residents also believed they order a high number of daily routine blood work, consistent with actual practice. This study can serve as an opportunity for further promotion of improving resident practice patterns.

MiR-195 represses Pim-1 expression and promotes endothelial cell apoptosis in sepsis

Dong Zheng, Yong Yu, Minghui Li, Grace Wang, Bainian Chen, Tianqing Peng.

Background: A group of circulating miRs including the miR-15 family members are increased in septic patients and may be associated with septic death. The miR-15 family members have been implicated in apoptosis. Apoptosis in endothelial cells contributes to organ failure in sepsis. This study investigated the role of miR-195, a member of the miR-15 family in endothelial cell apoptosis in sepsis. Methods and Results: MiR-195 was elevated in plasma of septic mice. Up-regulation of miR-195 was sufficient to induce apoptosis and enhanced lipopolysaccharide (LPS)-induced apoptosis in cultured mouse pulmonary micro-vascular endothelial cells. Inhibition of miR-195 prevented apoptosis in response to LPS. In addition to down-regulation of its known targets Bcl-2 and Sirt1, miR-195 mimic also reduced Pim-1 protein expression. Multiple computational algorithms predicted the Pim-1 3' un-translated region (UTR) to be a target of miR-195. Studies using luciferase reporters carrying wild-type and mutant Pim-1 3' UTR confirmed Pim-1 as a direct target for miR-195. Over-expression of Pim-1 prevented apoptosis in endothelial cells induced by LPS and miR-195 mimic. In mouse models of both LPS- and faeces-injection-in-peritoneum-induced sepsis, silencing of miR-195

reduced apoptosis and neutrophils infiltration, and increased protein levels of Bcl-2, Sirt1 and Pim-1 in lung tissues. However, these protective effects of miR-195 silencing were significantly attenuated by Pim-1 inhibitor in septic mice. Conclusions: This study demonstrates a critical role for miR-195 in pulmonary micro-vascular endothelial cell apoptosis in sepsis and identifies Pim-1 as a novel target of miR-195. Thus, miR-195 may represent a novel therapeutic target for sepsis.

Effective feedback: a resident's perspective

Tina Zhu, Myers K.

Background: Learners' perceptions of the credibility and utility of assessments regarding their clinical performance have implications on their internalization and application of this feedback. Purpose: This study explores the perceptions of Internal medicine residents regarding the quality and quantity of received feedback, and identifies the type of comments they view as most effective as feedback. Method: An anonymous 31 question online survey was distributed via email to the cohort of Internal Medicine residents at one university. Scaled items were designed to solicit residents' perceptions of the various types of feedback they receive. They also rated 16 sample feedback comments with regard to their overall valence (positive or negative) and their perceived utility as feedback. Results were analyzed using descriptive statistics. Results: Overall response rate was 52% (61/118). Residents were most interested in receiving feedback from attending physicians and other residents, however only 19% reported receiving frequent feedback from these sources. Most residents (90%) perceived face-to-face feedback as effective, while only 10% rated mini-clinical evaluation exercises as useful. Of the 7 CanMeds roles, residents are most interested in receiving feedback regarding their performance as medical experts. Of the sample comments, residents identified those with behaviourally specific content as the most useful, regardless of the perceived valence of the feedback. Conclusions: Although residents value face-to-face feedback from their clinical supervisors, they perceive these interactions as occurring infrequently. Residents view comments that are 'negative' in valence as useful if they target specific areas for improvement.

Clinical presentation and outcome of patients with false--positive ST--segment elevation myocardial infarction

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Background: Activation of cardiac catheterization laboratory through regional code STEMI programs by paramedics shortens treatment time but may increase the rate of false-positive STEMI. Methods: In this case-control study, 259 consecutive patients with true code STEMI were compared to 81 consecutive patients with false code STEMI activation. The clinical presentation, electrocardiographic features, etiology, and outcomes were assessed. We also compared the effectiveness of out of hospital and in-hospital activation of code STEMIs. Results: The false-positive and true STEMI groups were similar in their coronary artery disease risk factors except for dyslipidemia which was lower in the false-STEMI group (28.4% vs. 42.5%, P=0.02). Patients with false-positive STEMI were less likely to have typical chest pain (43% vs. 79%, P<0.01). The initial ECG in the false-positive STEMI group showed more concave ST elevation (60% vs. 31%, P<0.01), and less reciprocal ST-depressions (16% vs. 70%, P<0.01). The two groups had similar mortality at 30 days. In the true STEMI group, out-of-hospital activation reduced the first medical contact-to-device time by an average of 51 minutes, and 60% of the out of hospital activations achieved the 90 minutes first medical contact-to-device target compared to only 23% of the in-hospital activations. Conclusions: Patients diagnosed with false-positive STEMI have relatively poor outcome

due to other medical conditions. Careful history and review of ECG helps to differentiate this group from true STEMI. Activation of code STEMIs by paramedics reduces first medical contact-to-device time compared to in-hospital activations.

A Case Report of Warfarin and Carbamazepine Drug Interaction

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Warfarin is the most frequently prescribed anticoagulant worldwide, and is known to be highly efficacious in the prevention and management of thromboembolisms. Drug interactions remain a challenge in managing patients that require warfarin therapy. Many of these interactions are a result of induction or inhibition enzymes involved in warafarin metabolism. Carbamazepine widedly prescribed for epilepsy as well as chronic pain. We report the case of a 44-year-old prescribed warfarin after receiving mechanical mitral and aortic valves three months prior to being assessed by our team. Patient is also on carbamazepine CR 200 mg/day for seizure control. She showed warfarin resistance, as demonstrated by repeated sub-therapeutic INR values. Her observed warfarin maintenance dose of 13 mg/day was significantly higher than the predicted dose 6 mg/day using our genomics-guided dosing nomogram. We then measured S and R warfarin plasma levels. Despite her higher than predicted warfarin dose, her measured S-warfarin levels were within the expected therapeutic range for someone with her VKORC1 genotype. Since INR values were in the target range, it would appear that the higher than predicted dose of warfarin was required to maintain a therapeutically relevant S and R-warfarin levels. The observed phenomenon is consistent with induction of both CYP2C9 and CYP3A4 by carbamazepine. Our case illustrates the importance of integrating induction-related drug interactions, as well as pharmacogenomic parameters for optimal warfarin dosing, and such patients may require far higher than predicted dose of warfarin to attain therapeutic benefit.

Management of very severe hypertriglyceridemia with and without plasma exchange

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Background: Acute pancreatitis (AP) is a potentially life-threatening complication of severe hypertriglyceridemia (HTG). The risk of AP markedly increases with very severely increased triglyceride (TG) levels > 22.6 mmol/L (normal < 1.7 mmol/L).Usual management of HTG-induced AP includes: 1) cessation of oral intake; 2) fluid replacement; and 3) correction of secondary factors that predispose to HTG. Plasma TG levels typically fall with these conservative measures and patients typically stabilize and survive. Recently, several anecdotal reports of plasmapheresis in the early stages of HTG-induced AP have demonstrated dramatic TG reductions, prompting some clinicians to recommend this intervention in the acute setting. Description: We report three patients consecutively admitted to our hospital in 2013 with very severe HTG-induced AP: cholesterol and TG levels at baseline were: patient #1 - 17.4 (normal < 5.2) and >62.2 mmol/L; patient #2 -10.8 and 44.0 mmol/L; and patient #3 - 41.7 and >62.2 mmol/L respectively. Patients #1 and #2 received no PLEx, while patient #3 received a single course of PLEx within 24 hours of admission. By 72 hours, plasma TG was reduced by 68%, 77% and 73% in patients #1, #2 and #3, respectively. Dynamics of TG reduction followed a similar for trajectory over the next week for all three patients. All three patients were eventually discharged with essentially normal profiles. Conclusion: The clinical course in these three patients with severe HTG-induced pancreatitis suggests that PLEx is not necessary even in very severe cases, and that TG levels will correct rapidly with conservative measures and control of secondary factors.