University of Western Ontario
Department of Medicine

RESEARCH DAY

Thursday, May 7, 2015
Best Western Lamplighter Inn
591 Wellington Road South
London, Ontario N6C 4R3

This program has no commercial support.

CME INFORMATION

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification program of The Royal College of Physicians and Surgeons of Canada and approved by Continuing Professional Development, Schulich School of Medicine & Dentistry, Western University (5.25 hours). Each participant should claim only those hours of credit that he/she actually spent participating in the educational program.

Learning Objectives:

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

Department of Medicine
Resident Research Day 2015
Thursday May 7, 2015
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	The Perfect Storm - Transition to Research Career **Dr. Tamara Spaic** *(Crystal Ballroom North)*	
9:20	10:00	Keratin-19 Positive Stem Cells are Radioresistant Cancer-Initiating Cells in the Colon **Dr. Samuel Asfaha** *(Crystal Ballroom North)*	
10:00	11:00	**BREAK** *(Atrium)*	**Poster Presentation and Judging** *(Crystal Ballroom South)*
11:00	11:45	Facing Hospital Challenges Through Innovative Research and Knowledge Translation **Keynote Dr. Robin Walker** *(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)*	
16:45	17:00	*Please ensure that you fill out the evaluation form provided before you leave for the day and drop it in the box at the Registration Desk on your way out.*	

Oral Presentations

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2:00pm	Vighnesh Bharath	PGY-3	Incidence and natural history of intravenous immunoglobulin-induced aseptic meningitis: a retrospective review at a single tertiary care centre	14
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2:30pm	Meghan Garnett	PGY-4	Did changes to the Ontario Highway Traffic Act in 2009-2010 affect the proportion of alcohol-impaired motor vehicle collisions seen at a Level I Trauma Centre over a 10-year period?	19
2:45pm	Christine Ibrahim	PGY-3	ADrenal InsufficiEncy, QUAlity of life, and Treatment in the Emergency room [ADEQUATE Study]	22
3:00pm	**Refreshment Break**			
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3:30pm	Gitadokht Majdi	PGY-5	High dose levothyroxine absorption test to differentiate between malabsorption and non-adherence: 5 cases and discussion	30
3:45pm	Alpesh Shah	MSc Student	Methotrexate and cardiovascular events: systematic review and meta-analysis	43
4:00pm	Baekjun Sung	MSc Student	Loss of RIPK3 and Caspase-8 enhance intrinsic apoptosis in tubular epithelial cell (TEC) death and contributes to kidney ischemia reperfusion injury (IRI)	45
4:15pm	Xiaxin (Tony) Zhang	PGY-2	Is Rheumatoid Arthritis Cervical Spine Involvement Decreasing Over Time? Results from a Meta-Analysis	48

Poster Presentations

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106	John Basmaji	PGY-2	Impact of a Critical Care Outreach Program on Night time Discharges from the Intensive Care Unit (ICU)	12
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109	Robert Biswas	PGY-5	Caregiver-delivered delirium prevention in hospitalized patients - a pilot study	14
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Improving Hemodialysis Patient Vaccination Rates through HUGO Powerform and Module

Ali Alfageeh, Laila Sadagah, Alaa Alem, Seychelle Yohanna, Amit Patel, Andrew Burke, Nabil Sultan.

Hemodialysis patients are at increased risk for infectious disease due to their relative immunosuppression and the infectious exposures of their blood during treatment. We performed a quality improvement project to improve the appropriate vaccination rates for Hepatitis B, Influenza and Pneumococcus in hemodialysis patients at the Adam Linton Unit (ALU) of LHSC. Through a fishbone diagram, the primary barriers to timely and appropriate vaccination were the absence of digital documentation, communication gaps with primary care physicians and a lack of clinician prompts to vaccinate at the appropriate time. Baseline vaccination rates were assessed. Following consultation with representatives from ALU nursing and infection control, the most viable solution to the identified barriers was the creation of a new vaccination module within HUGO. A Powerform was designed to allow physicians and nurses to document vaccination status. This information was carried forward to provide a convenient record for future reference. The Powerform was linked to the results section, providing virus titres and previously received immunizations. To enhance communication, the data from the Powerform was displayed in a widget on the main clinical dashboard as well as a separate tab in the results section. The Powerform was piloted by physicians and nurses and implemented for ALU patients. The result of the program was improved clinician satisfaction with the reliability of the vaccination program and enhanced ability to monitor vaccination rates over time.

Hepatocellular Carcinoma Response to Local Regional Therapy; Correlations between Pre-Liver Transplants Imaging and explant pathology

Mansour Alghanem, M. Garisa, D. Driman, O. Bashir, B. Al Judaibi, N. Kakani, P. Marotta, K. Qumosani.

BACKGROUND: Hepatocellular Carcinoma (HCC) therapy includes Local regional Therapy (LRT) such as Radiofrequency Ablation (RFA) and Trans-Arterial Chemoembolization (TACE). Modified Response Evaluation Criteria in Solid Tumors (mRECIST) were developed to assess the response to treatment in patients with HCC, based on measurements of viable tumor using dynamic imaging (CT/MRI). AIM: To compare the estimate of viable HCC after LRT by CT imaging and before liver transplant, to the histopathological assessment of viable HCC in the hepatic explant. METHODS: We prospectively evaluated all patients with HCC who underwent both LRT and liver transplantation at london health science centre. Using mRECIST criteria, the response to LRT was assessed by two blinded radiologists. The results from the radiologists were compared to the findings of an expert pathologist reporting on viable tumour present . Both parties were blinded so prevent bias in the results. RESULTS: A total of twenty six transplant recipients fulfilled the inclusion criteria for the study. Six patients (23%) received RFA while twenty patients (77%) received TACE treatments as bridging therapy. twenty (76%) recipients (20/26) had accurate assessment for necrosis (mRECIST) within 20% comparing rCT to explant (i.e. concordant). thirteen (50%) of the 26 predicted 100% concordance. Only 3/26 (11.5%) had a poor concordance (>50%) between histology and reference CT images. positive correlation was detected with the correlation coefficient is calculated as 0.5723 CONCLUSION: Dynamic CT is

an accurate tool to evaluate the tumour response prior to liver transplantation and the likelihood of underestimating the tumour burden is low.

Improving Accuracy of Predicted Discharge Timing at Bullet Rounds: A Quality Improvement Project

Andrew Appleton, Andrew Smaggus, Saira Zafar, Alan Gob.

Context: The Clinical Teaching Unit at University Hospital, London Health Sciences Centre is a 71-bed acute care medicine service. Patients are cared for by internists, residents, medical students, patient care facilitators, nurses, and allied health staff. These stakeholders are involved in predicting the timing of each patient's discharge at daily "bullet rounds". Patients are assigned one of three colour statuses based on projected time until discharge (green <24h, yellow <72h, red >72h). Problem: Accurately predicting time of discharge is important in order to assign the right services at the right time. We are currently inaccurate with predictions. A one-week analysis demonstrated only 46% of green and 60% of yellow statuses discharged by 24 and 72 hours respectively. Process: We sought to understand the reasons for inaccuracies by discussion with stakeholders, observation of bullet rounds, and auditing delayed discharges. Analysis: Colour designation is largely a physician-led process, suggesting over-emphasis of medical status compared to functional status. Allied health services mainly use the colour statuses for triaging case priority. Bullet rounds are run in an environment fraught with distraction and attendance by stakeholder groups is variable. During a one-week audit there were 35 unique delayed discharges. The most common reason for delay was medical status in 49% of cases. Other common reasons included 14% social, 11% awaiting diagnostics, and 11% pending assessments. Future strategy: We aim to improve the environment for rounds, reduce variability in stakeholder participation and create guidelines/action plans for each colour status to more accurately predict discharge timing.

Septic Murine Pulmonary Microvascular Endothelial Barrier Dysfunction is Regulated by TIMP3

Valerie Arpino, Lefeng Wang, Cynthia Pape, Ryan Bird, Mark Keh, Sanjay Mehta, and Sean E. Gill.

Sepsis often causes dysfunction of pulmonary microvascular endothelial cells (PMVECs) leading to severe pulmonary edema. Metalloproteinases can regulate endothelial function through processing of cell surface proteins, including adherens junctions proteins, which has been associated with increased permeability. Tissue inhibitor of metalloproteinases 3 (TIMP3) regulates metalloproteinase function in the lung following injury. Thus, we hypothesize that TIMP3 promotes PMVEC stability via inhibition of metalloproteinase activity. To test this hypothesis, we used PMVECs isolated from WT and Timp3-/- mice. PMVECs were treated with PBS or cytomix (equimolar interferon γ, tumour necrosis factor α, and interleukin 1β) in order to mimic septic conditions. We found that TIMP3 levels (mRNA and protein) were decreased in WT PMVECs in a time-dependent fashion under septic conditions (cytomix). Analysis of leak (transendothelial electrical resistance, dextran, and albumin flux) revealed that Timp3-/- PMVECs had significantly higher permeability under resting conditions (PBS) vs. WT PMVECs. Although cytomix treatment significantly increased WT trans-PMVEC permeability, there was no effect on Timp3-/- PMVEC barrier function.

Additionally, the increased basal Timp3-/- PMVEC permeability was associated with disrupted surface vascular endothelial (VE)-cadherin localization, which was rescued by treatment with GM6001, a synthetic inhibitor of metalloproteinases. Together, our data suggest that TIMP3 supports normal PMVEC barrier function and that septic downregulation of TIMP3 may be an important contributor to septic PMVEC barrier dysfunction. A better understanding of the novel TIMP3-mediated endogenous protective mechanism against septic PMVEC dysfunction would support new therapeutic approaches for patients with sepsis, and help elucidate PMVEC dysfunction in other vascular diseases.

An antimicrobial peptide with pulmonary surfactant compound as a potential treatment of bacterial pneumonia

Brandon Banaschewski, Cory Yamashita, Ruud Veldhuizen.

Current treatment strategies of bacterial pneumonia are hampered by two major complications – the difficulty in administration of therapeutics to lower respiratory infections, and the development of multi-drug resistant bacteria. Antimicrobial peptides (AMP) are found to exhibit broad antimicrobial activity and lack typical resistance patterns against them. Pulmonary surfactant, when exogenously administered, has excellent spreading capabilities that could facilitate the delivery of therapeutics throughout the airways. The objective of this study was to investigate the safety and tolerability of a surfactant/AMP mixture, BLES+CATH-2, and the efficacy of this mixture in an acute bacterial pneumonia model. C57Bl/6 mice were administered either control or Pseudomonas aeruginosa, and then co-administered one of five treatments (Air, Saline, BLES, CATH-2, or BLES+CATH-2) via intratracheal instillation and left to spontaneously breathe for either four or 18 hours. After the mice were sacrificed, respiratory compliance, cell infiltration, inflammatory analysis, and bacterial counts were collected. Administration of BLES+CATH-2 appeared to be safe and well tolerated in naïve mice, with no significant differences observed in any of the parameters investigated. CATH-2 administration showed significant increases in lavage protein content and IL-6 levels. Administration of both CATH-2 and BLES+CATH-2 showed significant reductions in bacterial recovery compared to controls at four hours, but no effect was observed at 18 hours. BLES+CATH-2 appears to be a safe and tolerable therapy in mice, and shows efficacy in an acute bacterial pneumonia model up to four hours after administration, although benefits of this therapy is lost at 18 hours.

Impact of a Critical Care Outreach Program on Night time Discharges from the Intensive Care Unit (ICU)

Basmaji, John, Jariwala, Abhishek; Chehadi, Waleed; Priestap, Fran; Campbell, Eileen; Martin, Claudio; and Kao, Raymond.

Increasingly, discharges from intensive care units are occurring after normal working hours. The impact of these night time or early discharges have been of particular concern with respect to patient safety, with evidence suggesting a significant increase in in mortality. However, these studies were done prior to the inauguration of CCRT (Critical Care Response Team), an initiative developed with the intention of delivering timely access to treatments and services to non-residents of the intensive care unit (ICU). We investigated the impact that a CCRT has had on mortality related to nighttime or early discharges, and whether there is an increased amount of resources used by our CCRT for patients transferred

at night. A retrospective chart review was undertaken of patients transferred from the Critical Care Trauma Center (CCTC) to the ward over a 30-month period (January 2011 to June 2013). One thousand five hundred seventy nine patients were identified through the existing CCOT (Critical Care Outreach Team) database and classified according to whether transfer occurred during the daytime (0700-2059 hours) or nighttime (2100-0659 hours). Data was collected regarding reasons for CCOT interventions, duration and frequency of CCOT follow-up, interventions performed by CCOT, and readmissions to CCTC.

Right Ventricular Mass and Third degree Heart Block: A Rare Presentation of Cardiac Sarcoidosis

Dr. Mia Bertic, Dr. Shruti Tandon, Dr. Gerald Wisenberg.

Case Description: A 33-year-old male was assessed after presenting with a 10-day history of dyspnea on exertion, palpitations and dizziness. He was profoundly bradycardic. Transthoracic echocardiogram showed moderate RV hypertrophy, particularly at the apex, with moderately reduced systolic function. Cardiac MRI revealed a large ovoid mass-like area of thickening involving the mid RV free wall. Endomyocardial biopsy demonstrated non-caseating granulomata, highly suggestive of cardiac sarcoidosis. 18FDG PET scan suggested sarcoidosis-related myocardial inflammation predominantly and extensively involving the RV. Given the risk of ventricular arrhythmias in patients with cardiac sarcoidosis, the patient underwent implantation of a defibrillator and was started on Prednisone 50 mg daily. Three weeks after initiating medical therapy with prednisone, the patient presented to hospital with the sudden onset of shortness of breath and syncope. On interrogation of his defibrillator, it was discovered that it had fired shortly after the onset of these symptoms in response to episodes of ventricular tachycardia. Discussion: This report describes the first case to demonstrate a right ventricular (RV) mass representing cardiac sarcoidosis. With the use of advanced imaging modalities including MRI and 18 FDG PET, we were able to identify the extent of cardiac involvement. Given the variations in cardiac manifestations of sarcoidosis and the poorer prognosis in patients with cardiac involvement, early diagnosis using advanced imaging modalities can help identify patients with unique presentations of active cardiac sarcoidosis.

Neuropathy and Urinary Retention: a rare case of Autoimmune Syndrome Associated with Adjuvant.

Anurag Bhalla, Wassim Saad.

Silicone, considered biologically inert, has been widely used in various medical devices. Silicone breast implants (SBIs) causing systemic effects has been highly debated. We present a unique case of a 30-year-old female with a month-long history of low-back pain, perianal numbness, ascending paresthesias, and urinary retention, with a past history only significant for bilateral SBIs. She had been recently discharged from the hospital after inconclusive work-up for neurological disorders. Examination revealed reduced pinprick sensation in the perianal region, and slight asymmetry on the right breast implant. Positive investigations included ANA 1:1250, CRP 114, and ESR 52; and CT chest identifying right breast implant rupture. Treatment with high-dose prednisone resulted in resolution of symptoms and decrease in inflammatory markers. As part of the differential diagnosis, we hypothesized that our

patient's symptoms may be the result of an autoimmune reaction to the silicone antigen. A PubMed search containing the terms autoimmune, inflammatory, silicone, and breast implants identified seventy English articles published between years 1983 and 2014. Forty-five suggested a link between silicone breast implant and autoimmunity, but majority of these publications (24/45) were case reports. Although postulated, a direct relationship between silicone and autoimmunity has not been well established. The term Autoimmune Syndrome Associated with Adjuvants (ASIA), specifically Silicone Implant Incompatibility Syndrome has been used to describe such presentations. This case fits the diagnostic criteria for ASIA, a term that is resurfacing in the medical community. Future research should be conducted at both clinical and biochemical levels to establish causality.

Incidence and natural history of intravenous immunoglobulin-induced aseptic meningitis: a retrospective review at a single tertiary care centre

Vighnesh Bharath, Kathleen Eckert, Matthew Kang, Ian H. Chin-Yee, Cyrus C. Hsia.

Background: Aseptic meningitis is a rare but significant complication of intravenous immunoglobulin (IVIg) therapy. The majority of literature is limited to case reports, so the true incidence and natural history of this complication is uncertain. Study Design and Methods: A retrospective review of all cases of IVIg-associated adverse transfusion reactions was performed at London Health Sciences Centre (LHSC) from January 1, 2008 to December 31, 2013. All reported transfusion reactions were evaluated to identify cases of aseptic meningitis due to IVIg. All documented IVIg infusions and lumbar punctures performed during the study period were reviewed; patients with both interventions were identified and further chart review was performed to identify aseptic meningitis. Results: During our study period, 1324 unique patients received a total of 11,907 IVIg infusions (554,566 g) for various conditions. 8 cases of aseptic meningitis were identified, suggesting an overall incidence of 0.60% for all patients and 0.067% for all IVIg infusions. Patients presented with symptoms within 24-48 hours of the infusion, and were treated with antibiotics initially. The reactions were self-limited, as symptoms self-resolved within 5-7 days. Treatment was supportive, with subsequent IVIg infusions possibly requiring premedication or a switch in product formulation. Conclusion: This review of IVIg-induced aseptic meningitis over a 6-year period identifies a more robust estimate of incidence and risk of 0.60% and 0.067% for all patients and infusions, respectively. Given that this complication can mimic infectious meningitis and cause considerable morbidity, physicians need to be aware of this rare but important condition.

Caregiver-delivered delirium prevention in hospitalized patients - a pilot study

Biswas, Robert, Brymer, Christopher (MD, MSc) Mrkobrada, Marko (MD) Dasgupta, Monidipa (MD, MSc).

Background: A family-delivered intervention for modifying delirium risk factors was found to prevent delirium in Chile. The feasibility of doing a similar delirium prevention intervention was tested in a pilot study at LHSC. Methods: Participants were non-delirious on admission and were community dwelling seniors (≥70 years old) consecutively admitted to medical units. Patient-caregiver dyads were randomized (stratified by age and known dementia diagnosis) to receive a delirium prevention

pamphlet (with explanations of ways to prevent delirium) or general health brochure (placebo). Caregiver(s) were asked to complete a survey and maintain logs of time spent visiting the patient. The Confusion Assessment Method was used for delirium diagnosis. Results: Out of 146 eligible patient-caregiver dyads, 79 (54.1%) agreed to participate (67 of 146 eligible caregivers either refused or were unavailable to participate). Five patients (6.7%) became delirious in hospital; 2 patients (5.1%) in the placebo group and 3 patients (7.5%) in the intervention. Surveys were returned by 52 (66%) caregivers. Challenges caregivers faced were parking costs and overall time required (average of 5.6 hours/day were spent by caregivers). Caregivers did not find the study difficult to participate in (mean score 1.9 on 1 to 5 Likert scale; in the intervention group, 1.8), and 51 of 52 (98.1%) of respondents found the overall experience at least somewhat rewarding. Conclusions: Although 45.9% of caregivers were not interested in participating in this study, those who did participate found it to be rewarding. A family-delivered delirium prevention intervention may be another way to decrease delirium.

Lightning Strikes Twice: Thyroid Hormone Resistance Beta and Normophosphatemic Familial Tumoral Calcinosis in a Single Subject

Brahm AJ, Fraser LA, Ban MR, McIntyre A, Wang J, Hegele R.

Background: Thyroid hormone resistance syndrome (RTH) and normophosphatemic familial tumoral calcinosis (NFTC) are individually very rare conditions, with only ~3000 cases and 6 kindreds, reported respectively. They have never before been reported together in a single individual. Case: A 67 year old female presented with an 8 year history of progressive calcific tumors affecting multiple body sites, with the largest on her right hip (40cm). CT and plain film imaging, biopsy samples, laboratory testing and physical exam findings supported the diagnosis of normophosphatemic tumoral calcinosis. A trial of zolendronic acid was given intravenously, followed by stabilization of her tumors. Sequencing of GALNT3, FGF23, Klotho and SAMD9 revealed no potentially pathogenic mutations. She also had severe CHF (EF <20%), which remained unexplained despite cardiac biopsy and MRI. TSH was normal with elevated free thyroid hormone levels; she was clinically euthyroid, other than a 30 year history of tachycardia and palpitations. A known RTH-associated mutation (E460K) in THRB was found on sequencing. Discussion: This is the first case of NFTC reported outside the Jewish-Yemenite population and the first reported without a mutation in SAMD9. This suggests other unidentified molecular factors are involved in the etiology of NFTC. Bisphosphonate infusion was correlated with improvement in bone turnover markers and a halt in disease progression, and may represent an effective treatment for this poorly understood condition. This case generates the hypothesis that THRB mutations could lead to the development of tachycardia-induced cardiomyopathy via thyrotoxic effects on cardiac tissue, which predominately expresses functional THR-alpha receptors.

Effective outpatient management of denosumab-induced hypocalcemia in a long-standing hemodialysis patient

Sissi Cao BSc, MD(c), Lisa-Ann Fraser MD, MSc; Elizabeth Froats RN.

Case: A 58-year old man with chronic kidney disease (CKD) on hemodialysis, a history of chronic prednisone use and multiple fragility fractures including

spontaneous right jaw fracture while chewing food was referred for skeletal evaluation. His CKD-metabolic bone disease was being managed with cinacalcet (40 mg daily) and vitamin D3 (2000 IU daily). Investigations revealed a serum calcium of 2.16 mmol/L (2.15-2.60), albumin 40 g/L (40-50), PTH 24.4 pmol/L (1.3-8.2). He was started on denosumab (60 mg) for severe osteoporosis but by post-injection day 8, pre-arranged bloodwork revealed profound hypocalcemia (serum calcium 1.59 mmo/L). 1g of intravenous calcium gluconate was given acutely, and aggressive outpatient management, including calcitriol 0.25 mcg TID, was arranged. Follow up bloodwork was arranged every 2 days during dialysis to monitor progress. Within 20 hours, his serum calcium had risen to 2.11 mmol/L. On day calcium was 2.46 mmol/L and by day 35 calcium stabilized at 2.12 mmol/L. Calcitriol was tapered and he restarted his cinacalcet and vitamin D3 without issue. Discussion: Denosumab is an osteoporosis medication highly effective at reducing bone turnover and fracture risk. However, hypocalcemia has been documented as a side effect in CKD patients, and may be particularly severe in those on dialysis. We anticipated possible problems with hypocalcemia in our patient and therefore arranged bloodwork one week following initial denosumab injection. Our patient demonstrates how, with routine post-injection bloodwork and careful alteration of medications, dialysis patients can safely receive denosumab without undue suffering or the need for hospitalization.

A retrospective review of admission versus discharge diagnoses on CTU

Genevieve Chick, Dr. Andrew Smaggus.

Diagnostic errors are an under-investigated source of patient morbidity. The initial diagnosis that a patient is labeled with upon admission can have a profound effect on subsequent diagnostic pursuits. We sought to perform a clinical audit comparing admission versus discharge diagnoses over a 6-month period (416 patients) on CTU Team 2, with the aim of identifying discrepancies in diagnoses that can guide quality improvement initiatives. For each admission, the admitting diagnosis in the electronic medical record was compared with the most responsible diagnosis in the patient's discharge summary. Overall, the results showed that discharge diagnoses differed from the admission diagnosis in the majority of cases (56%). The data also demonstrated clinical conditions where the admitting diagnosis was almost always consistent with the discharge diagnoses (i.e. "COPD exacerbation"), and where the two labels were frequently different (i.e. "sepsis"). As an extension to this audit, we analyzed how often a clear "most responsible diagnosis" appeared in discharge summaries. This was identified in only 47% of discharge summaries. Overall, this audit demonstrates that, based on the initial admitting diagnosis label, there are more discrepancies than there are consistencies between the admitting and discharge diagnoses. Furthermore, in the group of discharge summaries examined in this audit, the "most responsible diagnosis" is not consistently documented. The clinical implications of these discrepancies will be the subject of future studies, but the results may inform short term clinical practice by alerting clinicians to the admitting diagnoses that suggest the need for persistent diagnostic vigilance.

An Audit of Laboratory Investigation Ordering Practices on the Medicine Clinical Teaching Unit

Dr. Lucas Ciprietti, Dr. Andrew Smaggus.

Many academic institutions are launching quality improvement initiatives to identify unnecessary laboratory investigations as a means to reducing costs, venipunctures, and other consequences of excessive testing. The current study is an audit of laboratory investigation ordering on the Medicine Clinical Teaching Unit at a tertiary care centre. Twenty-three common tests were studied to determine the frequency with which they were ordered, their yield regarding changes is diagnosis, therapy, or consultations, and if the rationale for the test could be identified in clinical notes. A total of 259 consecutive admissions were studied over a one-month period, with a total of 8328 individual tests. Complete blood counts, electrolytes, and renal function were ordered in over 90% of admissions, and accounted for 44.9% of all tests. Coagulation studies, liver and cardiac enzymes were each ordered in approximately 50% of admissions, yet had low rates of new diagnoses or therapeutic change. Common outpatient tests such as TSH, glycated hemoglobin, and B12 offered low rates of utility as well, however they were not ordered as frequently as expected. Folate and fecal occult blood, which are not recommended in the inpatient setting, were ordered in less than 5% of admissions. Clinical reasoning with respect to ordering a test or repeating it was infrequently documented. Overall, this audit demonstrates the quantity of laboratory investigations on the ward, and suggests that targeted interventions may be beneficial in reducing unnecessary laboratory investigations without risking patient care.

Ventilation Heterogeneity in Older Never-Smokers and Ex-smokers with COPD: The Poorly Communicating Fraction and MRI Ventilation defects

Christopher Davis, Damien Pike, Sarah Svenningsen, David G McCormack, Denis O'Donnell, J Alberto Neder, Grace Parraga.

Pulmonary imaging and lung function measurements have quantified the heterogeneity of lung dysfunction in Chronic Obstructive Pulmonary Disease (COPD). However, the clinical consequences of ventilation heterogeneity in COPD patients is not well-understood. Our objective was to evaluate the relationship between magnetic resonance imaging (MRI) measurements of ventilation heterogeneity and the "poorly communicating fraction" (PCF), previously described as the ratio of total lung capacity (TLC) to alveolar volume (VA) from a single-breath measurement. Both PCF and inhaled noble gas MRI provide measurements of ventilation heterogeneity but their relationship in never-smokers and COPD patients has not yet been evaluated. 146 participants provided written informed consent including 45 never-smokers and 101 COPD ex-smokers. During a single two-hour visit, spirometry, plethysmography, the St George's Respiratory Questionnaire, Six-Minute-Walk-Test , thoracic CT and hyperpolarized 3He MRI were acquired. From MRI, the ventilation defect percent (VDP), and from plethysmography and VA measurements, the poorly communicating fraction were derived. Linear regression, Pearson correlations and Bland-Altman analysis were used to evaluate the relationship between PCF and MRI ventilation heterogeneity. Both PCF ($p<0.001$) and VDP ($p<0.001$) increased with increasing COPD severity and there was a significant linear correlation for MRI ventilation defect percent and PCF ($r = 0.68$, $p<0.001$) in all subjects and COPD subjects alone ($r = 0.61$, $p<0.001$), although PCF was biased to larger values in severe grade COPD. PCF and MRI VDP are measured under the same physiological conditions (static breath-hold of inert gas) and may be reflecting similar pathophysiologies in COPD patients.

Emergency department point-of-care ultrasound in symptomatic early trimester patients: a description of practice management patterns

Dong, Alex Xin, McLeod, S.L., Thompson, D., Roebotham, R..

Point-of-care-ultrasound (POCUS) has played an increasing role in the emergency department (ED) evaluation of symptomatic women in their first-trimester. Although numerous studies highlight benefits of POCUS when an intrauterine pregnancy (IUP) is confirmed, many patients have indeterminate scans. This study describes the current management of patients with determinate and indeterminate POCUS scans. 100 patients aged 18-52 were randomly selected from all ED visits in a one-year period with a positive βHCG during their visit. Those not pregnant, >20-weeks gestation, or not complaining of abdominal/pelvic pain, vaginal bleeding, and/or syncope/pre-syncope were excluded. 11 were excluded based on the exclusion criteria. 73% (65) had a documented POCUS examination, 52% of which were documented as IUP. Patients with IUP on POCUS alone were more often discharged with family physician follow-up (70%) than non-determinate (NDIUP) patients (9.7%) or no-POCUS patients (29%). Specialist referral was less frequent in patients with IUP (5.9%, 24%) than NDIUP (23%, 58%) and no-POCUS (25%, 29%), respectively. Formal radiology consultation was also reduced in IUP patients; (12%) compared to NDIUP (32%) and no-POCUS (29%). In patients with determinate studies, there was reduction in formal radiology and specialty service consultation. Despite this benefit in resource utilization, 27% did not have a POCUS study. This may represent a lack of training or comfort with this modality, or lapse in documentation. Management strategies in NDIUP and no-POCUS patients were heterogeneous with specialist service consultation. Further research will examine differences in practice after implementation of a multi-disciplinary care pathway incorporating the use of POCUS.

"Type 1, or Not Type 1? That is the Question"

Esmaeilbeigi F, Hegele RA, Hramiak I, Liu SL..

Case: A 21 year old male Aviation Management student originally from Africa had glucosuria on routine screening and was sent to the Emergency Room. Investigations showed A1C 17.7%, small serum ketones, and he was referred to the Diabetes Clinic for possible type 1 diabetes (T1DM). He reported 3 months of polyuria/polydipsia, and type 2 diabetes in his parents. BMI 21.2 kg/m2 and physical exam unremarkable. Negative anti-islet cell/anti-glutamic acid decarboxylase antibodies. He started on insulin glargine and aspart. After 3 months, A1C was 7.2%, c-peptide slightly low. Since a T1DM diagnosis would preclude continuation of his pilot training, genetic testing for Maturity Onset Diabetes of the Young (MODY) was done. This showed a heterozygous mutation—namely p.A71T—in the B lymphocyte kinase (BLK) gene, which has been associated with MODY subtype 11 (MODY11). He started Diamicron MR 30 mg daily, weaning off insulin. His glycemia has been excellent for 3 months off all insulin—most recent A1C 6.3% with normal c-peptide. However, due to possibility of a T1DM "honeymoon phase", he is being followed closely. Conclusion: MODY is characterized by non-insulin dependent diabetes diagnosed at young age, with autosomal dominant transmission and lack of autoantibodies. In our case, MODY testing was pursued due to the discordance between family history, ethnicity, and clinical phenotype, and also the impact of the diagnosis on his career. The consistency of

the clinical presentation provides support for a contributory role of the BLK gene and of this particular rare variant in the MODY phenotype.

Musculoskeletal complications of systemic lupus erythematosus: risk factors for and prevalence of avascular necrosis and osteoporosis.

Maeve Gamble, Janet Pope.

Objective: Osteoporosis (OP) and avascular necrosis (AVN) are well-recognized musculoskeletal complications of systemic lupus erythematosus (SLE). Steroid therapy and the underlying disease process are major contributors and the degree to which each influences their development is unclear. The aim of this study was to identify the mean prevalence of OP and AVN as well as modifiable risk factors associated with the development of OP and AVN in patients with SLE. Methods: A comprehensive review of both published articles and unpublished abstracts was conducted using the PubMed, EMBASE, and Cochrane databases. All articles relating to risk factors for AVN and OP in patients with SLE were included. Results: Ten articles pertaining to AVN and 13 pertaining to OP met the inclusion criteria. The prevalence of OP was 12% and osteopenia 38%. The prevalence of AVN was 31%. In the studies of steroids in SLE, patients receiving high dose steroids did not have an increased risk of AVN. Similarly, disease activity did not have a significant impact on AVN in SLE patients. Patients with renal involvement were more likely to develop AVN. The potential protective effect with antimalarial use for AVN was not significant. Conclusion: The prevalence of OP and AVN is higher in SLE patients compared with the general population. Though we did not identify many modifiable risk factors for AVN, it is important to identify those at higher risk with the goal to reduce morbidity, identify AVN early and ultimately improve quality of life.

Did changes to the Ontario Highway Traffic Act in 2009-2010 affect the proportion of alcohol-impaired motor vehicle collisions seen at a Level I Trauma Centre over a 10-year period?

Meghan Garnett, Tanya Charyk Stewart, Michael Miller, Rodrick Lim, Kristine Van Aarsen, Wanda Millard.

Introduction: Impaired driving is the leading cause of criminal death in Canada. Since May 2009, all drivers in Ontario with a blood alcohol concentration (BAC) between 0.05-0.08% receive a minimum 3-day roadside license suspension under the Highway Traffic Act. Since August 2010, all novice drivers and drivers under 22 years must maintain a BAC of zero. Methods: This was a retrospective review of the trauma registry at a Level I Trauma Centre from 2004-2013. Descriptive statistics were calculated for all alcohol-impaired (ethanol > 0 mmol/L) drivers in a motor vehicle collision (MVC) with Injury Severity Score (ISS) ≥ 12 or Trauma Team Activation. A time series analysis was performed. Results: 377 severely injured alcohol-impaired drivers were treated at our trauma centre over the 10-year period, representing 20.9% of the MVCs. The majority (330; 87.5%) were male. The median age was 31 years and median ethanol was 35.3 mmol/L. Over three-quarters (292; 77.5%) were single-vehicle MVCs. Only 44.1% (n=143) of drivers were wearing their seatbelts. The median ISS for impaired drivers was 21 (IQR=20). A total of 29 patients (7.7%) succumbed to their injuries. The time series analysis showed no significant change in the number of alcohol-impaired drivers presenting to the hospital before and after changes to the law. Conclusion: Alcohol-

impaired driving results in devastating injuries and a substantial impact on the health care system. We were unable to detect a significant difference in the number of alcohol-impaired drivers presenting to our trauma centre, as a result of toughening the law.

Do emergency physicians educate patients about the dangers of drinking and driving after a motor vehicle collision, and what are the barriers or motivators to do so?

Meghan Garnett, Tanya Charyk Stewart, Rodrick Lim, Kristine Van Aarsen, Michael Miller, Wanda Millard.

Introduction: Impaired driving is the leading cause of criminal death in Canada and results in numerous emergency department (ED) visits each year. Methods: An online survey was distributed to 94 emergency physicians and emergency medicine residents at an academic tertiary centre in Southern Ontario. Descriptive statistics were calculated. Results: We received 76 responses (81% response rate). 56 (74%) physicians reported seeing an injured driver with a blood alcohol concentration greater than zero in the last year. Physicians widely varied in the frequency that they discussed the dangers of drinking and driving with patients. Only 13% had consulted the ED social worker and 32% had used an alcohol screening questionnaire in the past 12 months. The vast majority (96%) of residents have never received any teaching on how to counsel patients on impaired driving. Physicians were of the opinion that their advice would have little effect (3.44 on a 7-point Likert scale), however 89% thought they could do more to educate patients. The greatest barriers to addressing drinking and driving with motor vehicle collision patients were severity of injury, lack of time, and intoxication. The greatest motivators were a sense of personal responsibility, concern for patients' health and safety, and having the time. Conclusion: The information from this survey brings awareness to the longstanding problem of drinking and driving, explores the barriers and motivators to addressing this topic in the ED, and can be used to develop new strategies to educate trauma patients on the dangers of impaired driving.

Clinical-pathologic correlates of proteoglycan deposition in human thoracic aortopathy

Abdulaziz Hashi, Dr. G. Pickering, Hao Yin, Caroline O'Neil.

It has been known that proteoglycan deposition is a feature of diseased aorta and may be both a biomarker and driver for aortic dilation. It is critical to better understand the circumstances in which excess proteoglycan deposition occurs. This association study involves examining the thoracic aorta of patients, both those with known aortic disease and those without, and aims to elucidate these relationships further. In March 2015, sections of human thoracic aorta from over 75 unique patients were examined in the Vascular Biology Laboratory of Dr. G. Pickering at Robarts Research Institute. Sections were stained with Alcian blue followed by an acetic acid wash to serve as a surrogate marker for sites of excessive proteoglycan deposition. These sections were then viewed under a microscope at twenty times magnification. Images of random areas of the tunica media were taken using the Northern Eclipse computer program and a Hitachi HV-F22 camera with an exposure of 12.08 ms. The Image J program was used to quantify percent area of Alcian blue deposition. The percent areas were then averaged for each patient. Correlates of this study will include

the type of aortic disease, age, ascending aorta diameter, and convexity vs. concavity of the aorta and its relation to proteoglycan deposition. This study is ongoing.

Overexpression of junctophilin-2 prevents lipotoxicity-induced endoplasmic reticulum stress and apoptosis in cardiomyocytes

Yifan Huang, Dong Zheng, Tianqing Peng.

Background and Aims: Obesity and type-2 diabetes are prevalent in westernized countries. In both conditions, lipotoxic cardiomyopathy commonly ensues due to excessive fatty acid uptake by cardiomyocytes. The outcomes of patients with lipotoxic cardiomyopathy will be severe heart failure, leading to death or heart transplantation. Endoplasmic reticulum (ER) stress and apoptosis in cardiomyocytes contribute to lipotoxic cardiomyopathy. However, the underlying mechanisms remain poorly understood. This study investigated the role of junctophilin-2 in lipotoxicity-induced ER stress and apoptosis in cardiomyocytes. Methods: Lipotoxicity was induced by incubation with palmitate in cultured neonatal mouse cardiomyocytes and rat cardiomyocyte-like H9C2 cells. To up-regulate junctophilin-2, the cells were infected with an adenoviral vector containing junctophilin-2 (Ad-JPH2). Apoptosis was determined by caspase-3 activity and DNA fragmentation. ER stress was assessed by measuring C/EBP homologous protein (CHOP), phosphorylated c-Jun N-terminal kinase-1/2 (JNK1/2) and immunoglobulin heavy chain-binding protein (BIP) using western blot analysis. Results: Incubation with palmitate (200 μM) for 24 hours increased the protein levels of CHOP, Bip and phosphorylated JNK1/2, indicative of ER stress, and induced apoptosis in neonatal mouse cardiomyocytes and H9c2 cells. In contrast, incubation with oleatic acid did not have any effects on ER stress and apoptosis. Infection with Ad-JPH2 up-regulated the protein levels of JPH2, significantly attenuated ER stress and prevented apoptosis in cardiomyocytes induced by palmitate incubation. Conclusions: Over-expression of JPH2 prevented ER stress and apoptosis in cardiomyocytes during lipotoxicity.

Curriculum Mapping: Structured resident input identified the importance of informal teaching and clinical encounters

Nicole Hugel, Joan Binnendyk, Sheri-Lynn Kane.

Introduction: Curriculum mapping is a tool used to link elements of a curriculum to specific objectives. This is a key step for the transition to competency-based medical education (CBME). One challenge of curriculum mapping is to understand where objectives are being covered outside of formal clinical teaching. We used structured resident-focus groups to help address this gap in the development of our curriculum map. Methods: The Royal College Objectives of Training in Internal Medicine formed the template for our curriculum map. We retrospectively linked objectives from structured clinical teaching (Academic Half Day, Grand Rounds, Morning Report) to the template. Resident focus groups disclosed the perceived location of objective-specific training in nine curriculum categories (ex. Morning Report, Noon Rounds), as well as areas of inadequate objective coverage. Results: Focus groups were held over two nights and a total of 25 residents in PGY1-3 attended. Residents identified the largest percentage of objectives as being met through clinical encounters, with 69% of objectives covered in general internal medicine rotations and 75% in subspecialty

rotations. Informal teaching met 46% of the objectives. Clinical encounters and informal teaching covered the largest number of objectives in the Communicator, Collaborator, Health Advocate, and Medical Expert roles. Conclusion: Many residency objectives are covered outside of structured teaching sessions, in clinical encounters and informal teaching. This presents a challenge, as programs will have to develop a way to track these encounters in the CBME model.

Glycemic Control and Acute Diabetes Complications during Transition from Pediatric to Adult Care

Jennifer Huynh and Tamara Spaic (MD, MSc, FRCPC), Cleril Clarson (MD, FRCP), Jeffery L. Mahon (MD, MSc, FRCPC).

Transition from paediatric to adult diabetes care is a high-risk period marked by increased disengagement from care and diabetes-related complications. We conducted a population based cohort from 2007-2014 using uniquely linked pediatric and adult electronic medical records. We determined the impact on glycemic control and acute diabetes-related complications in the three years prior and subsequent to the transition. Transition occurred at 18 years of age in 147 patients. The majority of patients (98%) had type 1 diabetes. At the baseline visit (age 15 yrs), median duration of diabetes was 5 yrs (range 0-14). There were 45 (31%) patients on an insulin pump, and 96 (65%) on multiple daily injections. The mean A1C was 8.66 % (95 % CI 5.77-13.66) prior to transition and 8.89% (95 % CI 5.65-16.9) following transition. A1C changed by a mean (SD) value of 0.30% (1.47) (p=0.014). There were 65 and 101 emergency department visits and/or hospitalizations for acute complications (hypoglycaemia and hyperglycaemia) respectively before and after transition. Diabetic ketoacidosis (DKA) admissions were 3 times higher after transition (OR 3.0, 95% CI 1.19-7.5) compared to before transition. Assist-requiring hypoglycemia occurred in 12% of patients before and 8% of patients after transition (OR 0.42, 95% CI 0.12 to 1.27). Urine albumin creatinine ratio (ACR) testing decreased after transition, from 47 patients pre-transition versus 29 patients post-transition. Our results suggest that transition of young adults with diabetes to adult care has a negative impact on glycemic control and is associated with a significant increase in risk for DKA.

ADrenal InsufficiEncy, QUAlity of life, and Treatment in the Emergency room [ADEQUATE Study]

Christine Ibrahim, Lisa-Ann Fraser, Jeff Mahon, and Stan Van Uum.

Adrenal insufficiency (AI) is a chronic disease requiring on-going glucocorticoid, and often mineralocorticoid, replacement. Patients may develop an adrenal crisis and require a hospital visit to receive parenteral stress-dose glucocorticoids. We created a survey to assess: patients' knowledge of their illness, disease stability, stress-dosing, hospital experiences, and the utility of medical alert identifiers (MAIs). In early 2014, an invitation to participate was provided to patients with AI in our endocrinology clinic and to the Addison's Society of Canada members. Of the 304 patients invited, 134 completed the survey. Ninety-six (71.6%) were female. Mean age was 56 (18-89), with a mean AI duration of 14 (0-54) years. Most (82.7%) had been on stable therapy in the preceding 6 months. Patients commonly stress-dosed for illness and surgical procedures, and dose duration varied from one day to four weeks. Of 66 respondents who presented to hospital, all received stress-dosing within 12 hours, with 84.9% in the first 6 hours. A MAI was

carried by 85% of patients, but checked by only 27% of paramedics and 26% of ER personnel. Many respondents expressed frustration at the medical system for its lack of awareness and delay in triaging. Although patients are aware of the need for stress-dosing, there is misinterpretation for how long to do this. There are barriers to patient care within hospitals that need to be addressed. There needs to be re-education on the purpose of MAIs. A quality of life questionnaire found significantly reduced physical well-being and energy in this population.

Assessing the Benefits of Referral to Infectious Diseases for Consultation of Cellulitis Diagnosed in the Emergency Department.

Shilpa Jain, Phil Dwek, Tehmina Ahmad, Sonia Poenaru, Kaveri Gupta, Seyed Hosseini, Michael Silverman.

Background: Despite established guidelines for diagnosis and management of cellulitis, failure rates for treatment of cellulitis in the Emergency Room (ER) remain high. Recurrent cellulitis is often the result of an underlying infection or condition that can be difficult to diagnose without specialist consultation. Additionally, several "mimickers" of cellulitis have been identified that often lead to over-diagnosis of cellulitis (and therefore inappropriate antibiotic use), and under-treatment of the true presenting condition. Infectious Diseases (ID) consultation may be beneficial in differentiating true cellulitis from its mimickers, and identifying and treating underlying conditions that lead to recurrent cellulitis and treatment failure. Objectives: The objective of this study was to identify whether referral to a specialized ID Cellulitis Clinic following diagnosis of cellulitis in the ER changed diagnosis and outcomes. Design: A retrospective chart review was performed on 136 patients referred to the ID Cellulitis Clinic following diagnosis of cellulitis in the ER. Results: Of 136 patients diagnosed with cellulitis in the ER, 56 (41%) were given an alternative diagnosis by ID specialists. Antibiotics were discontinued in 16 (12%) patients following ID consultation. Of 80 patients diagnosed with true cellulitis, 19 (24%) had an additional complicating condition identified and treated. Of 56 patients diagnosed not to have cellulitis, 37 (66%) were identified as having a different infection requiring alternative treatment. Conclusions: ID consultation following diagnosis of cellulitis in the ER was beneficial in differentiating mimickers from true cellulitis, and identifying underlying factors that may result in recurrent cellulitis, leading to more definitive management.

Utility of Ambulatory Holter monitoring in patients with permanent atrial fibrillation

Umjeet S Jolly, George Klein.

Background: Ambulatory Holter monitors are ordered for the evaluation of rate control in patients with permanent atrial fibrillation to determine the average heart rate. Despite this, the use of Holter monitors for this purpose are not mentioned in current CCS or ACC atrial fibrillation guidelines. We evaluated as to whether ambulatory Holter monitors provided additional information than a resting ECG in an outpatient population with permanent atrial fibrillation. Methods: The electronic Holter database at London Health Sciences Centre was searched retrospectively for the terms 'AF', 'Afib', and 'atrial fibrillation'. Inclusion criteria were the presence of continuous atrial fibrillation throughout the Holter monitor, a resting outpatient 12-lead ECG performed within 1 week of the Holter monitor with atrial fibrillation, or the absence of other atrial or ventricular rhythms on the Holter

monitor. Mean heart rate on holter was compared to resting heart rate on 12-lead ECG. Statistical analysis was performed using SPSS software. Results: From the 1039 Holters reviewed, only a total of 276 met the inclusion criteria. The Pearson's correlation coefficient for resting heart rate and mean Holter heart rate was 0.77. ROC analysis revealed that a resting heart rate of 78 bpm had a sensitivity of 87% and a specificity of 62% to predict a mean heart rate greater than 100 bpm on Holter monitor. Conculsions: In patients with permanent atrial fibrillation, mean heart rate from Holter monitors correlate with resting heart rates, and provide incremental information if the ECG shows a heart rate greater than 78 BPM.

The role for rituximab as an induction agent in ANCA-associated vasculitis

Emily Jones, William F. Clark, Jessica Sontrop, Kelly Hatch.

Background: Cyclophosphamide and glucocorticoids have been the mainstay of remission induction therapy for ANCA associated vascultis (AAV) for many years. Recent studies have suggested, however, that rituximab may be a comparable, and potentially safer alternative that traditional therapies. Objectives: We undertook a systematic review and conducted a descriptive analysis of the literature to analyze the impact of Rituximab on remission induction and renal improvement among patients suffering from AAV. Methods: We included prospective studies of rituxumab on patients with specifically ANCA vasculitis. We searched 6 electronic databases and grey literature for eligible trials. Two investigators independently assessed trial eligibility and abstracted data. Results: Our search identified 851 citations, and 8 trials met our eligibility criteria. There was a comparable risk of death in patients that received rituximab to previously reported results in standard therapy studies. Remission was achieved in 79% of patients treated with rituximab (RR 1.37; 95% CI .87-2.16). Conclusions: Our descriptive analysis provides evidence as to the function of rituximab in treating AAV, its future potential, and outlines how perception of treatment with rituximab is framed by the style of the study in which it is conducted. Our systematic review helps to establish the legitimacy of rituximab's role in treating AAV, particularly in patients with refractory disease, or that not amenable to treatment with conventional therapy.

Reasoning During Admission Case Review: What Physicians Reason About and When They Do It

Salina Juma, Mark Goldszmidt.

PURPOSE: Little is known about the 'what', 'when', and 'why' of physician reasoning during case review – prior research has largely focused on 'how' physicians reason. Answers to these questions are essential for improving clinical training, patient-care, and reasoning research. METHODS: A constant comparative approach was used to analyze clinical records and transcripts from 38 admission case reviews between junior trainees, senior residents and faculty supervisors. Using a previously identified list of 24 reasoning tasks, the analysis focused on: what tasks were performed, when they occurred, and the relationships among them. RESULTS All 24 tasks were observed in at least one of the reviews with a mean of 16.6 (SD=1.5;Min=13,Max=19) tasks per review. Two new reasoning tasks – assess severity of illness and assess patient capacity – were identified. We found four overarching tasks – assess priorities, determine and refine the most likely diagnosis, establish and refine management plans, and self-reflection – that occurred

throughout all stages of case review, from the patient identification to the assessment and plan. The other 22 tasks appeared to be context dependent, serving to support and refine the overarching ones. Tasks were non-sequential and the same supporting task could serve more than one of the overarching tasks. CONCLUSIONS This study provides new insights into the 'what' and 'when' of physician reasoning during case review. Our findings can be used to support professional development and clinical training. Further research is needed to explore how physicians decide why a supporting task is required for a particular context.

A Case of Mixed Connective Tissue Disease with Features of SLE and SSc, Livedoid Vasculitis, and Severe Vasculopathy.

Michelle Jung, Janet Pope.

This case is of a 51-year-old woman with mixed connective tissue disease with features of SLE and SSc (ANA 1:640 with a speckled nucleolar pattern, double stranded DNA, RNP, SSA, low C3 and C4), livedoid vasculitis, severe vasculopathy with multiple amputations of fingers. She presented with a longstanding history of Raynaud's phenomenon. During the last few years, it substantially worsened to the point of being spontaneously triggered, affecting her toes in addition to her fingers, and occurring up to 12 times a day. She also began to notice puffiness involving the entire length of her fingers. She had no pertinent medical or family history at the time of initial assessment. Initial examination revealed multiple telangiectasias on her face, upper chest and hands as well as dilated capillaries in several nail folds. Initial investigations including bloodwork, pulmonary function test, and echocardiogram were non-contributory. She rapidly deteriorated with marked cyanotic changes with Raynaud's phenomenon, which progressed to digital infarction of both hands. Arteriogram showed small vessel long segment variable narrowing almost exclusively within the hands, with multiple small vessel occlusions in the digits, compatible with severe vasculopathy. During this period, she also developed interstitial lung disease and lost significant weight due to dysphagia, lack of appetite, and recurrent vomiting, likely due to the gastrointestinal tract involvement. She was treated with nifedipine, sildenafil, iloprost, prednisone, cyclophosphamide, rituximab and various analgesics. However, we were unable to salvage her digits, and she required amputation of fingers.

Rate of severe infection in anti-neutrophilic cytoplasmic antibody vasculitis patients treated with cyclophosphamide: a meta-analysis.

Michelle Jung, Lillian Barra.

Objective: To determine the rate of severe infection in cyclophosphamide (CYC) induction therapy for anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis. Methods: We searched the following bibliographic databases: Medline, Embase, and Cochrane database from 1947 to July 2014. Systemic reviews, meta-analysis, case reports, and abstracts were excluded. Our search strategy combined the terms: ANCA or ANCA-associated vasculitis (granulomatosis with polyangiitis, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis) treated with CYC. We performed a random effects meta-analysis. Both oral and intravenous CYC were included. The cumulative dose of CYC was calculated based on the study description of the CYC dosing regimen and the duration of treatment. Results: Fifty-nine studies met the criteria (14 RCTs and 41

observational studies). Only the RCTs were meta-analyzed. The sample size ranged from 25-197, mean age 42.9-67.8 and total cumulative CYC dose 114.5-5333 g. Everyone in the trial received corticosteroid as part of the induction regimen for AAV. 2 trials compared CYC vs. rituximab, and 5 trials compared oral CYC vs. intravenous CYC. Duration of follow-up ranged from 6 to 60.8 months. Random effects analysis showed the rate of severe infection per 100 g of CYC was 9.49 per 1000 person years (95% CI: 9.48-9.49; p-value ≤ 0.0001). Conclusion: The rate of severe infection among patients with AAV treated with CYC and corticosteroid induction therapy was 9.5 per 1000 person years. The rate was highly variable between studies even accounting for cumulative CYC dose. Other factors, such as patient age, disease severity, and co-morbidities should be considered.

Retrospective analysis of cardiac arrest patients and their outcomes at London Health Sciences Centre

CAROLINE JUSZCZYNSKI, Varinder K Randhawa, Shahar Lavi.

Background and Rationale: Cardiac arrest (CA) has a huge burden on mortality and neurological morbidity. The objectives of this study were to define the characteristics of CA patients and their outcomes, and its relationship to ischemic heart disease. Methods: We have undertaken a retrospective chart review of all adult CA patients at our institution over the past 10 years. Baseline demographic data (i.e., age, gender, comorbidities, ejection fraction, and cardiac arrest details as per Utstein guidelines) will be collected, along with outcomes of mortality, length of stay, neurological status, and coronary revascularization. Results: Sixteen patients have been analyzed to date. Eighty percent suffered out-of-hospital CA (OHCA), with 33% males at a mean age of 63±15 years. Over half had hypertension (73%), dyslipidemia (53%), and diabetes (40%). Fewer had known ischemic cardiomyopathy or smoking history (27%), and renal insufficiency (20%). About half the patients were on aspirin, beta-blocker, and statin therapy that were continued. Anti-platelet therapy was increased from 13% to 26%. The mortality was high at 67%, with an average intensive care length of stay of 5.8±4.5 days. Survivors achieved good neurological status post-therapeutic hypothermia. Conclusions: At our institution, the survival and neurological outcomes of CA patients is quite poor. The majority of these patients suffered from an OHCA, and had a significant burden of cardiovascular risk factors.

Novel Imaging Modalities in Diagnosis and Disease Activity Assessment of Takayasu Arteritis: Systematic Review and Meta-Analysis

Tahir Kanji, MD, Jacqueline Malette, MD, Lillian Barra, MD, FRCPC.

Background. Takayasu arteritis (TAK) is a rare large vessel vasculitis affecting predominantly women under the age of 40. Despite being in clinical remission, 42% of TAK patients have evidence of active inflammation on biopsy. Early recognition of disease activity may reduce the risk of vascular complications. **Objective.** To assess the role of novel imaging modalities for early diagnosis and disease activity assessment in patients with suspected or diagnosed TAK. **Methods.** We searched MEDLINE and EMBASE; we excluded case reports, case series and reviews. Two authors independently screened articles, assessed risk of bias and extracted data. Measurements obtained include correlations, sensitivity, specificity, positive predictive value, negative predictive value,

and diagnostic accuracy. **Results.** From the 932 citations screened, 33 studies enrolling 698 participants met our inclusion criteria. Studies comprised 20 articles and 13 conference abstracts. 8 studies examining disease activity with Positron Emission Tomography (PET) were meta-analyzed. Pooled estimates for sensitivity and specificity were as follows: 0.84, 95% CI 0.76-0.91, and 0.71, 95% CI 0.62-0.80, respectively. Magnetic Resonance Angiography (MRA) demonstrated concordance with biochemical and clinical indices of activity in 5 studies but discordance in 2. **Limitations.** Primary literature was dominated by small, retrospective, single centre studies. Inconsistent definitions for imaging and clinical indices of activity were a source of heterogeneity. **Conclusions.** PET is moderately sensitive for identifying disease activity in TAK. MRA has demonstrated inconsistent results. Larger prospective studies incorporating a validated gold standard are needed to better define the role of novel imaging modalities.

Medical Research Council (MRC) dyspnea score as a measure of disease progression in patients with ILD other than IPF

Hadeel Khadawardi, Marco Mura.

Background: Dyspnea is the main complain in patients with interstitial lung disease (ILD). Medical Research Council (MRC) dyspnea score has been showed to be a reliable method to monitor disease progression in patients with idiopathic pulmonary fibrosis (IPF), but has not been investigated in patients with ILD secondary to other causes. Objective: To investigate whether MRC dyspnea score is a predictor of disease progression in patients with ILD other than IPF. Methods: Sixty-five patients with ILD other than IPF were retrospectively studied. Baseline MRC dyspnea score and 3-month changes were considered. The endpoint was clinical progression within 17 months. Clinical progression was defined as either: > 10% absolute reduction in FVC percent predicted; >50 m decline in 6 minute walk distance (6MWD); hospitalization for respiratory causes; or death. Results: Twenty-six (40%) patients progressed, including 5 deaths. MRCDS at baseline was not significantly different between progressors and non-progressors. However, 3-month worsening of MRCDS was significantly more frequent in progressors (84%) than in non-progressors (23%) ($p<0.0001$). Worsening of MRCDS was a significant predictor of progression (HR 11.9, C.I. 4.4-41.8, $p<0.0001$), with 85% sensitivity and 77% specificity. MRC categorical change (from 0-3 to 4-5) predicted progression (HR 5.6, C.I. 2.5-12.5, $p<0.0001$) with improved specificity (92%) but worse sensitivity (58%). Conclusion: Three-month changes of MRCDS, are significant predictors of clinical progression of ILD other than IPF. MRCDS reflects response to therapy and may be a very useful parameter to follow the clinical course of ILDs other than IPF.

Site Specific Prevalence of Fragility Fractures and their Relationship with Body Mass Index in Patients with Type 1 Diabetes

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The increased risk of fragility fractures associated with type 1 diabetes (T1DM) is thought to be mediated by mechanisms different from those of primary osteoporosis. How these differences alter the fracture risk at different bone sites, or the relationship between BMI and fracture site, is unknown. Consecutive patients, over age 40, with T1DM completed a bone health

questionnaire. Characteristics of those with fragility fractures, defined as occurring from standing height or less, were reviewed using descriptive statistics. For BMI analysis, only patients whose fractures occurred within 5 years of BMI measurement were included. 201 patients with T1DM participated, and 52 fragility fractures were identified. Of these, most occurred at the ankle/metatarsal (13/52; 25.0%), followed by hip (11/52; 21.1%), and wrist (10/52, 19.2%). No association between BMI and fracture site was identified. However, we noted that the BMI of most patients who fractured was high (average 28.3), with 5.9% of patients in the overweight, and 52.9% in the obese category. The average age of patients with fragility fractures was 42.1 for ankle, 57.2 for hip, and 49.2 years for wrist. In this cohort of patients with T1DM, fragility fractures occurred at younger ages than expected. Similarly, although low BMI is thought to be important in the pathophysiology of fracture in T1DM, we found patients were more likely to be overweight/obese. This study confirms that the characteristics of patients with T1DM who fracture are different from those of other populations and need further evaluation to facilitate appropriate preventative care and treatment.

Microvascular endothelial cells undergo RIPK3 independent, CD4+ T-cell mediated death in chronic cardiac allograft rejection

Cecilia Kwok, Alexander Pavlosky Xuyan Huang Aaron Haig Anthony Jevnikar Zhuxu Zhang.

Necroptosis is a form of programmed necrotic cell death that is dependent on receptor-interacting protein kinase (RIPK) 1/3 and can be induced by death-receptor ligation with cytokines. Our previous study found that RIPK3-mediated necroptosis regulated microvascular endothelial cell (MVEC) death in acute rejection. This study aims to establish the role of RIPK3 in CD4+ T cell-mediated chronic rejection by using the single MHC class II mismatch [C57BL/6 (H-2b) to bm12 (H2-Ab1bm12)] chronic rejection transplantation model. MVEC death in-vitro was induced by cytokines or CD4+ T-cells and measured by flow cytometry and SYTOX® Green Nucleic Acid staining. Released HMGB1 protein was measured by immunobot. Hearts were transplanted from C57BL/6 wild type and B6;129R1-RIPK3tm1Vmd (RIPK3-/-) into Bm12 mice and followed by histological examination. TNFα-induced necroptosis in MVECs was enhanced with SMAC-mimetics and zVAD-fmk, and confirmed by RIPK1 inhibition with Necrostatin-1. Necroptosis was significant at all tested time points. Interestingly, no significant differences were found between CTL-induced cell death in wild type and RIPK3-/- MVECs. Intimal thickening and vessel narrowing, hallmarks of chronic rejection, were found in both wild type and RIPK3-/- cardiac grafts within 60 days, and no significant difference was found between days survival of wild type and RIPK3-/- hearts. Contrary to our previous study that showed RIPK3 deficiency protected MVECs in acute rejection; RIPK3 does not seem to have an effect on CD4+ T cell-mediated cell death. Next, we will study the mechanisms of CD4+ T cell-mediated death in wild type and RIPK3-/- MVECs after cardiac allograft transplantation.

The role of homocitrulline in Rheumatoid Arthritis

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

Background: Anti-homocitrullinated protein antibodies (AHCPA) have recently been

recognized in patients with Rheumatoid Arthritis (RA). Recent evidence suggests immunological similarity between AHCPA and anti-citrullinated protein antibodies (ACPA). ACPA are an established biomarker for RA and have been demonstrated to be arthritogenic. While AHCPA and ACPA are generated quite differently, it is not known whether AHCPA play a similar role to ACPA in the pathogenesis of RA. Objective: Compare the expression of AHCPA and ACPA in RA patient sera, and examine antigen specificity of AHCPA. Methodology: Serum samples were collected from patients with RA attending the rheumatology clinic at St. Joseph's Hospital in London, Ontario. Expression of AHCPA and ACPA in RA patient sera were examined by enzyme-linked immunosorbent assay (ELISA) using synthetic homocitrullinated and citrullinated peptides respectively. Specificity of AHCPA was examined by inhibiting homocitrulline binding using citrullinated and homocitrullinated peptides by inhibition ELISA. Results: In our cohort, AHCPA, similar to ACPA, were found to be expressed in RA patients but not in other related diseases or in healthy individuals. In addition, levels of AHCPA and ACPA were highly correlated in the serum of RA patients. AHCPA binding activity was inhibited to a similar extent by both homocitrullinated and citrullinated peptides. Conclusions: AHCPA are detected in RA patients and have a similar level of expression as ACPA. Furthermore, AHCPA are cross-reactive and capable of binding both homocitrullinated and citrullinated peptides. This suggests that AHCPA are immunologically similar to ACPA and may play a role in the development of RA.

Does Methotrexate Lower Serum Uric Acid Levels? Yes. Data from the CATCH Cohort

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Background: Methotrexate is an important medication in the treatment of rheumatoid arthritis. The exact mechanism of action is elusive, but it may be related to increase in adenosine levels. Methotrexate may be increasing the adenosine levels by blocking its natural conversion to uric acid. Objectives: The purpose of this study was to determine if methotrexate therapy lowers serum uric acid levels in patients with early rheumatoid arthritis. Methods: Data were obtained from Canadian Early Arthritis Cohort, a prospective cohort. This was a nested case control study. All patients with methotrexate use and a diagnosis of early rheumatoid arthritis were included. Results: Forty-nine ERA patients, out of 2524, in the CATCH database on methotrexate therapy with serial serum uric acid measurements were identified. In this group, the mean pre-methotrexate uric acid level was 300 µmol/L with a mean post-methotrexate uric acid level of 273 µmol/L (p 0.035). The control group of ERA patients not taking methotrexate during this time had a mean baseline uric acid level of 280 µmol/L and a follow-up level of 282 µmol/L (p 0.448). Patients who experienced a decrease in serum uric acid levels in relation to their methotrexate treatment had a DAS28 score of 2.37 at 18 months, while the control group had a DAS28 of 3.26 (p = 0.042). Conclusions: Uric acid levels were shown to be decreased in a clinical setting for patients taking methotrexate for ERA. This could provide a mechanistic basis for improved monitoring of methotrexate therapy.

Design and Implementation of a Collaborative Health Research Informatics System for Specialized Ambulatory Geriatric Care

Joseph Lindsay, Michael Borrie.

In the fall of 2012, the Division of Geriatric Medicine at Western University in London Ontario and the Cognitive Clinical Trials Group at the Lawson Health Research Institute began the development of a longitudinal clinical research registry system for a specialized ambulatory geriatric cognition clinic. Through the use of different open source development platforms, as well as usability engineering techniques, the Collaborative Health Research Informatics System (CHRIS) was designed and implemented as a masters in Health Informatics research project. CHRIS uses an open approach to bridge the gap between clinical care and clinical research, fostering cooperation and reducing compartmentalization. CHIS allows for the automatic generation of clinical dictations and visit summaries; visualization of clinical data at the point of care; data to be auto-completed and auto-saved; data to be extensively validated; and its system use to be tracked though an enhanced audit trail. Although CHRIS functions very much like a clinical documentation system, its primary focus is to allow for all clinical data to be used for clinical research. As the Canadian population is quickly aging, the use of CHRIS could have many positive implications including greater access to medical information, greater practice efficiency, easy identification of patients for clinical trials, and advanced facilitation of longitudinal investigator initiated clinical research through the process of providing regular clinical care.

High dose levothyroxine absorption test to differentiate between malabsorption and non-adherence: 5 cases and discussion

Gitadokht Majdi, Tirona RG[2], [3]Goldberg A, Van Uum SH[1].

Background: Consistent gastrointestinal absorption of levothyroxine (LT4) is essential for proper thyroid hormone replacement. Increase in LT4 dose requirements can be caused by non-adherence or by impaired absorption, e.g. due to gastrointestinal disorders or interaction with other drugs. In practice, it can be challenging to differentiate between malabsorption and non-adherence. Objective: We evaluated the ability of a high dose LT4 absorption test to differentiate between non-adherence and malabsorption of LT4 in 5 patients with therapy resistant hypothyroidism. Methods: We evaluated patients whose TSH did not normalize with prescribed doses of LT4 or required an LT4 dose over 3 microgram/kg. Patients underwent an absorption test involving an oral dose of 1000 mcg LT4 given under supervision. Plasma total T4, free T4, free T3 and TSH were determined at 0, 30, 60, 90, 120, 180 and 240 minutes after LT4 intake. Total T4 was quantified using LC-MS/MS and the pre-dose level corrected Area Under the Curve (AUC) was calculated as the % of standard AUC previously determined in healthy subjects. Results:The AUC in the patients indicated non-adherence in one patient (case 1, 140%), delayed absorption in one patient (case 5, 20%), and no/minimal absorption in 3 patients (cases 2,3 ,4: -7%, 15%, and -9%, respectively). Conclusions:The oral LT4 absorption test can be used to differentiate between non-adherence and impaired or no LT4 absorption. The results can inform clinical decision making focused on improved adherence, increase of oral LT4 dose, or even consideration of parenteral LT4 administration.

Management of dabigatran overdose in a case of acute kidney injury

Alison Martin, MD, Alejandro Lazo-Langner, MD, FRCP; Louise Moist, MD, FRCP; Rommel Tirona, PhD.

Introduction: Dabigatran is an oral direct thrombin inhibitor approved for use in prevention and treatment of thromboembolism. There is no reliable strategy for reversing its anticoagulant effects. This report describes a case of dabigatran overdose and management with factor eight bypassing activity (FEIBA) and hemodialysis. Case Presentation: A 62-year-old man taking dabigatran 110 mg twice daily presents with hematemesis, shock, acute kidney injury, INR greater than 8 and PTT greater than 150s. Last dose of dabigatran was within 10 hours of presentation. Additional complications included hematuria, pulmonary hemorrhage, rectal bleeding and cardiac arrest requiring multiple blood transfusions. He received 42 units/kg of FEIBA. A dialysis catheter was then placed and intermittent hemodialysis (IHD) was initiated for high clearances, followed by continuous renal replacement therapy (CRRT). No further blood transfusions were required. He had resolution of hemorrhage and partial recovery of kidney function. Dialysis was discontinued day 3 and he was discharged day 34. Results: Bloodwork drawn every 2 hours was analyzed for INR, PTT and dabigatran levels using Hemoclot assay. Two hours following FEIBA administration, INR decreased from 7.4 to 3.6 and a dialysis catheter was placed without complication, despite no significant change in dabigatran levels (1.26ug/mL – 1.30ug/mL). In the first 3.5 hours of IHD, dabigatran levels decreased from 1.15ug/mL to 0.86ug/mL. Conclusions: This study supports the use of FEIBA for rapid reversal of dabigatran allowing for urgent procedures. Dialysis appears helpful in cases of acute kidney injury to clear dabigatran, with IHD decreasing drug concentrations more quickly than CRRT.

Investigation of Admissions to Internal Medicine Lasting Less Than 12 hours

Kathryn McIntyre, MD, Saira Zafar, MD, FRCPC.

The objective of this study was to identify the characteristics of patients admitted from the Emergency Department (ED) to Internal Medicine who were discharged within 12 hours of admission. The patients were admitted to Internal Medicine at Victoria Hospital between January 1, 2013 and December 31, 2013. The inclusion criterion was length of admission less than 12 hours. Patients who died or left hospital against medical advice were excluded. Reason for admission, patient age, time of admission, and length of admission were recorded for all patients who met the criteria. During the period of study, 119 (3%) of 3824 admissions were under 12 hours. The median length of admission was 8 hours and 42 minutes and the median patient age was 56. Gastrointestinal conditions were the most common reason for admission, followed by respiratory conditions, and intoxication. In the bottom quartile for patient age, intoxication was the most common reason for admission. In the top quartile, respiratory conditions were the most common. Only a small number of patients required intervention from Internal Medicine or Subspecialties such as endoscopy or management of diabetic ketoacidosis. Of the 119 admissions, 103 (86%) occurred between midnight and eight in the morning. Many patients admitted briefly to Internal Medicine require observation longer than is feasible within the ED but otherwise do not require specialist care from the Internal Medicine

Service. Given the high percentage of patients in this sample admitted overnight, logistical and social reasons likely contributed to difficulty discharging patients from the ED.

Should effective Pulmonary Arterial Hypertension-targeted drug therapy be withdrawn, as per Ontario Drug Benefit's cost-saving strategy

Mauli Mehta, Sanjay Mehta.

Introduction: Pulmonary arterial hypertension (PAH) is a significant cause of morbidity and mortality. Combination drug therapy is becoming standard of care, but ODB funding requires that PAH patients be weaned off the initial medication within 6 months of adding a second therapy. We assessed the efficacy and safety of this cost-saving treatment strategy in PAH. Method: We performed a retrospective study of 42 patients diagnosed with PAH and treated with PAH-targeted medications based on ERS/ESC guidelines. Clinical, functional, and echocardiographic data were collected at prior to combination therapy, and reassessed at 4 months and 1 year post-combination therapy. Individual patient clinical status was compared on combination therapy and after withdrawal of the initial medication, and clinical outcomes were compared between patients weaned off initial PAH medication and patients maintained on combination PAH-targeted therapy. Results: Prior to starting combination therapy, patients had severe PAH characterized by mean 6MWT (284±116m), NYHA functional class (2.9±0.4), echo RVSP (77±20 mmHg) and moderate RV dilation and function. Following significant improvement 4 months after combination PAH-therapy, 22 (51.3%) patients were weaned off the initial medication as per ODB strategy. By 1 year mark, 100% of these patients demonstrated worsening PAH by clinical and objective criteria and combination PAH therapy was reinstituted. Conclusion: In PAH patients treated with sequential combination PAH-targeted therapy, attempts at weaning are unsuccessful due to clinical and objective worsening of PAH. We suggest Ontario's cost-saving PAH therapy withdrawal strategy is not appropriate, and may be harmful to PAH patients.

Iron-dependent ferroptosis mediates microvascular endothelial cell survival following cardiac allograft transplantation.

Natalie Montwill, Alex Pavlosky, Cecilia Kwok, Ye Su, Xuyan Huang, Zhuxu-Zhang and Anthony Jevnikar.

Activation of programmed cell death (PCD) pathways results in destruction of tissue cells and ultimately leads to allograft rejection. The field of PCD has recently been expanded to include novel forms of regulated necrosis (RN) such as iron-dependent ferroptosis, which has been implicated in renal ischemia reperfusion injury (IRI) but has yet to be studied in a heart allograft model. Ferroptosis occurs when the cystine-glutamate Xc- antiporter is inhibited and also in the absence of extracellular glutathione. We have shown that when murine renal tubular epithelial cells (TEC) and microvascular endothelial cells (MVEC) were treated with erastin, an Xc- antiporter inhibitor, both cell lines experienced increased necrotic cell death in comparison to their untreated counterparts. Furthermore, treatment of human cardiac microvascular endothelial cells (HCMEC) with a glutathione depletor, buthionine sulfoximine (BSO), also resulted in significantly increased necrotic cell death compared to untreated HCMEC. Based on these results, cardiac cells exhibit similar cell death kinetics to renal epithelial cells

and therefore ferroptosis may be an important mechanism regulating cardiac allograft transplantation.

Administration of mitochondrial targeted anti-oxidant reduces cardiomyopathy 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 anti-oxidant on diabetic cardiomyopathy in both type-1 and type-2 diabetic mice. Methods: Type-1 diabetes was induced in mice with multiple injections with streptozotocin (STZ, 50 mg/kg/day for 5 days, i.p.). Both type-1 and type-2 (db/db) diabetic mice received mito-Tempo (0.7 mg/kg/day, i.p.) treatment for 30 days. Mito-Tempo, a physicochemical compound as one of superoxide dismutase (SOD) mimics, is a mitochondria-targeted antioxidant with superoxide and alkyl radical scavenging properties. One month after treatment with mito-Tempo, myocardial function was assessed by echocardiography. Cardiomyocyte apoptosis, cardiac hypertrophy, cardiac fibrosis, mitochondrial ROS generation and protein carbonyl contents were determined thereafter. Results: In both type-1 and type-2 diabetic mice, mitochondrial ROS production, cardiomyocyte apoptosis and oxidative damage were increased. Diabetes also induced myocardial hypertrophy and decreased myocardial function. Administration of mito-Tempo significantly attenuated myocardial dysfunction , decreased cardiomyocyte apoptosis and oxidative damage, and reduced myocardial hypertrophy as determined by decreased cardiomyocyte size and a reduction in hypertrophic gene expression (ANP and beta-MHC) in both type-1 and type-2 diabetic mice. Conclusions: Administration of mitochondrial targeted anti-oxidant reduces cardiomyopathy 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.

Establishing an in vivo Pneumonia Model in Sprague-Dawley Rats

Michael Nicholson, Brandon Banaschewski, Lynda McCaig, Ruud Veldhuizen and Cory Yamashita.

Critically ill patients and those with underlying lung disease are at increased risk to develop bacterial pneumonia with associated impairments in lung function and bacterial colonization. The increasing antibiotic resistance patterns and the diminishing availability of conventional antibiotics thus requires the urgent development of novel treatment approaches. Furthermore, current in vitro systems utilizing these novel therapies, albeit quite promising, are limited by clinical applicability and therefore these strategies should be further examined in animal model of pneumonia. Based on this information, our objective was to establish a reproducible animal model, specifically a Pseudomonas aeruginosa (PA) induced pneumonia. Adult male Sprague-Dawley rats were intubated and mechanically ventilated for four hours after receiving 500 mcL of intratracheal PA inoculum. Varying concentrations, from 1-4 x10^8 CFU/mL, were given after 30 minutes of ventilation. Dynamic monitoring consisted of various

physiological measures including arterial blood gases. Colony growth analysis involved the lungs, spleen, liver and blood. The results showed that higher PA doses (4x10^8 CFU/mL) induced greater response in hypoxemia with PF ratios averaging 260 and 224 at 3 and 4 hours, respectively, compared to a PF ratio of 458 and 459, at 3 and 4 hours, respectively, in the low dose (1x10^8 CFU/mL) inoculum. Preliminary analysis of the colony growth data demonstrates that the higher inoculum insults resulted in the lung, spleen, liver, and blood to grow PA in subsequently higher concentrations. The decreased lung function and bacterial colonization provides evidence that we have established a robust in vivo pneumonia model.

In-Hospital Assessment and Management of Falls in the Elderly

Anna O'Connor MD, Monidipa Dasgupta MD, Lisa-Ann Fraser MD, MSc.

Objective: A thorough falls assessment can successfully reduce future fall events and injuries, making it an important part of fall care in the elderly presenting to hospital with a fall. The frequency with which patients receive such an assessment is not known. We sought to characterize the assessment and management of elderly patients presenting to hospital with a fall. Methods: Records from a tertiary care center between 2003-2014 were searched. A random sample of 180 charts (96 ED and 84 inpatient), describing visits for a "fall" in individuals ≥ 65 year, were selected. Paper and electronic charts were reviewed using a detailed pre-specified data abstraction form. Results: Of the 180 patients studied, mean age was 80.2 years (SD±8.46), and 66.1% were women. Fall related injuries were common, with 59.5% sustaining a new fracture. Only 1.1% of patient charts had a documented presumed etiology of their fall on the discharge summary. Orthostatic blood pressure was documented in 1.7%, 11.1% underwent formal assessment of cognition, and 17.8% had a medication review. Of those discharged, 19.2% had no follow-up arranged. The majority of patients had new fractures, including 83 (46.1%) lower limb fractures; however, only 30 (17.1%) were discharged on Vitamin D, 25 (14.3%) on calcium, and 17 (9.7%) on a bisphosphonate. Conclusions: Despite the potential for a thorough falls assessment to reduce future events, very few patients received a proper assessment or an adequate treatment plan. These results suggest a significant care gap and highlight an area of opportunity for quality improvement.

The Rapid Kinetics of Subcutaneous Methotrexate in Early Inflammatory Arthritis

Anna O'Connor, Hyeon Kang, Carter Thorne, Diane Tin and Janet E. Pope.

Objective: To determine the speed of onset of subcutaneous (sc) methotrexate (MTX) in early rheumatoid arthritis (ERA). Methods: Patients with ERA were studied at baseline, 6 and 12 weeks to determine the speed of onset of sc MTX. Outcomes included swollen joint count (SJC), tender joint count (TJC), pain, fatigue, sleep, physician global assessment (MDGA), patient global assessment (PTGA), ESR, CRP, health assessment questionnaire (HAQ), and composite scores including the disease activity score (DAS28), clinical disease activity index (CDAI), and simplified disease activity index (SDAI). Results: 103 patients from a single site with a mean age 56.2 (16.0); 64.0% females; 58.6% RF+; 29.4% ACCP+; mean disease duration 5.3 (3.5) months; in whom 82.5% met ACR 2010 criteria for RA were included. On repeated measures ANOVA, the change in disease

activity score was greater between 0-6 weeks vs. 6-12 weeks for SJC, pain, fatigue, sleep, PTGA, MDGA (all p<0.001), CRP (p=0.04), and the DAS28, CDAI and SDAI (all p<0.001). There was a significant improvement when using combination DMARD therapy compared to MTX monotherapy for TJC, DAS28, CDAI, SDAI, HAQ (all p<0.01), and CRP (p=0.04). Co-medication with intra-articular steroids yielded the most disease measures with significant improvement in the early (0-6weeks) vs. later group (6-12weeks). Conclusions: Subcutaneous methotrexate operates rapidly as the change in many disease activity scores was significantly greater between 0-6weeks compared to 6-12weeks. Intra-articular steroid injections may contribute to this early effect. Combination DMARDs seem to enhance the response to MTX.

Analyzing the effects of an epicutaneous peptide treatment to induce tolerance to citrullinated proteins in DR4tg mice.

Ashish Patel, Leanne Taylor, Eva Turley, David Bell, and Ewa Cairns.

Introduction: Rheumatoid arthritis is a chronic, inflammatory autoimmune disease that primarily effects the joints. Disease pathology is mediated by an immune response against citrullinated proteins found in the joints. We investigated an epicutaneous treatment of a citrulline-rich peptide (JED) to induce immunological tolerance towards citrullinated proteins in DR4tg mouse model for RA. Methodology: Fluorescent microscopy was used to visualize labelled JED that was administered to the skin of mice using a hyaluronan-phosphatidylethanolamine (HA-PE) cream, skin patch, or intradermal injection to determine the best delivery method. DR4tg mice were immunized with citrullinated fibrinogen, and 28-days post-immunization they were treated once with 100µg of JED in HA-PE cream for 3 or 7 days. Splenocyte proliferation and cytokine ELISAs were used to measure T cell response to citrullinated proteins. Anti-citrullinated protein antibody ELISAs were used to assess B cell response to citrullinated proteins. Results: HA-PE cream was the most effective method to deliver JED to mice, and it allowed for the best retention of JED in the skin 72 hours after application. There was no significant difference (P>0.05) in the T cell or B cell response to citrullinated proteins between the mice treated with JED in HA-PE cream compared to control treatments. Conclusion: Although the HA-PE cream is an effective way to deliver JED to deep dermal tissue in mice, the current treatment protocol has no effect on the immune response to citrullinated proteins. Further experiments are needed to optimize the treatment to effectively induce tolerance against citrullinated proteins.

A Case of Polycythemia Rubra Vera or Myomatous Erythrocytosis Syndrome or Both?

Christina Paul, Joy Mangel.

There are many potential mechanisms for the development of polycythemia. We describe a case of polycythemia likely related to both PolycythemiaRubraVera (PRV), a primary myeloproliferative neoplasm, and to a secondary cause, Myomatous Erythrocytosis Syndrome (MES), a condition where uterine leiomyomas produce elevated levels of Erythropoietin (EPO). A 55 year-old woman was found to have an isolated polycythemia on routine CBC: hemoglobin 206g/L, hematocrit 0.62, normal WBC and platelet counts. Despite a normal serum EPO level of 20.4IU/L (normal range: 5-29.5) and

negative JAK-2 mutation, no alternate cause was identified, and she was diagnosed with PRV. Initial treatment was with ASA 81mg and phlebotomies, but these were poorly tolerated, requiring addition of Hydroxyurea. Her hematocrit kept <0.45 for years using low dose Hydroxyurea and intermittent small volume phlebotomies. Five years into treatment, her hematocrit became harder to control. Attempts to increase the Hydroxyurea dose led to unacceptable decreases in her WBC's and platelets, and more frequent phlebotomies. She also began to experience pelvic pressure and urinary urgency, and ultrasound identified a 10x11cm leiomyoma. Postulating a link between the fibroid and worsening polycythemia, EPO level was rechecked and found to be elevated (64.7IU/L; normal range 2.6-18.5). Post hysterectomy, EPO level dropped to 10.5IU/L. She remains on low dose Hydroxyurea with good control of her counts. It remains to be seen whether she will be able to discontinue hydroxyurea altogether in the future and whether she ever truly had PRV, or whether this was simply a case of MES all along.

The Effect of Alcohol Consumption on Patient Reported Outcomes in Ankylosing Spondylitis

Matthew Piche, Nigil Haroon, Robert Inman, Sherry Rohekar.

This study examined the effect of alcohol intake on patient reported outcomes (PROs) in ankylosing spondylitis (AS). Using data from the Spondyloarthritis Research Consortium of Canada (SPARCC) cohort, data sets from patient visits were analyzed to determine correlations between alcohol intake prior to diagnosis (PreDx), at diagnosis (Dx) and at current visit (CS). PROs included Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), AS Quality of Life (ASQoL) Short Form Health Survey (SF-36), Patient Global Assessment of Disease Activity (PGA), EuroQoL (EQ5D) Scores, Health Assessment Questionnaire (HAQ) scores, and Functional Severity Score (FSS). Analysis included simple statistics and Pearson Correlation with statistical significance at a level of $p<0.05$. There were 1330 patients (57.3% males), mean age of 49.92 years (SD 13.3). Mean weekly alcohol intake was 1.6 units PreDx, 1.4 units at Dx and 2.2 at CS. EtOH use at CS was statistically significantly, but weakly correlated with poorer outcomes as assessed by BASFI, BASDI, ASQoL, HAQ, FSS, and SF-36 (Physical Component Score [PCS] and Mental Component Scores [MCS]) ($r2$ all <-0.2 or 0.2; many $r2 <0.1$). Alcohol use at Dx had only one weak, but statistically significant negative correlation ($r2 = -0.05$). Alcohol use prior to diagnosis also had one statistically significant, negative correlation with EQ5D ($r2=0.06$). Current alcohol intake and HAQ pain and stiffness scores correlate negatively whereas there was a positive correlation between current alcohol intake and SF scores. Further studies into the physical and psychological mechanisms underlying these relationships are ongoing.

The Effect of Cigarette Smoking and Alcohol Intake on Patient Reported Outcome Measures in Psoriatic Arthritis

Matthew Piche, Vinod Chandran, Lihi Eder, Dafna Gladman, Sherry Rohekar.

The goal of this study was to assess the effect of alcohol and smoking on patient reported outcome measures (PROs) in psoriatic arthritis (PsA). Data from the International Psoriasis And Arthritis Research Team (IPART) cohort was used to assess alcohol intake prior to diagnosis

(PreDx), at diagnosis (Dx), and at current study (CS). PROs included EuroQoL, HAQ, FSS, FACIT, DLQI, BASDAI, BASFI, ASQoL and SF-36. Analysis included simple statistics and Pearson correlation, deemed statistically significant at $p<0.05$. Smoking at Dx, number of years of smoking at Dx, smoking at CS and number of years smoking at CS were each significantly negatively correlated with HAQ, HAQ pain, HAQ stiffness, FSS, FACIT, BASDAI, BASFI, ASQoL and both physical and mental components of SF-36 ($r2<0.2$ for all correlations). Alcohol use at CS was weakly, but significantly correlated with poorer outcomes on EQ5D, HAQ pain, HAQ stiffness, FSS, FACIT, DLQI, BASDAI, BASFI, ASQoL, and physical and mental components of SF-36 ($r2<0.2$ for all correlations). Significant but weak correlations were found between alcohol at Dx and worse outcomes on physical component of SF-36 ($r2<0.1$). Alcohol use Pre-Dx was significantly correlated with poorer outcomes on HAQ pain, HAQ stiffness, FSS, FACIT, BASDAI, BASFI, ASQoL and both components of SF-36 ($r2 < 0.1$ for all correlations). Smoking weakly correlated with several PROs, with the notable exception of the DLQI. Alcohol intake during the course of PsA also negatively impacted several PROs. However, while these correlations were statistically significant, they were quite weak.

Evaluation of the Classic Clinical Signs When Screening for Endogenous Cushing Syndrome: A Retrospective Validation Study

Serena Pisani, MD, Alaa Khalil Monjed, MBBS, ABIM, FRCPC, Cert. Endo, Lisa-Ann Fraser, MD, MSc,FRCPC, Cert. Endo, and Stan Van Uum, MD, PhD, FRCPC3..

Background: Guidelines for evaluation of CS suggest assessment for the presence, or absence, of classic signs. However, it is not known if evaluation of these signs is useful for assessing the full clinical spectrum of disease. Objectives: To validate previously published LRs for classic signs of CS in all patients referred for screening. Subgroup analysis to investigate if these signs help to assess patients with low to medium pretest probability of CS. Methods: We performed a retrospective chart review of all patients, >18 years old, undergoing biochemical testing for endogenous CS between 2003 and 2009. We determined the presence or absence of classic signs of CS. LRs were calculated and compared to previously published LRs. For the subgroup analysis, we excluded patients with high clinical suspicion of CS, defined as having ≥ 4 classic signs, and again calculated LRs. Results: We reviewed 123 patients, 18 were excluded. Of the 105 remaining, 14 were diagnosed with CS. Positive LRs for all patients with CS were similar to previously published: easy bruising 3.06, osteoporosis 9.75, facial plethora 3.08, hypertension 1.76, purple striae 6.50, and proximal myopathy 6.50. In the subgroup analysis, patients with low to moderate pretest probability of CS, only proximal myopathy was a useful sign: LR= +6.96. Conclusion: This study suggests that classic signs, known to have high positive LRs, are helpful in identifying patients with florid CS; but are less helpful when assessing patients with low to medium clinical suspicion. In this group, proximal myopathy is the most useful.

Supporting the Link Between Thyrotoxicosis and New Onset Sleepwalking: An Unusual presentation of a Common Condition.

Dr. Megha Poddar, FRCPC, Dr. Lisa Ann Fraser, FRCPC.

A 17-year-old female presented with typical symptoms of thyrotoxicosis. She had prominence of one eye, diplopia and compressive symptoms concerning for Graves' disease. She had no history of psychiatric illness or sleep disorders in childhood. Her most notable symptom was the new onset of sleep walking which occurred with the onset of her other symptoms. She had been found wandering around the house throughout the night with no recollection of these events upon awakening. Biochemically she had an elevated free T4 of 72.6 pmol/L (7.2-21.0), free T3 of 38.5 pmol/L (2.9 – 6.0) and a suppressed TSH of < 0.03 pmol/L (0.3 – 5.6). Her ultrasound showed diffuse enlargement of her thyroid gland, with no prominent nodules. Her elevated TBII of 20.7 IU/L (0 – 0.19) confirmed her diagnosis of Graves' thyrotoxicosis. She was treated with Methimazole 30mg and Atenolol 25mg daily. As her free hormones improved, her sleepwalking behaviour diminished and eventually subsided with normalization of her hormone levels. Thyrotoxicosis may exacerbate triggers for abnormal sleep behavior including stress and insufficient sleep. Eight cases of patients with thyrotoxicosis exhibiting new sleep walking behavior have been documented in the literature, but none in North America. In a previous case, the sleep walking behavior re-occurred with non-adherence to anti-thyroid medications; increasing the plausibility of a relationship between these disorders. New onset sleepwalking may be an under-recognized symptom of thyrotoxicosis and seems to resolve with treatment of the thyroid disorder. It may be beneficial for physicians to inquire about sleep behaviours in these patients.

The InPatient Osteoporosis Future Fracture Assessment (TIPOFF) Quality Improvement Project

Megha Poddar, MD, Gita Majdi MD, James Howard MD, MSc, FRCSC, TerryLyne McLaughlin NP, Lisa-Ann Fraser MD, MSc.

Introduction: Thirty thousand Canadians experience hip fractures annually, with mortality rates of 28-37% within the following year. Guidelines recommend osteoporosis treatment for all hip-fracture patients, with proven fracture and mortality reductions. However, 80% of patients in Canada with a hip-fracture do not get evaluated or treated. We sought to improve hip-fracture assessment and treatment rates at our center. Methods: Hip-fracture inpatients at University Hospital were identified post operatively one week prior to, and then 8-weeks during, the intervention. Bloodwork was ordered by the orthopaedics-NP who identified patients over age 50 with a fragility-fracture. Twice weekly an Endocrinologist assessed patients, and initiated osteoporosis medications in hospital if no contraindications were noted. Family Physicians were notified of treatment and follow up recommendations. Results: Prior to the intervention 11 hip-fracture patients were observed, 0 were discharged on osteoporosis therapy. During the intervention, 24 of 25 hip-fracture patients underwent an osteoporosis assessment; 1 patient died. Mean patient age was 77.87±11.5. Fourteen patients had a previous fragility fracture, including 4 with previous hip-fractures. Eight patients were already on medications for osteoporosis, which were continued or changed, and 8 patients were started on treatment. Eight patients were unable to start medications due to contraindications including renal failure and hypocalcemia that were identified. No delays to discharge or adverse effects occurred in patients started on treatment. Conclusion: The TIPOFF project lead to osteoporosis assessments in 96% of hip-fracture inpatients, and 66% left hospital on osteoporosis treatment;

significantly improving our care gap without any adverse events.

Risk of Ventricular Arrhythmia with Citalopram and Escitalopram

Elena Qirjazi, Eric McArthur, Danielle M Nash, Stephanie N Dixon, Matthew Weir, Akshya Vasudev, Lorne Gula, Matthew Oliver, Ron Wald, Amit X Garg.

Objective: To investigate the 90-day risk of ventricular arrhythmia associated with citalopram or escitalopram. Design: Population-based retrospective cohort study. Setting: Ontario, Canada, from 2002 through 2012. Participants and Exposures: Older adults (mean age 76 years) who were newly prescribed citalopram (n= 137 701) or escitalopram (n = 38 436), compared to those prescribed referent antidepressants sertraline or paroxetine (n = 96 620). After statistical weighting using a propensity score, the baseline characteristics of patients prescribed citalopram and the referent antidepressants were similar; likewise for patients prescribed escitalopram and the referent antidepressants. Outcomes: Outcomes were assessed within 90 days of a new prescription. The primary outcome was a hospital encounter (emergency room or hospital admission) with ventricular arrhythmia - assessed using hospital diagnostic codes (good positive predictive value but limited sensitivity). The secondary outcome was all-cause mortality. Results: Citalopram was associated with a higher risk of a hospital encounter with ventricular arrhythmia compared with the referent antidepressants (0.06% vs. 0.04%, RR 1.53, 95% CI 1.03 to 2.29), and a higher risk of mortality (3.49% vs. 3.12%, RR 1.12, 95% CI 1.06 to 1.18). Escitalopram was not associated with a higher risk of ventricular arrhythmia compared with the referent antidepressants (0.03% vs. 0.04%, RR 0.84, 95% CI 0.42 to 1.68), but was associated with a higher risk of mortality (2.86% vs. 2.63%, RR 1.09, 95% CI 1.01 to 1.18). Conclusion: Citalopram was associated with a modest but statistically significant increase in the 90-day risk of a hospital encounter for ventricular arrhythmia and all-cause mortality.

Are Homocitrullinated Lipoproteins Involved in the Pathogenesis of Rheumatoid Arthritis-Associated Atherosclerosis?

Arthi Rajamohan, Sallie ElHayek, Ewa Cairns, Murray Huff, Geoffrey Pickering, David Bell, Lillian Barra.

Background: Rheumatoid Arthritis (RA) patients who express antibodies targeting citrullinated proteins have up to 8 times the risk of CVD compared to the general population. The mechanism by which these antibodies contribute to CVD pathogenesis is unknown. Citrullinated proteins are structurally similar to homocitrullinated proteins, which have been identified in atherosclerotic plaque. Also, homocitrullinated LDL (HcitLDL) has been shown to promote the formation of lipid-laden macrophages (foam cells), which are implicated in the pathogenesis of atherosclerosis. We aim to study the effects of homocitrullinated and citrullinated proteins/lipoproteins on macrophage function in vitro. Methods: Human LDL and fibrinogen was homocitrullinated by incubating with potassium cyanate and citrullinated using peptidyl arginine deiminase in a calcium- containing buffer. Homocitrullination and citrullination was confirmed using Western Blot analysis. RAW 264.7 cells were cultured and differentiated into macrophages using phorbol myristate acetate. After 24 hours, macrophages were treated with LDL, acetylated LDL, HcitLDL, citrullinated fibrinogen (CitFib) + LDL, homocitrullinated

fibrinogen (HcitFib) +LDL. Foam cells were visualized using oil red staining and phase contrast microscopy. Results: HcitLDL strongly induced foam cell production in macrophages (89%). This was significantly higher than unmodified LDL (16%, P<0.001) and comparable to acetyated LDL (92%), which is a known potent inducer of foam cells. There were no statistically significant differences between LDL (16%), CitFib + LDL (23%), HcitFib+LDL (20%) and untreated macrophages (10%). Conclusion: HcitLDL appears to promote foam cell production in vitro. Further studies are needed to determine the effect of citrullinated proteins/lipoproteins on macrophage function.

Pre-hospital versus In-Hospital Hypothermia for Out-of-Hospital Cardiac Arrest: A Meta-Analysis of Randomized Trials

Varinder K Randhawa, Janet Martin, Shahar Lavi.

Background: There remains controversy whether earlier initiation of hypothermia for patients with out-of-hospital cardiac arrest (OHCA) improves outcomes. This study aims to determine if pre-hospital (in the field) versus in-hospital (after hospital arrival) initiated hypothermia improves clinically-relevant outcomes in OHCA. Methods: All randomized trials of pre-hospital versus in-hospital hypothermia in OHCA with at least one predefined outcome were identified in MEDLINE, Cochrane, EMBASE, and abstract databases up to July 2014. A composite of death and poor neurological status with cerebral performance category (CPC) score over 2 was the primary outcome. Subgroup analyses included arrhythmia type, cooling modality, and hypothermia duration. The random effects model was used to calculate risk ratios (RR, 95% confidence intervals [CI]). Heterogeneity was quantified by the I2 statistic. Results: Seven randomized trials involving 2,367 patients were included. Pre-hospital hypothermia did not reduce the composite of death or poor neurologic outcome compared with in-hospital hypothermia, (69.7% vs 69.3% for pre-hospital vs in-hospital; RR 1.01, 95% CI 0.82 to 1.26, p=0.90; I2=0%). All-cause mortality (RR 0.97, 95%CI 0.93 to 1.02; I2=0%), poor neurologic outcome (RR 0.99, 95%CI 0.84 to 1.16; I2=0%), acute kidney injury (RR 0.54, 95%CI 0.05 to 6.03; I2 = 0%), and pulmonary edema (RR 1.82, 95%CI 1.44 to 2.30; I2 = 0%) for pre-hospital vs in-hospital initiated hypothermia were not improved. Effects were similar across subgroups. Conclusions: Overall, the evidence from randomized trials indicates that pre-hospital hypothermia does not improve outcomes including death or adverse neurologic outcomes compared with in-hospital hypothermia.

Hypothermia versus Normothermia, and Outcome Dependence on Target Temperature, in Out-of-Hospital Cardiac Arrest: A Meta-Regression of Randomized Trials

Varinder K Randhawa, Janet Martin, Shahar Lavi.

Background: Recent studies indicate aggressive hypothermia for out-of-hospital cardiac arrest (OHCA) may be unnecessary. This study aims to determine whether different target temperatures improve clinically-relevant outcomes. Methods: We identified all randomized trials (RCTs) of temperature in OHCA (hypothermia versus normothermia, and <36°C versus ≥36°C for primary and secondary analyses) in MEDLINE, Cochrane, and EMBASE since July 2014. A composite of death and poor neurological status with cerebral performance category

(CPC) score over 2 was the primary outcome. Risk ratios (RR) and 95% confidence intervals [CI] were calculated, and meta-regression was performed by temperature achieved. Heterogeneity was calculated using I2 statistic. Results: For normothermia versus hypothermia, 7 RCTs involving 570 patients were included. For <36°C versus ≥36°C, 8 RCTs involving 1509 patients were included. Hypothermia versus normothermia significantly reduced the composite of death/poor neurologic outcome (RR 0.79, 95% CI 0.68 to 0.92, p=0.002; I2=40%). All-cause mortality (RR 0.79, 95%CI 0.67 to 0.92; p=0.003; I2=0%) was reduced and good neurologic outcome of CPC 1 or 2 (RR 1.42, 95%CI 1.15 to 1.74; p=0.001, I2=4%) was significantly improved with hypothermia. Results were similar in secondary analysis of lower versus higher temperature (i.e., for <36°C versus ≥36°C). Meta-regression showed a significant relationship between target temperature and death/poor neurologic outcome (p<0.0001). Conclusions: Existing evidence indicates that lower temperatures improve all-cause mortality and neurologic outcomes compared with higher temperatures in OHCA, and meta-regression suggests that lower temperatures are associated with the greatest improvement.

First Trimester Patients With Surgical Diagnoses: Clinical Factors and ED Management

M. Riggan, J.A. Koichopolos, S.L. McLeod, M. Klingel, R.W. Roebotham, D. Thompson.

Introduction: First-trimester pregnancy concerns may be related to normal pregnancy, signs of miscarriage or serious surgical diagnosis. The shift to outpatient management of early pregnancy complications makes ED identification of patients at risk for surgical intervention essential. Objective: to examine the clinical factors and ED management of patients with early pregnancy concerns that required surgery within 14 days Methods: Retrospective chart review of first-trimester pregnancies presenting to the ED in 2013 for concerns requiring surgical intervention within 14 days of ED visit. Exclusion criteria: direct to another service, >12 weeks gestational age, known ectopic or incomplete abortion. Results: 33 patients were included, 25 had a Point of Care ultrasound (POCUS). No patient who received POCUS had an incorrect diagnosis of intrauterine pregnancy (IUP). 15 were referred for admission; 8 were referred to an Early Pregnancy Assessment Unit; 1 had pre-arranged outpatient follow-up and 1 had a planned ED return for formal US; 3 were taken to the OR. 8 patients did not have a POCUS; 3 were referred for admission, 3 had EPAU follow-up, 1 had a planned ED return for formal US, and 1 had no follow-up. Final Surgical diagnoses: 16 (48%) ectopics, 10 (30%) incomplete abortions; 1 (3%) molar pregnancy; 2 (6%) appendicitis; 2 (6%) LIUPs; 1 (3%) cholecystitis; Conclusion: In this review, all ectopic pregnancies (the predominant diagnosis) were either identified in the ED or via appropriate follow-up. No patient with ectopic pregnancy was misdiagnosed on ED POCUS. POCUS expedited surgical intervention in 3 patients.

Toxic Megacolon from Shigella infection: A case report of a 26 year old.

Steven Russell, John Snider & Jeffery Shum.

Introduction: While fever and bloody diarrhea are common features of Shigella gastroenteritis, the disease is normally self-limiting. Progression to toxic megacolon is both rare and life-threatening. A case of toxic megacolon caused by Shigella flexneri

that needed to be managed with surgical resection is described here. Case Report: A 26 year old, otherwise healthy male, presented to Emergency Department with 5 day history of bloody diarrhea and fever. He was tachycardic and febrile with a tender and distended abdomen. Blood work showed an elevated WBC and abdominal x-ray revealed a dilated transverse colon of 12cm. Blood and stool cultures were positive for Shigella flexneri. Despite antibiotics, his condition worsened with subsequent x-rays showing free-air in the abdomen. Surgical exploration revealed pan-necrosis of the colon and sub-total colectomy with end-ileostomy was performed. Discussion/Conclusion: Shigella causing dysentery is a well-known medical condition but its complications are rarely seen and very serious. Intestinal obstruction, colonic perforation and toxic megacolon occur in less than 3% of cases. The condition can progress rarely to toxic megacolon and even more rarely to requiring surgical intervention. Through this case, we demonstrated that the correct diagnosis is essential because delayed or inappropriate (i.e. corticosteroids) treatment could prove disastrous. This case also highlights the significance of stool culture follow-up after discharge in the patient with dysentery.

Comparison of carotid intima media thickness in those with and without diabetes mellitus in a southwestern ontario population

Sabreena Sadat, Tamara Spaic, Irene Hramiak, Michael Weingert, Selina Liu
Abstract.

Introduction: Carotid intima media thickness (CIMT) is an established index of generalized atherosclerosis. Several large epidemiological studies have demonstrated association between increased CIMT and future cardiovascular events in the general population, and in those with diabetes (DM). However, each laboratory must develop its own normative data based on local technique, equipment, and patient population. This study characterized the CIMT and other cardiovascular risk factors of a local cohort of patients with and without DM. Methods: A retrospective cohort study (2001-2014) of patients from a local Cardiology clinic in London, Ontario was performed. Demographic (age, gender) and clinical (body mass index, blood pressure, smoking, anti-hypertensive/diabetic/lipid medications) characteristics and CIMT measurements from 1581 patients (323 with DM, 1258 without DM) were summarized and associations between these characteristics and CIMT were assessed by multivariable linear regression. Results: Overall, median CIMT ranged from 0.55-0.87mm. In both genders, CIMT increased with age: 0.05mm every 10 years ($p<0.001$). CIMT was significantly higher in subjects with DM vs. those without: mean 0.782±0.147 mm vs. 0.731±0.153mm ($p=0.005$). However, this difference no longer remained significant when adjusted for age, gender, BMI, blood pressure, smoking, and anti-hypertensive/diabetic/lipid medications. Conclusion: There was no significant difference in CIMT between patients with and without DM after adjustment for other traditional cardiovascular risk factors. This suggests that better primary prevention therapies in patients with DM (i.e. control of lipids, blood pressure, obesity) may have helped prevent progression of CIMT thickening, thus reducing the future atherosclerotic risk in this population.

Executive function, gait function, and regional cerebral glucose metabolism in healthy older women

Ryota Sakurai, Kenji Ishii, Yoshinori Fujiwara, Masashi Yasunaga, Naoko Sakuma, Shoji Shinkai, Manuel Montero-Odasso.

Background: Low executive function is associated with gait dysfunction in older adults. However, little is known about the neural basis underlying this association. We aim to investigate the relationship between regional cerebral metabolic rates of glucose (rCMRglc) and executive / gait functions in physically and mentally high-functioning community-dwelling older women. Methods: Eighty-six healthy older women (mean age [SD], 74.7 [5.4] years) underwent positron emission tomography using [18F]fluorodeoxyglucose (FDG-PET) to assess brain activity at rest. We measured rCMRglc in 15 regions of interest. Within 6 months before and after the FDG-PET, MMSE, TMT-A, TMT-B, maximum gait speed and TUG test were measured. Associations between variables were examined using multiple linear regression analyses adjusted for demographic variables, height, weight, blood pressure, and comorbidities. Results: Lower TMT-B scores (i.e., executive function) were associated with poor performance in maximum gait speed and TUG. For the cerebral glucose metabolism, lower TMT-B score was associated with lower rCMRglc in the posterior cingulate, parietal and primary sensorimotor cortices whereas lower TUG ability was associated with lower rCMRglc in the primary sensorimotor cortex. There was no significant association between maximum gait speed and rCMRglc. Conclusion: The known relationship between lower executive function and lower gait ability in seniors may be explained by reduced metabolic activity in the primary sensorimotor cortex. To best our knowledge, this is the first study to point out this association. Future longitudinal studies are needed to examine causality in this intriguing association.

Methotrexate and cardiovascular events: systematic review and meta-analysis

Alpesh R. Shah, Dr. Lillian J Barra, Dr. Daniel G Hackam.

Background: Chronic autoimmune disease is a leading cause of cardiovascular morbidity and mortality. Methotrexate (MTX) is a commonly used treatment for a variety of autoimmune conditions to reverse progressive disease. Methods: We conducted a systematic review and meta-analysis to assess the association of MTX with cardiovascular morbidity, cardiovascular mortality and all-cause mortality in patients with autoimmune disease. Our primary outcome was incident cardiovascular events. After screening 13,479 citations, we identified 30 eligible studies (20 cohort studies, 7 case-control studies and 3 randomized controlled trials). We synthesized adjusted risk estimates using a random effects model to compute pooled risk ratios and 95% confidence intervals for each outcome of interest. Results: MTX was significantly associated with a 25% reduction in cardiovascular events (pooled RR: 0.75, 95% CI: 0.65, 0.86, I2: 11%), a 55% reduction in cardiovascular mortality (pooled RR: 0.45, 95% CI: 0.26, 0.80, I2: 33%) and a 40% reduction in all-cause mortality (pooled RR: 0.60, 95% CI: 0.48, 0.76, I2: 45%). The evidence for cardiovascular events was rated as moderate using GRADE. In a dose-response analysis, low-cumulative dose MTX was associated with a stronger effect size for reducing cardiovascular events than high-cumulative dose MTX (RR: 0.61, 95% CI: 0.51, 0.74 versus RR: 0.88, 95% CI: 0.78, 0.99, respectively). Conclusion: The findings from this systematic review are

suggestive of a significant associative reduction in cardiovascular events with the use of low-dose MTX in patients with autoimmune disease.

Morbidity and mortality associated with pre-hospital "lift assist" calls.

Shephard L, Klingel M, McLeod SL, Dukelow A, Lewell M, Davis M.

Introduction: When an individual requires assistance with mobilization, emergency medical services (EMS) may be called. If a patient does not receive treatment on scene and is not transported to hospital for medical attention, these are referred to as "Lift Assist" (LA) calls. It is possible this need for assistance represents a subtle-onset of a disease process or decline in function. Without recognition or treatment, the patient may be at risk for recurrent falls, repeat EMS visits or worsening illness. Objective: To determine the 14 day morbidity and mortality associated with LA calls. Methods: All LA calls from a single EMS agency were collected over a one-year study period (Jan - Dec 2013). These calls were linked with hospital records to determine if LA patients had a subsequent visit to the emergency department (ED), admission, or death within 14 days. Results: There were 42,055 EMS calls in the study period; 808 (1.9%) were LA calls. These calls were for 428 individuals; 313 (73.1%) patients had 1 LA, and 115 (26.9%) patients had >1 LA call; with a range of 2 to 34 calls. There were 169 (20.9%) ED visits, 93 (11.5%) hospital admissions and 9 (1.1%) deaths within 14 days of a LA call. Conclusions: LA calls are associated with short-term morbidity, mortality and considerable use of EMS and hospital resources. These calls may be early indicators of problems requiring comprehensive medical evaluation. Further research is required to identify predictors associated with higher risk of morbidity and mortality in LA patients.

Use of a self-administered Malnutrition Universal Screening Tool (MUST) is not a valid means of identifying inpatients at risk for malnutrition in the setting of the Clinical Teaching Unit.

Dr. Erin Spicer, Dr. Adam Rahman.

BACKGROUND: Evidence exists validating patient self-screening with the Malnutrition Universal Screening Tool (MUST) in a variety of outpatient settings. The validity of MUST in hospitalized patients has not yet been demonstrated. OBJECTIVE: To determine the feasibility of self-screening for malnutrition among inpatients, this study assessed acute medicine patients' ability to self-administer the MUST, as compared to a healthcare provider (HCP) facilitating the MUST. DESIGN: Single day audits of patients admitted to each clinical teaching unit team were conducted. Patients eligible for participation provided signed consent before undergoing malnutrition screening by first independently completing the MUST, and subsequently with the HCP completing the MUST. Each participant then completed an ease-of-use questionnaire. RESULTS: One hundred and twenty-five patients admitted to the London Health Sciences' clinical teaching units (CTU) were considered for enrolment of which 65.6% (82/125) were excluded on the basis of a cognitive impairment preventing them from providing informed consent, or a physical impediment that prevented safe participation in self-screening. A total of 17 inpatients (13.6%) were enrolled, only ten of whom completed the MUST and generated a risk score. Agreement between self-screening and HCP-screening was 70% (7/10). CONCLUSIONS: Owing to the degree of cognitive and physical impairments found in this patient population,

this study concludes that self-screening with the MUST is not a safe, practical, or accurate tool to assessing for the risk of malnutrition on the CTU.

A meta-analysis of multicomponent, non-pharmacological interventions targeting identified barriers to patient flow on the Clinical Teaching Units at University Hospital.

Erin Spicer, Alan Gob Marko Mrkobrada Matthew Ramer.

BACKGROUND: The expanding elderly population is stressing already congested inpatient services. Interventions must be identified to minimize patient complications that hinder patient flow. OBJECTIVE: (1) Identify barriers to patient flow on the Clinical Teaching Units at University Hospital. (2) Evaluate, using systematic review and meta-analysis (SR/MA), the evidence for multicomponent, non-pharmacological interventions for preventing inpatient complications that impede patient flow. DESIGN: (1) Focus groups involving 60 team members from various inpatient services identify perceived barriers to inpatient flow. Barriers were coded, categorized by themes, and prepared as a 'driver diagram'. (2) A SR/MA was conducted to evaluate interventions targeting the identified barriers. Data sources included OVID Medline and EMBase from 1998 to 2015. Two reviewers independently abstracted data on outcome measures. Quality ratings for each study were based on the Cochrane risk-of-bias criteria. RESULTS: The 'driver diagram' identified 5 categories of barriers to patient flow (orientation, cognition, nutrition, communication, and mobility). The SR/MA isolated 11 interventional studies. Five studies demonstrated a reduction in number of falls (odds ratio [OR] 0.43; 95% CI, 0.24 to 0.74). Incidence of delirium decreased in 9 studies (OR 0.52; 95% CI, 0.41 to 0.6. Interventions in four studies resulted in a trend towards decreasing length of stay (OR -0.35; 95% CI, -0.48 to -0.22). CONCLUSIONS: The use of multicomponent non-pharmacological interventions is effective in preventing falls, functional decline, and delirium, and shows a trend towards decreasing length of stay. Multicomponent non-pharmacological interventions can improve identified barriers to patient flow on the CTU.

Loss of RIPK3 and Caspase-8 enhance intrinsic apoptosis in tubular epithelial cell (TEC) death and contributes to kidney ischemia reperfusion injury (IRI)

Baekjun Sung, Ye Su, Arthur Lau, Jifu Jiang, Aaron Haig, Douglas Green, Zhuxu Zhang, Anthony Jevnikar.

[Background] Ischemia-reperfusion injury (IRI) is detrimental in allograft survival and is related to cell death by apoptosis and necroptosis. Eliminating RIPK3-mediated necroptosis provides benefit against IRI while variable results follow Caspase-8 inhibition. We aim to test the benefit of both RIPK3 and Caspase-8 deletion in renal IRI in a mouse model. [Results] 48-hour post renal clamping, DKO mice do not gain additional benefit in protection from RIPK3-/- alone as serum creatinine levels increased compared to RIPK3-/- null mice (74±33 vs. 53±20, umol/L, n=3, $p>0.05$). Compared to RIPK3-/- TECs, DKO TECs displayed enhanced caspase-9 activity (10670±1881 vs. 19367 ± 2397, lum, n=3, $p<0.05$) and intrinsic apoptotic death (18±3 vs 36±2% survival at 24 hr, n=3, $p<0.01$) with IL-1-beta+IFN-gamma. Survival (46±6 vs 62±5 % survival, n=3, $p>0.05$) and caspase-9 activity (11070±1342 vs 10670±1881, lum, n=3, $p>0.05$) of DKO TECs are restored to basal levels of RIPK3-/- with BIP. mRNA of pro-apoptotic BAX

(2.12-fold, n=3, p<0.05) and BAK (3.84-fold, n=3, p<0.0001) are increased in DKO TECs by RT-PCR. Infection with Murine CMV (MCMV) which encodes inhibitors for both BAX and BAK achieved a complete salvage in the TECs. [Conclusion] For the first time, we demonstrate elimination of both caspase-8 and RIPK3 can augment TEC death via up-regulation of caspase-9 mediated apoptosis. These results highlight the complex biology resulting from perturbations of death pathways. Inhibition of multiple forms of cell death will be required to maximize clinical benefit.

Sleep Apnea and Atrial Arrythmias

Erik M. van Oosten, Wonju Song, Amro Qaddoura, Diego Conde, Andrew Hamilton, Dimitri Petsikas, Darrin Payne, Alexander Boag, Damian Redfearn, Shetuan Zhang, Adrian Baranchuk.

Obstructive sleep apnea (OSA) is a common breathing disorder that affects approximately 5% of North American adults but is largely underdiagnosed. It is associated with a myriad of medical conditions including increased cardiovascular morbidity and mortality. Studies have shown that cardiac arrhythmias are common in patients with OSA. Proposed mechanisms of this association include increased sympathetic tone, systemic and pulmonary hypertension, intermittent hypoxia, and inflammation, all of which facilitate structural and electrical remodelling. This review intends to summarize recent works by our group exploring the relation between cardiac arrhythmias and OSA. We investigated OSA as a predictor of recurrence of atrial flutter (AFL) in patients who have undergone AFL ablation, finding that OSA was not a predictor of AFL recurrence following AFL ablation. A prospective study found that OSA was a predictor of post-coronary artery bypass grafting atrial fibrillation (PCAF), and, by extension, with increased length of stay. We further investigated this relationship in a meta-analysis concluding that OSA is independently associated with the development of PCAF. We also performed a study investigating the relationship between inter-atrial block and PCAF but failed to demonstrate an association. We were the first to perform studies looking at human atrial tissue for the effects of OSA on ion channel expression and on histological changes. We found that human right atrial cardiomyocytes in patients with OSA tended to have decreased hERG expression. However, we found no observable histological differences in human right atrial tissue from individuals at high- versus low-risk for OSA.

Percutaneous Mitral Clip Insertion in Severe MR patients from LHSC

Dr.Shahar Lav**i**, **Ying Wang**.

Mitral regurgitation (MR) is a common valvular disease. When severe and symptomatic, surgical intervention is indicated. MR leads to deterioration in patients' functional status, increasing hospitalization and mortality. However, many patients who have high-risk comorbidities in particular severe LV dysfunction and previous CABG, are at high risk for conventional surgery. Percutaneous Mitral Clip Insertion is an alternative intervention. Correcting the Mitral regurgitation surgically has shown to reduce the severity of MR, reverse left ventricular remodeling, improve HYHA functional class, and reduce hospitalization for heart failure. LHSC Cardiology Department in conjunction with Cardiovascular Surgery has performed 16 percutaneous mitral clip insertion procedures up-to-date. Patients are followed in clinic on regular intervals.

Echocardiography was done pre, during and post procedure as well as at follow-up appointments to measure LV function, and degree of MR. The patients' mean age is 75.8 +/- 7.88 who have multiple common comorbidities including HTN, LV dysfunction, dyslipidemia, CAD, CHF, DM, prior CABG and COPD. Patients were having NYHA class 3 or 4 and severe MR prior to procedures. Five patients died during follow-up, including two during the same admission. None of the patients died during the procedure. Our patients post-procedures have measurable severity reduction in MR and NYHA class. Percutaneous Mitral Clip Insertion is a novel procedure at LHSC. This procedure has shown to reduce MR severity and improve NYHA class. Long-term data will be required to further categorize benefits and adverse outcomes from LHSC.

CRicothryoidotomy In-situ simulation Curriculum (CRIC) improves surgical airway performance in Emergency Medicine residents

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Introduction: Cricothyroidotomy is a required Emergency Medicine (EM) skill, despite few real life-training opportunities. In-situ simulation (ISS), a training technique that occurs in the actual emergency department (ED), is a promising method to promote environmental fidelity for rare procedures. The aim of this study was to evaluate cricothryoidotomy performance by EM residents after completion of a curriculum consisting of deliberate practice and ISS. Methods: Twenty EM residents were enrolled. The curriculum consisted of 3 sessions. Session 1 - established participant baseline technical skill. Session 2 – didactic teaching followed by deliberate practice using a task-training manikin. Session 3 - unannounced, high fidelity ISS, during an ED shift, two weeks later. The primary outcome was the difference in skill performance time between session 1 and session 3. ISS feasibility was evaluated based on total ISS time, impact on patient care due to resident absence and post-course surveys. Results: Cricothyroidotomy performance times improved significantly from session 1 to 3 (mean difference 59 seconds, $p<0.0001$). Performance times did not differ significantly between junior (PGY1-2) and senior (PGY3-5) residents ($p = 0.99$). Post course survey responses were favorable for both the curriculum and the unannounced ISS. The mean duration of Session 3 was 17 minutes. Absence from clinical duties during ISS participation resulted in no adverse patient events. Conclusion: This novel curriculum resulted in a significant improvement in cricothyroidotomy performance time among EM residents. ISS proved to be a feasible and effective technique for realistic and more frequent cricothyroidotomy training in an EM residency.

CRicothyroidotomy In-situ Simulation Curriculum (CRIC): A novel competency-based training program for Emergency Medicine residents

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Innovative Concept: The CanMEDS 2015 framework emphasizes the importance of competency-based education within residency programs. Emergency medicine (EM) residents are required to achieve competence in cricothyroidotomy performance, however clinical opportunities are rare. Simulation-based technical skill education offers a training alternative when skills cannot be acquired within the clinical environment. In-situ simulation (ISS), a training strategy that occurs within the

actual patient care environment, can be used to further augment environmental fidelity. We developed a novel training curriculum using ISS to develop cricothryoidotomy competency among EM residents. Methods: A national survey of Canadian EM residents found that most had never performed a cricothryoidotomy in clinical practice thus a need for further training. The curriculum consisted of: 1) deliberate practice-specific skill components that are practiced followed by immediate feedback, and 2) unannounced ISS during the resident's ED shift – to recreate the urgency and realism of a cricothyroidotomy. The curriculum was offered to Royal College EM residents as a pilot for focused competency-based procedure training and to evaluate the feasibility of unannounced ISS during an ED shift. Curriculum: Core skill knowledge was delivered through a didactic session. Using task-training models, participants performed a cricothyroidotomy until competency was met. Two weeks later, an unannounced high-fidelity ISS scenario was conducted in the ED, requiring the performance of a cricothyroidotomy. Conclusion: This curriculum demonstrated the feasibility of ISS as a technical skill training technique within the ED and may provide a transferable framework for skills training in other emergent but rarely performed procedures.

Rheumatologist practices for primary and secondary cardiovascular risk prevention in Giant Cell Arteritis

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Chronic inflammation is a risk factor for cardiovascular disease. Previous studies have demonstrated that the presence of traditional cardiovascular risk factors (including hypertension, hyperlipidemia, diabetes, and smoking) increased the risk of vascular disease in Giant Cell Arteritis (GCA). Methods: We identified a retrospective cohort of patients with GCA between 1998 and 2015 in the Rheumatology Clinic at St. Joseph's Health Care, London, Canada. Cardiovascular complication (CVC) was defined as a composite outcome (any acute coronary syndrome, stroke, transient ischemic events, or peripheral vascular disease). Risk factors for cardiovascular disease (hypertension, dyslipidemia, smoking, and diabetes), Framingham risk stratification score, and medications were extracted from health records. Results: 39 patients were identified: 26 females (66%) and 13 males (33%) with a mean age of 72 and a median follow-up of 34 months. 7 patients (17%) had a CVC and these patients also had higher rates of cardiovascular risk factors. 3 of those 7 patients (43%) were treated with an antiplatelet or anticoagulant at time of GCA diagnosis. At last follow-up, 24 (61%) of the total patients were risk stratified by the Framingham risk score, and 23 of those 24 patients (96%) had been initiated on statin therapy as per Canadian Cardiovascular Society guidelines. Conclusion: In this Canadian cohort, cardiovascular risk factors were associated with a risk of vascular complications in GCA patients; however despite this, management of cardiovascular risk factors at last follow-up was suboptimal in terms of risk stratification and risk factor optimization.

Is Rheumatoid Arthritis Cervical Spine Involvement Decreasing Over Time? Results from a Meta-Analysis

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Objective: RA complications seem less common. The prevalence and progression

of anterior atlanto-axial subluxations (aAAS), vertical subluxations (VS), subaxial subluxations (SA) and associated cervical myelopathy in rheumatoid arthritis (RA) over the past 50 years were determined. Methods: A literature search was performed using Medline-OVID/EMBASE, PubMed, and Scopus (from 1960 to June 21, 2014). Prevalence studies were included if the sample size was at least 100 or the prevalence/progression of cervical subluxations was reported. Prevalence of cervical subluxations was calculated for each study. Student's t test and meta-regression was used to evaluate for significance. Results: A total of 12,249 citations were identified with 59 studies included. The prevalence of aAAS decreased from 36% (95%CI: 30%-42%) before 1980s to 24% (95%CI: 13%-36%) in 2000s (p=0.04). The overall prevalence of VS was 11% (95%CI: 10%-19%), 13% (95%CI: 12%-20%) for SA and cervical myelopathy 5% (95%CI: 3%-9%) without significant temporal changes. Rate of progression of aAAS, VS, and SAS subluxations was 4, 6, and 3 lesions per 100 patients per year, respectively. The incidence of new or progressive cervical myelopathy occurred at 2 cases per 100 patients with known cervical subluxations per year. Conclusions: Since 1960s, only aAAS has decreased dramatically. It is still more than twice as common as VS or SAS. No temporal changes in development of cervical myelopathy in affected RA patients were noted. The progression rate of cervical subluxations and myelopathy was unchanged over time.