University of Western Ontario
Department of Medicine

RESEARCH DAY

Thursday, May 26, 2016
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 2016
Thursday May 26, 2016
Best Western Lamplighter Inn
591 Wellington Road South

Schedule of Events			
Start	End		
8:00	8:30	**Breakfast**	**Poster Setup** (Crystal Ballroom South)
8:30	8:40	**Welcome & Opening Remarks** (Crystal Ballroom North)	
8:40	9:20	Developing a career in clinical research- an example from gastroenterology **Dr. Vipul Jairath** (Crystal Ballroom North)	
9:20	10:00	Arrhythmia Genetics: Implications for Common and Rare Diseases **Dr. Jason Roberts** (Crystal Ballroom North)	
10:00	11:00	**BREAK**	**Poster Presentation and Judging** (Crystal Ballroom South)
11:00	11:45	Targeting Regulated Forms of Cell Death to Attenuate Inflammation: Paradigm Change in Organ Transplantation? **Keynote - Dr. Anthony Jevnikar** (Crystal Ballroom North)	
11:45	13:45	**LUNCH**	**Poster Presentation and Judging** (Crystal Ballroom South)
Afternoon Session – Highlight Research by Department of Medicine Trainees			
14:00	15:00	**Trainee Oral Presentations** (Crystal Ballroom North)	
15:00	15:15	**REFRESHMENT BREAK**	
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

Time	Presenter	Status	Abstract Title	Page Number
2:00pm	Grace Yang	PGY-5	Pharmacologic Management of Takayasu's Arteritis: a Systematic Review	33
2:15pm	Brittany Balint	PhD Student	Ascending aortic dilation in patients with bicuspid aortic valve disease is marked by accelerated vascular smooth muscle cell aging	10
2:30pm	Amanda Brahm	PGY-4	Genetic confirmation rate in clinically suspected maturity-onset diabetes of the young	14
2:45pm	Jacqueline Dron	MSc Student	Elucidating the genetic determinants of extreme high-density lipoprotein phenotypes using next-generation sequencing	17
3:00pm	**Refreshment Break**			
3:15pm	Mike Nicholson	PGY-3	A Novel Surfactant-Based Host-Defense Peptide for the Treatment of Bacterial Pneumonia	27
3:30pm	Jonatan Snir	Post-Doctoral Fellow	Brain White Matter Integrity is Associated with Future Falls In Seniors With Mild Cognitive Impairment	31
3:45pm	Lauren Leggatt	PGY-4	Comparison of vital sign documentation for pre-hospital lift-assist calls and non lift-assist calls	23
4:00pm	Justin Zhu	PGY-2	Comanagement by Nephrologists is Associated with Increased Likelihood of Appropriately Dosed Prescriptions in Patients with Chronic Kidney Disease	34

Poster Presentations

Presenter	Abstract Title	Poster Number	Page Number
Al-Ani, Fatimah	Thromboprophylaxis in Multiple Myeloma Patients Treated with Lenalidomide – A Systematic Review	101	9
Alnahdi, Haifa	Yield of screening for previously undiagnosed acromegaly: A Review of the Literature	102	9
Anand, Nick	The effect of a high fat diet on Rheumatoid Arthritis using a mouse model	103	10
Ballantyne, Emily	Comparison of Patients with Low Bone Mineral Density With and Without Spinal Fracture	104	11
Ballantyne, Brennan	Performance of the EuroSCORE II and Society of Thoracic Surgeons scoring systems in the prediction of in-hospital and 30-day mortality in patients undergoing transcutaneous aortic valve implantation (TAVI).	105	11
Banaschewski, Brandon	CATH-2 is an effective antimicrobial peptide against multi-drug resistant bacteria derived from cystic fibrosis patients as well as tracheostomized pediatric patients	106	12
Berbenetz, Nicolas	Mineralocorticoid receptor antagonists for heart failure: systematic review and meta-analysis	107	12
Bertic, Mia	Variation in Aortic Pressure Upstroke and Amplitude in Elderly Patients with Severe Symptomatic Aortic Stenosis and Preserved Left Ventricular Ejection Fraction	108	13
Bhalla, Anurag	In vivo Morphometry of Emphysema: Alpha-1 Antitrypsin Deficiency	109	13
Boese, Kaitlyn	Everyday advocacy on the clinical teaching unit: Recognizing the importance of ‘Chance Encounters’	110	14
Breadner, Daniel	Impact of Relative Dose Intensity and G-CSF Use in the Adjuvant Treatment of Resected Colon Cancer	111	14
Burke, Amy	Bempedoic acid lowers low density lipoprotein-cholesterol and attenuates aortic atherosclerosis in LDL receptor-deficient (LDLR+/- and LDLR-/-) Yucatan miniature pigs.	112	15
Creider, Julia	Euglycemic diabetic ketoacidosis (DKA) in a trauma patient taking a sodium-glucose co-transporter 2 (SGLT2) inhibitor empagliflozin	113	15
Cui, Fulan	Etomidate use in critically ill patients: A review of current practice patterns in North America	114	16

Presenter	Abstract Title	Poster Number	Page Number
Dilliott, Allison	Identifying the genetic basis of neurodegeneration in 75 patients using a targeted resequencing panel.	115	16
Dong, Alex	Profiling the burdens of night work in an academic emergency department – Traditional 8-hour night shifts versus staggered 6-hour casino shifts	116	17
Durocher, Daniel	Quality Improvement of Heart Failure Clinics: Defining and Developing Quality Indicators to Improve Health Care	117	18
Enzevaei, Atoosa	What proportion of the published articles in critical care journals are valid and relevant	118	18
Esmaeilbeigi, Faranak	Cardiovascular Comorbidity in Systemic Lupus Erythematosus has a Large Care Gap	119	18
Gong, Zhaowei (John)	Reducing 30-Day Readmission Rates in the Elderly: A Systematic Review	120	19
Gupta, Manika	Does cell size matter?: Utilizing mean cell volume in hospitalized patients as a screen to determine common causes of anemia including iron deficiency anemia, vitamin B12 and folate deficiency	121	19
Hewson, Carly	Changes in antibodies to extractable nuclear antigens, double stranded DNA and complement over time in systemic lupus erythematosus.	122	20
Hugel, Nicole	Developing a resident-driven post-graduate academic half-day curriculum	123	20
Kyle, Rachel	ReCoM: The Development of the Resident Communication Manual	124	21
Lac, Patrick	Immune responses to homocitrulline and citrulline in patients with Rheumatoid Arthritis	125	21
Lac, Patrick	Immune responses to homocitrulline and citrulline in a mouse model of Rheumatoid Arthritis	126	22
Landman, Simon	Improving Patient Flow: The Impact of an Emergency Department Consults Rotation in Two Canadian Teaching Hospitals	127	22
Lau, Vincent	Factors Associated with the Increasing Rates of Discharges Directly Home from Intensive Care Units (Directly from ICU Sent to Home: Changing Trends in Intensive Care Unit Discharges – DISH Study)	128	22

Presenter	Abstract Title	Poster Number	Page Number
Lebert, Julie	Improving the Quality of Care of Patients with Systemic Vasculitis using an Interdisciplinary Approach	129	23
Leggatt, Lauren	Factors predicting morbidity and mortality associated with pre-hospital “lift assist” calls	130	24
Lu, Mary	A case of Leprosy contracted in a North-American Extreme Tourist	131	24
Maddison, Andre	Inpatient referrals from LHSC clinical teaching units to palliative care: A seamless transition?	132	25
Malette, Jacqueline	Utility of Biomarkers for the Diagnosis and Management of Takayasu’s Arteritis: A Systematic Review	133	25
Masciantonio, Marcello	The role of metalloproteinases and TIMPs in regulation of pulmonary microvascular endothelial cell barrier function during sepsis	134	26
Milos, Scott	The Impact of Ventilation Induced Lung Injury on the Intracellular Pulmonary Surfactant System	135	26
Mount, Gillian	Safety of Weight-Adjusted Dosing of LMWH in Clinically Obese Patients with VTE	136	27
Nguyen, Khoa Binh	Mentorship experience across specialties: Resident’s perspective	137	27
Paul, Christina	Successful treatment of steroid-resistant fibrosing organising pneumonia causing respiratory failure with mycophenolic acid	138	28
Rao, Sanath	Use of three dimensional rendering of point of care ultrasound images to assess static body structures in healthy volunteers and patients in the intensive care unit	139	28
Robinson, Brianne	Maternal Diabetes diet supplemented with or without olive oil differentially impacts pancreas development	140	29
Russell, Steve	Gaucher Disease Screening at a General Adult Hematology Referral, Single Canadian Tertiary Care Centre: A Prospective Study	141	29
Samotus, Olivia	Kinematic measures of bilateral upper limb essential tremor personalize botulinum toxin type A therapy	142	30
Sangha, Navjeet	Risk Factor Management in Vascular Surgery Patients	143	30
Sathiyapalan, Arani	Use of Alkylating Chemotherapy in High Grade Neuroendocrine Tumours: Evaluation of real world data.	144	30

Presenter	Abstract Title	Poster Number	Page Number
Shapiro, Roman	The BMi: A Novel Clinical Decision Tool to Guide Azacitidine Therapy in Myelodysplastic Syndrome patients	145	31
Song, Hao Yuan	Polypharmacy increase risk of falls probably by affecting gait velocity and stability	146	32
St. Bernard, Rosanne	Safe utilization of Ibrutinib with or without steroids in patients with Chronic Lymphocytic Leukemia with Autoimmune Hemolytic Anemia	147	32
Townsend, Cassandra	Polymicrobial bacteremia with Actinomyces odontolyticus, Fusobacterium and Atopobium parvulum secondary to septic thrombophlebitis in an immunocompetent patient	148	33
Yu, Jeffrey	Reducing wait time for radiological investigations in Urgent Medical Clinic	149	33

Thromboprophylaxis in Multiple Myeloma Patients Treated with Lenalidomide – A Systematic Review

Fatimah Al-Ani, Jose Maria Bastida Bermejo, María-Victoria Mateos, Martha Louzada.

Background: The optimal approach of thromboprophylaxis in patients with newly diagnosed multiple myeloma (NDMM) or relapsed refractory multiple myeloma (RRMM), receiving lenalidomide-based therapy (LBT) has not yet been established. Objective: To compare the efficacy of aspirin (ASA) with low molecular weight heparin (LMWH) prophylaxis in myeloma patients on LBT. Results: Six studies were included with 1125 adult participants (Table1 and 2). There was a significantly higher VTE risk for patients receiving lenalidomide plus high-dose dexamethasone (RD) on ASA prophylaxis compared to lenalidomide plus low-dose dexamethasone (Rd) [RR=2.5 (95% CI: 1.68-3.96), p <0.0001]. Patients who received lenalidomide and dexamethasone alone had a significantly higher risk of VTE compared to those on MPR while on ASA prophylaxis (RR=6.4 [(95% CI: 4.11- 9.91), P < 0.0001]). Conclusion: More studies comparing the efficacy and safety of ASA to LMWH are warranted, incorporating the IMWG VTE risk stratification criteria. Study Design Rx N VTE N (%) 95% CI Zonder, 2010 Rajkumar, 2010 Phase III RCT RD 195 52 (26.6) 20.0-33.2 Larocca, 2011 Rajkumar, 2010 Phase III RCT Rd 262 27 (10.3) 7.18-14.58 Palumbo, 2012 Stewart, 2014 Phase III RCT MPR 458 19 (4.1) 2.67-6.38 Total 915 98 (10.7) 8.86-12.88 Table1. VTE rate in NDMM using ASA. Paper Design Rx Setting N VTE N (%) 95% CI Klein, 2008 Retrospective RD RRMM 45 1(2.2) 0.39-11.57 Larocca, 2011 Phase III RCT Rd NDMM 166 2(1.2) 0.33-4.28 Total 211 3(1.4) 0.48-4.09 Table2. VTE rate in myeloma patients using LMWH.

Yield of screening for previously undiagnosed acromegaly: A Review of the Literature

Stan VanUum, **Haifa Alnahdi**, Alescia Azzola, Ali Imran.

Background: Acromegaly has an insidious onset and in most patients there is a considerable delay in diagnosis. Guidelines indicate there is a need for improved screening for acromegaly, and recommend screening in patients with known comorbidities of acromegaly. The objective was to determine the usefulness of screening for previously undiagnosed acromegaly in different clinical settings. Study design: We searched the biomedical literature for studies evaluating screening approaches for acromegaly were analyzed their findings. Results: Five articles were identified using the search criteria. Four out of five concluded that screening for acromegaly is useful in certain clinical settings. The yield was less than 0.6%, except for the study that used a questionnaire inquiring for acral (shoe and/or ring size) increase in whom a 2% prevalence of previously undetected acromegaly was found. Conclusion: There is a paucity of studies on screening for acromegaly, and the results have been relatively disappointing, except for use of the questionnaire on increase in acral size. There is a need for further studies to determine which population groups should be screened, what screening tools should be used and what the cost-effectiveness of these approaches is.

Infertility in patients treated with cyclophosphamide for non-cancerous indications: a meta-analysis and systematic review

May Alzahrani, Lillian Barra.

BACKGROUND: Cyclophosphamide (CYC), an alkylating agent, which was used initially as an anti-cancerous drug, is a potent immunosuppressant that has been used successfully in various autoimmune diseases with major organ involvement. There are concerns about gonadal toxicity as a serious side effect of this drug. The rate of premature ovarian failure was approximately 50% in studies of patients who received high doses of CYC for cancer treatment. OBJECTIVE: to determine the prevalence of infertility in males and females treated with CYC for non-cancerous indications. METHOD: We searched the English language

literature using PubMed, EMBASE and the Cochrane library and included studies that report an association between CYC and infertility in men and women of childbearing age for patients with non-cancerous, autoimmune diseases. Case reports and case series were excluded. RESULT: 121 out of 315 papers met the inclusion criteria. Data has been extracted from 43 studies with 987 subjects, most of them females treated with CYC for lupus nephritis. Other conditions included vasculitis and multiple sclerosis. Cumulative CYC dose was extracted. The following outcomes were reported: premature ovarian failure, transient amenorrhea, oligo- or azoospermia, miscarriage, stillbirth, and neonatal death. These outcomes occurred infrequently; however, studies with women >35 years suggest a significant risk for premature ovarian failure. CONCLUSION: Infertility in men and young women treated with low dose CYC for severe autoimmune disease appears to be uncommon. Studies suggest an increased risk of infertility in older women and patients who received higher cumulative doses.

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

Nick Anand, Julia St. John, Murray Huff, Geoffrey Pickering, David Bell, Ewa Cairns, Lillian Barra.

Objective: Rheumatoid Arthritis (RA) is a chronic autoimmune disorder characterized by the production antibodies to citrullinated proteins. Obesity is a risk factor for RA. We aim to investigate the effect of a high fat diet on arthritis using a mouse model of RA. Methods: Mice expressing human leukocyte antigen DR4 (DR4Tg) are known to develop arthritis by day 35 after immunization with citrullinated proteins. DR4Tg mice and C57BL/6 (B6) controls were fed a high fat high cholesterol (HFHC) diet or standard chow for 40 days, and immunized at day 0 and 20 with PBS, fibrinogen (Fib) or citrullinated fibrinogen (CitFib). Mice were monitored weekly for joint swelling (change in ankle width using calipers) and some were sacrificed at day 30 for joint pathology. Serum IgG anti-CitFib antibody responses were measured using ELISA. Results: Although not obese, HFHC-fed B6 mice (N=6) gained more weight than chow-fed B6 mice (N=6) ($p<0.05$). HFHC-fed (N=13) vs. chow fed (N=13) DR4Tg mice did not gain more weight. Caloric intake and antibody levels did not differ among groups. At day 30, there was no swelling or histologic evidence of arthritis in any of the mice. After day 35, CitFib immunized chow-fed DR4Tg mice (N=6) displayed a significant ankle swelling compared to the other groups ($p<0.01$). Conclusion: In a mouse model of RA, short-term feeding of a HFHC diet did not induce obesity or increase arthritis severity. Future work will investigate the impact of longer exposures to a HFHC diet in DR4Tg mice.

Ascending aortic dilation in patients with bicuspid aortic valve disease is marked by accelerated vascular smooth muscle cell aging

Brittany Balint, Hao Yin, Zengxuan Nong, Fuyan Li, Oula Akawi, Stephanie Fox, Stephanie Rogers, Caroline O'Neil, Lindsay Chase, Michael M.W. Chu, J. Geoffrey Pickering

Background: Individuals with a bicuspid aortic valve (BAV) are at increased risk for ascending aorta dilation and rupture. Aortic smooth muscle cell (SMC) loss and extracellular matrix disruption are well-recognized pathologies, but the cellular mechanisms remain elusive. We hypothesized that aortic dilation in BAV patients is marked by accelerated cellular aging. Methods/Results: Ascending aorta samples were obtained from BAV patients undergoing aorta replacement (n=40, age 55.5±2.3, aortic diameter 4.8±0.1cm) or patients with a tricuspid aortic valve and non-dilated aorta undergoing coronary bypass (n=10, age 64.1±7.6, aortic diameter 3.2±0.2cm). Assessment of fresh tissue for senescence-associated β-galactosidase (SA-ß-Gal) activity revealed that 4.8% of SMCs in BAV-associated aortas were senescent, whereas SA-ß-Gal activity was rare in non-dilated aortas (0.03%, $p=0.04$). Interestingly, γH2A.X immunostaining revealed DNA double-strand breaks in 25.8% of SMCs in BAV-associated aortas, which was 7.3-fold higher than in controls ($p<0.0001$). Stress-activated p38 MAPK was activated in 38.9% of SMCs in BAV-associated aortas, but only in

21.6% of control aorta SMCs (P=0.0002). Quantitative real-time PCR revealed that expression of collagenase (MMP-1, MMP-8 and MMP-13) was increased in BAV SMCs compared to controls ($p<0.05$). Remarkably, incubation of BAV SMCs with a clinically relevant inhibitor of p38MAPK decreased SA-ß-Gal by 51% ($p=0.0002$), and decreased collagenase expression by 68% ($p<0.0001$). CONCLUSION: These findings identify a previously unrecognized phenomenon of accelerated SMC aging in the BAV-associated aorta. This phenomenon could be a driver of aortic wall degeneration in these patients and a potential therapeutic target.

Comparison of Patients with Low Bone Mineral Density With and Without Spinal Fracture

Emily Ballantyne, Jessica Sennet, Dr. Richard Crilly

It is common to see post-menopausal women with low spinal bone mineral density (BMD) without spinal fractures. Whether they are in early stages of osteoporosis, or whether the low BMD is an artifact is unknown. We hypothesized that low BMD may be an artifact as BMD is an areal density, influenced by vertebral body shape. Wider vertebrae have a greater surface area and may be calculated to have a lower BMD than vertebrae which are deeper and narrower, but of similar mass and strength. Postmenopausal women attending the osteoporosis clinic with a BMD T-score ≤-3.0 at L2-L4 sites, with and without spinal fractures, were studied. Height, weight, age, bone mineral content (BMC), vertebral area, and spine, hip total, neck, and intertrochanteric BMD were collected. Lateral thoracic and lumbar radiographs were assessed for compression fractures. Of 112 women assessed, 39 patients had vertebral fractures. They did not differ in terms of vertebral morphometry, refuting the primary hypothesis. Fracture patients were significantly older (71.3±10.6 vs. 64.2±8.5, $p<0.001$) and had small but significantly greater reductions in BMD at all sites. After multiple-regression analysis, only age ($p=0.001$) and spine T-score ($p=0.014$) remained significant. Low BMD in patients without fractures is not the result of differences in vertebral body shape. These patients may represent an earlier phase in the development of osteoporosis, and may end up with vertebral fractures due to passage of time (risk exposure), or drop in BMD. These patients should be considered at risk and treated accordingly.

Performance of the EuroSCORE II and Society of Thoracic Surgeons scoring systems in the prediction of in-hospital and 30-day mortality in patients undergoing transcutaneous aortic valve implantation (TAVI).

Brennan Ballantyne, Rodrigo Bagur.

Background: Transcatheter aortic valve implantation (TAVI) has emerged as a successful alternative to surgical aortic valve replacement. TAVI is appropriate in selected patients with symptomatic, severe aortic valve stenosis who are at high risk for mortality with conventional open valve replacement. The most commonly used scoring systems for stratifying patient surgical risk and assisting in the selection of patients for TAVI are the EuroSCORE II (ESII) and the Society of Thoracic Surgeons (STS) scoring systems. However, the performance of these risk scores to predict mortality after TAVI remains unclear. Furthermore, the comparative accuracy of the two scoring systems is unknown. Objective: The objective of this study is to evaluate the performance of the ESII and STS mortality scoring systems to predict post-surgical in-hospital and 30-day mortality outcome in patients undergoing TAVI. Methods: This is a single centre, retrospective, case series. ESII and STS risk scores for mortality were calculated in 225 consecutive patients who underwent TAVI from 2009 – 2015 at London Health Sciences Centre. Outcomes were recorded according to the standardized Valve Academic Research Consortium-2 (VARC-2) consensus. Discrete variables were analysed using Student's t-test and continuous variables using Fisher's exact test. Discriminative power was assessed using receiver operating characteristic (ROC) curve. Results and Conclusions: Full results pending completion of data collection and analysis.

CATH-2 is an effective antimicrobial peptide against multi-drug resistant bacteria derived from cystic fibrosis patients as well as tracheostomized pediatric patients

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

Bacterial pneumonia is the leading cause of mortality associated with bacterial infections. With the increasing prevalence of multi-drug resistant (MDR) bacterial infections, there is a dire need for the development of new therapeutics. Previous studies have shown bactericidal efficacy of the antimicrobial peptide CATH-2, in suspension with the exogenous surfactant BLES against laboratory bacterial strains. However, there is currently no data to investigate the potential of CATH-2 or BLES+CATH-2 against clinically isolated bacteria. We hypothesize that CATH-2 and BLES+CATH-2 will be effective antimicrobial agents against multiple clinical bacterial strains. Bacteria from cystic fibrosis and tracheostomized pediatric patients were isolated and identified by the LHSC clinical microbiology lab. Overnight bacterial cultures were suspended at a concentration of ~2 x 106 CFU/ml, and incubated with CATH-2 or BLES+CATH-2 for three hours, plated on chocolate agar plates and counted the following morning. CATH-2 showed bactericidal activity against all P. aeruginosa strains tested, with MIC values of 5-10μM independent of resistance patterns. BLES+CATH-2 exhibited reduced bactericidal activity, but was able to consistently inhibit pediatric-derived P. aeruginosa growth at 100μM concentrations. CATH-2 showed reduced activity against S. aureus samples regardless of clinical source, while BLES+CATH-2 showed no bactericidal effect against any S. aureus samples. CATH-2 has been shown to be an effective antimicrobial agent, as it has bactericidal activity against clinically isolated MDR bacteria. Future directions will investigate the potential of CATH-2 and BLES+CATH-2 to synergize with conventional antibiotics, in order to improve therapeutic options.

Mineralocorticoid receptor antagonists for heart failure: systematic review and meta-analysis

Nicolas Berbenetz, Marko Mrkobrada.

Mineralocorticoid receptor antagonists (MRA) have been associated with improved patient outcomes in patients with heart failure with reduced ejection fraction (HFrEF) but not preserved ejection fraction (HFpEF). We conducted a systematic review and meta-analysis of selective and nonselective MRAs in HFrEF and HFpEF. Methods: We searched Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE. We included randomized controlled trials (RCT) of MRAs in adults with HFpEF or HFrEF if they reported data on major adverse cardiac events or drug safety. Results: We identified 15 studies representing 16321 patients. MRAs were associated with a reduced risk of cardiovascular death (RR 0.81 [0.75-0.87], I2 0%), all-cause mortality (RR 0.83 [0.77-0.88], I2 0%), and cardiac hospitalizations (RR 0.80 [0.70-0.92], I2 58.7%). However, an a-priori specified subgroup analysis demonstrated that these benefits were limited to HFrEF (cardiovascular death RR 0.79 [0.73-0.86], I2 0%; all-cause mortality RR 0.81 [0.75-0.87], I2 0%; cardiac hospitalizations RR 0.76 [0.64-0.90], I2 68%), but not HFpEF (all-cause mortality RR 0.92 [0.79-1.08], I2 0%; cardiac hospitalizations RR 0.95 [0.68-1.31], I2 21%). MRAs increased the risk of hyperkalemia (RR 2.03 [1.78-2.31], I2 0%). Nonselective MRAs, but not selective MRAs increased the risk of gynecomastia (RR 7.37 [4.42-12.30], I2 0% vs. RR 0.74 [0.43-1.27], I2 0%). The quality of evidence was moderate. Conclusions: MRAs improved outcomes in HFrEF but not HFpEF by reducing adverse cardiac events. Selective MRAs do not increase the risk of gynecomastia compared to nonselective MRAs. There is evidence for harm without benefit for MRAs in HFpEF patients.

Variation in Aortic Pressure Upstroke and Amplitude in Elderly Patients with Severe Symptomatic Aortic Stenosis and

Preserved Left Ventricular Ejection Fraction

Mia Bertic, Teefy, Patrick MD. Bagur, Rodrigo MD. Diamantouros, Pantelis MD.

Methods: We analyzed the echocardiographic and hemodynamic data obtained at cardiac catheterization from 24 elderly patients with severe calcific aortic stenosis and preserved LVEF. Peak aortic systolic and aortic pulse pressures are inverse indices for pulsus parvus. The slope of aortic pulse during systole (an inverse index of pulsus tardus) was the quotient of dP (peak aortic pressure) and dT (time difference in msec between these pressure points). These indices were correlated with the degree of valvular stenosis (mean pressure gradient and valve area) utilizing. A subset of 12 patients underwent CT scanning, with quantification of ascending aortic calcification and correlated with the aortic pulse characteristics. Results: Mean age was 78.4 +/- 7.56 years and mean valvular pressure gradient was 48.2 +/- 17.0 mmHg. The slope of aortic systolic pressure upstroke correlated with peak aortic systolic pressure (r=0.71). However, there was no correlation between the peak aortic systolic pressure with aortic valve mean pressure gradient (r=-0.012, r=-0.013 respectively). Correlation between the slope of aortic pulse during systole and aortic valve area was also poor (r= 0.274). Measures of pulsus parvus and tardus correlated poorly with the average percent calcification of the aorta by area (r=0.238, r=0.049 respectively). Conclusion: There is significant variation in aortic pulse characteristics such that the classical findings of pulsus parvus et tardus are not universally present in severe aortic stenosis with preserved left ventricular function. These findings are not correlated with the magnitude of the stenosis nor with the degree of calcification of the ascending aorta.

In vivo Morphometry of Emphysema: Alpha-1 Antitrypsin Deficiency

Anurag Bhalla, Alexei Ouriadov, Eric Lessard, David G McCormack and Grace Parraga.

INTRODUCTION Alpha-1-Antitrypsin-Deficiency (AATD) is a genetic disorder that manifests as early-onset panlobular emphysema. Unfortunately, there are few tools that provide sensitive measures of disease evolution. Hyperpolarized noble gas magnetic-resonance-imaging (MRI) provides a non-invasive way to generate structure-function measurements of pulmonary ventilation and apparent diffusion coefficients (ADC) that help explain symptoms, disease progression and response to therapy, not easily measured using conventional pulmonary function tests and x-ray computed-tomography-imaging (CT). HYPOTHESIS In patients with AATD, MRI generates sensitive regional estimates of emphysema that change significantly over time. METHODS Six patients with AATD (59±6 years) were evaluated using spirometry, plethysmography, MRI, CT, St.-George-Respiratory-Questionnaire (SGRQ) and 6-minute-walk-test (6MWT). One patient was followed longitudinally over four years on five occasions. MRI was performed to obtain ADC and ventilation defect percent (VDP). CT was performed to measure relative lung area <-950 Hounsfield units (RA950). RESULTS Forced-expiratory-volume in 1-second %predicted (FEV1%pred) (54±19%; 25-77%), diffusing-capacity-of-the-lung for carbon monoxide (DLco%pred) (43±10%; 26-80%), RA950 (19±9.0%; 3.0-27%), VDP (24±17%; 10-49%) and ADC 51±.09cm2/s (0.41-0.67cm2/s) were abnormal. For the patient evaluated longitudinally, there was worsening ADC (0.58cm2/s vs 0.54cm2/s), VDP (36% vs 14%), RA950 (19% vs 17%) and FEV1%pred (55% vs 63%). An increase in MR ventilation abnormalities and CT emphysematous zones was primarily in the lower lobes. There was deteriorating 6MWT (480m vs 521m) and SGRQ (43 vs 29). DISCUSSION This is the first demonstration of longitudinal MRI Morphomics in AATD adults for whom lifelong treatment and monitoring is required.

Everyday advocacy on the clinical teaching unit: Recognizing the importance of 'Chance Encounters'

Kaitlyn Boese, Lisa Faden, Sandra DeLuca, Noureen Huda, Mark Goldszmidt.

Background: CANMEDS 2015 emphasizes the importance of partnership in advocacy. While patients, their caregivers, nurses and allied health providers are all fellow advocates, much of their advocacy activities take place during unscheduled or informal communication events. The purpose of this study was to further characterize these encounters and their role in supporting clinical decision making on the clinical teaching unit (CTU). Methods: Constructivist grounded theory was used to guide data collection and analysis in an iterative process. Data included field interviews, field notes, and de-identified copies of patient charts. Results: Informal encounters were observed to provide clinically salient information that informed thinking about diagnosis, management, goals of care, and discharge planning. Moreover, the potential power of unscheduled communication events resonated strongly with individuals in diverse roles on CTU. However, these seemingly 'chance encounters' often arose as a result of a great deal of effort on the part of the advocate. Family members, nursing staff and allied health waited around, interrupted or positioned themselves in order to engage in conversations regarding patient care. The challenges of engineering these unscheduled communication events reflect the barriers to communication on CTU. Conclusions: CTU team members need to understand the importance of unscheduled communication events with patient advocates and the difficulties that these advocates may experience. In some cases, the advocate lacks the skill or influence to initiate the encounter successfully. Advocacy training should address strategies that physician teams can use to better support everyday advocacy and decrease barriers to unscheduled communications.

Genetic confirmation rate in clinically suspected maturity-onset diabetes of the young

Amanda J. Brahm, Grace Wang, Jian Wang, Adam D. McIntyre, Henian Cao, Matthew R. Ban and Robert A. Hegele.

Introduction: Maturity-onset diabetes of the young (MODY) is the most common form of monogenic diabetes, accounting for 2-5% of all diabetes cases. MODY is characterized by autosomal dominant inheritance of mutations in one of 12 genes. Clinical features suggesting MODY include non-insulin dependent diabetes, onset before age 25, lack of obesity and negative autoantibodies. Methods: Between 1999 and 2015, our centre received requests for DNA sequencing from unrelated Canadian patients with clinically suspected MODY. Sanger sequencing was used initially for samples received prior to 2012; after 2012 targeted next-generation sequencing was used. Results: Of 96 samples received, 50 (52.1%) had a likely rare causal variant in one of nine known MODY genes. Of these, 31 (62.0%) were diagnosed by Sanger and 19 (38.0%) by targeted next generation sequencing. The 50 mutation-positive samples comprised 45 unique rare variants, of which the majority were in genes encoding either glucokinase (GCK, or MODY2) or hepatocyte nuclear factor 1-alpha (HNF1A, or MODY3). Furthermore, 15 (33.3%) of the detected rare variants were previously unreported, but were likely clinically significant according to standard bioinformatic methods. An additional six samples had rare variants in MODY genes that were of uncertain clinical significance. Conclusions: These findings suggest that clinical suspicion for MODY has a diagnostic yield of ~ 50% at the molecular level. Patients meeting the criteria for suspicion of MODY should undergo confirmatory genetic testing to allow for definitive diagnosis, identification of other family members and to permit for more appropriate management of their diabetes.

Impact of Relative Dose Intensity and G-CSF Use in the Adjuvant Treatment of Resected Colon Cancer

Daniel Breadner, Frances Whiston Larry Stitt Stephen Welch.

Background: The consequences of dose delays and modifications in adjuvant colon cancer treatment are not well established. Relative dose intensity (RDI) and dose index (DI) have been shown to have prognostic significance in a

number of cancers. Methods: A retrospective review was conducted for patients with stage III CC presenting between 2006 and 2011. The RDI and DI were calculated and examined for correlation with DFS and OS. Results: FOLFOX was used more commonly than capecitabine, 64% vs. 36%. Within the FOLFOX regimen median RDI for oxaliplatin was 76.3%, and 83.5% for 5-FU. Median capecitabine RDI was 73.8%. Median DI were similar at 75.4%, 86.5%, and 69.1%, respectively. 3-year DFS was higher when RDI or DI was >80%, compared to ≤80%, for each chemotherapeutic, however the differences did not reach significance. 3-year OS trended towards being higher in patients with an RDI and DI > 80%. Over half of patients on FOLFOX experienced a dose delay, 64.9% then received G-CSF. Patients who received G-CSF had a higher DI than those who did not, 74.9% and 87.4% versus 66.5% and 76.8%. 3-year DFS and OS was higher in patients who received G-CSF versus those who did not, 78.3% and 97.5% vs. 69.8% and 91.5%, respectively. Conclusions: In patients with stage III colon cancer an RDI or DI is associated with improved 3-year DFS and OS, although the difference did not reach significance in our review. G-CSF as secondary prophylaxis improves RDI, DI, DFS and OS.

Bempedoic acid lowers low density lipoprotein-cholesterol and attenuates aortic atherosclerosis in LDL receptor-deficient (LDLR+/- and LDLR-/-) Yucatan miniature pigs.

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Bempedoic acid (BA, ETC-1002) is a drug that targets hepatic adenosine triphosphate-citrate lyase to inhibit cholesterol biosynthesis. In Phase 2 studies, BA lowers LDL-cholesterol (C) in hypercholesterolemic patients. In the present study we examined the ability of BA to decrease LDL-C, and attenuate atherosclerosis in a model of familial hypercholesterolemia. Yucatan minipigs heterozygous (LDLR+/-) (n=12) or homozygous (LDLR-/-) (n=12) for LDL-receptor (R) deficiency were fed a diet containing 34% kcal fat with 0.2% cholesterol, and administered placebo or BA (120 mg/d or 240 mg/d) for 160 days. BA was well tolerated; weight gain, caloric intake, liver enzymes and clinical chemistries were unaffected. In LDLR+/- pigs at 160 days, compared to placebo, BA decreased plasma-C and LDL-C up to 43% ($P<0.01$) and 63% ($P<0.002$), respectively. Compared to LDLR-/- placebo pigs, in which plasma-C and LDL-C were 5-fold higher than in LDLR+/- placebo pigs, BA decreased plasma-C and LDL-C up to 26% ($P<0.04$) and 29% ($P<0.03$), respectively. Plasma triglycerides, HDL-C, fasting glucose and insulin, and liver lipids were unaffected by treatment in either genotype. In the aorta of LDLR+/- pigs, BA attenuated total lesion area (-58%, $P<0.02$) and abdominal aortic raised lesion area (-58%, $P<0.03$). In LDLR-/- pigs, in which total (6-fold) and abdominal raised lesions (12-fold) were larger compared to LDLR+/- pigs, BA decreased total aortic lesion area (-47%, $P<0.01$) and abdominal raised lesion area (-50%, $P<0.03$). In summary, BA treatment reduces LDL-C and attenuates aortic atherosclerosis in both LDLR+/- and LDLR-/- minipigs.

Euglycemic diabetic ketoacidosis (DKA) in a trauma patient taking a sodium-glucose co-transporter 2 (SGLT2) inhibitor empagliflozin

Julia Creider, Alex Dong, Emily Chen, Rob Leeper, and Terri Paul

SGLT2 inhibitors are a new class of medications approved for type 2 diabetes (DM2) that target the kidney to excrete excess glucose. Via this mechanism they may mask the signal of high serum blood glucose (BG) usually seen in patients with DKA. To date there has been only one published case report of euglycemic DKA associated with empagliflozin. A 64-year-old man was admitted to hospital with poly trauma due to a tire explosion that required operative fixation of facial and upper extremity fractures. He had a medical history of DM2 treated with insulin and empagliflozin. On day 2 of his hospitalization, his blood work demonstrated a drop in his bicarbonate to 10. During the next 2 days his bicarbonate continued to be low and an anion gap (AG) developed. His BG during this time

remained between 10-13 using a sliding scale only for his glycemic control while NPO for surgery. Empagliflozin was held on admission. On day 5 further investigations revealed frank ketoacidosis. Another factor in this case is that the patient was likely misdiagnosed with DM2. Further history, including a poor response to oral agents and significant weight loss at diagnosis, indicated he has underlying type 1 diabetes (DM1). The lack of basal insulin during his hospitalization likely triggered the DKA. This case demonstrates that health care providers need to be aware of the possibility of euglycemic DKA in patients treated with SGLT inhibitors. It also exemplifies that not all adults who develop diabetes later in life have DM2.

Etomidate use in critically ill patients: A review of current practice patterns in North America

Fulan Cui, Adrian Millman, Stacy Ridi, Eric Bruder, Ian Ball.

BACKGROUND: Use of etomidate for rapid sequence intubation (RSI) in patients with septic shock remains controversial. It's favourable hemodynamic profile is ideal for unstable patients, however, etmoidate is known to cause adrenal suppression of unclear clinical significance. OBJECTIVE: We aim to describe the practice habits of etmoidate use by emergency physicians in Canada and the United states. METHODS: An survey study was conducted with 200 randomly selected Emergency Physicians across North America in 2014. Surveys were distributed through e-mail and responses were collected using Survey Monkey. RESULTS: The overall response rate was 43%. There was agreement that controversy still exists regarding the safety of etomidate use (62% US and 52% Canada). There was also agreement in the belief that etomidate caused clinically significant adrenal suppression in septic patients (36% US and 48% Canada). However, a difference was seen in the usage pattern of etmoidate with 82% of American physicians declaring it the agent of choice in septic patients requiring RSI vs. 19% of Canadians. There was also a difference in the availability of etomidate with 100% respondents in the US stating it was easily available and only 61% in Canada. CONCLUSION: There is still controversy over the safety of etomidate use in RSI for septic patients. Currently, it remains the agent of choice for emergency physicians in the US while less frequently used in Canada. This could be due to drug availability and user experience. More research is needed on the clinical significance of adrenal suppression caused by etomidate.

Identifying the genetic basis of neurodegeneration in 75 patients using a targeted resequencing panel.

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The Ontario Neurodegenerative Disease Research Initiative (ONDRI) is a multidisciplinary study aimed to characterize five neurodegenerative diseases: 1) Alzheimer's disease and/or mild cognitive impairment (AD/MCI); 2) amyotrophic lateral sclerosis (ALS); 3) frontotemporal dementia (FTD); 4) Parkinson's disease (PD); and 5) vascular cognitive impairment (VCI). We used a custom-designed, next-generation sequencing based disease-specific panel to elucidate the genetic basis of the diseases in 75 ONDRI participants. DNA from participants was extracted from blood and sequenced using a next-generation sequencing based panel, ONDRISeq. A bioinformatics workflow was then used to obtain non-synonymous, rare variants. APOE genotypes were also extracted using ONDRISeq and were subsequently validated via TaqMan allelic discrimination assay. Over 70% of participants carried at least one genetic variant, with a total of 91 unique non-synonymous, rare variants identified in 44 of 80 genes represented on ONDRISeq. Three particular genes were more frequently mutated, namely: 1) LRRK2, 2) NOTCH3, and 3) DNAJC13. Additionally, four ONDRI participants were homozygous for the APOE E4/E4 genotype, which confers risk for late-onset AD. The APOE genotypes of the 75 individuals were determined using ONDRISeq

and were independently validated using a TaqMan allelic discrimination assay. To test whether candidate variants observed are disease causing, they will need to be functionally validated. Methods described in this paper will also be reproduced on all 600 participants of the ONDRI study. Novel variants and genes with multiple disease associations allow us to further understand mechanisms of these diseases and allow for the development of new therapeutic targets.

Profiling the burdens of night work in an academic emergency department – Traditional 8-hour night shifts versus staggered 6-hour casino shifts

Alex Dong, Melanie Columbus, Robert Arntfield, Drew Thompson, Michael Peddle.

In response to the deleterious effects of night work, traditional 2300-0700 night shifts have been replaced with casino shifts (22:00-04:00 and 04:00-10:00). Though purported to permit better sleep and recovery, no evidence in the literature exists. We examined the impact of transitioning from traditional to casino shifts on the quality-of-life and job satisfaction of emergency physicians (EP) in an academic emergency department (ED). Online surveys were sent to EPs working in the ED in 2010 and 2016, before and after transitioning to casino shifts. Participants rated their agreement about the burdens of night work on a 7-point Likert scale. Results from both surveys were compared. 43 2010-surveys, and 47 2016-surveys were completed. In 2016, recovery to baseline function after one 22:00-04:00 was most common after 1 day (52.4%), and after multiple 22:00-04:00 shifts was ≥2 days (66.7%). Recovery after one 04:00-10:00 was most common at 1 day (54.8%), and after multiple 04:00-10:00 shifts was ≥2 days (59.5%). In 2010, 55.8% recovered from single 23:00-07:00 shifts after 1 day, and 95.3% required ≥2 days to recover from multiple shifts. In 2016, 40.5% stated night shifts were the greatest drawback of their job (79.1% previously). Some stated teaching (36.5%), diagnostic test interpretation (23.2%), and handovers (33.5%) were inferior on night shifts (74.4%, 58.1%, and 60.5% in 2010 respectively). 95.0% preferred casino over traditional shifts. Our study demonstrated a benefit in quality-of-life, productivity, and sleep after implementing casino shifts.

Elucidating the genetic determinants of extreme high-density lipoprotein phenotypes using next-generation sequencing

Jacqueline S. Dron, Jian Wang, Adam D. McIntyre, John F. Robinson, Matthew R. Ban, Henian Cao, David Rhainds, Guillaume Lettre, Marie-Pierre Dubé, Jean-Claude Tardif, and Robert A. Hegele.

HDL cholesterol (HDL-C) levels associate with cardiovascular disease risk, and as a complex trait, are influenced by genetic and environmental factors. Extreme HDL-C concentrations are largely genetically determined; monogenic disorders have been well-characterized, including candidate genes driving each extreme phenotype, which typically show autosomal recessive or co-dominant inheritance. Within genes causing syndromes of both HDL-C extremes, numerous disease-causing variants have been identified and functionally validated. In a unique cohort of patients with extreme HDL-C profiles, we applied our targeted next-generation sequencing panel LipidSeqTM, which is designed for re-sequencing of genes associated with dyslipidemia and other metabolic disorders. We found that 20.6% and 11.8% of low (N=136) and high (N=119) HDL-C patients, respectively, carry heterozygous, large-effect mutations in pertinent genes explaining their phenotypes. To further characterize the genetic variation contributing to HDL-C levels, we investigated the integrated polygenic contribution from multiple small-effect genetic variants using a polygenic trait score (PTS). We developed two scores to assess an individual's burden of small-effect variants: one each for lowering and raising HDL-C. Low HDL-C patients had a significantly greater mean PTS for low HDL-C than normolipidemic controls ($P<0.001$); surprisingly, there was no difference in mean PTS between carriers and non-carriers of large-effect variants. Likewise, high HDL-C patients had a significantly greater mean PTS for high HDL-C than normolipidemic controls

(P<0.001), and no difference in mean PTS between carriers and non-carriers. These findings support the complexity of extreme HDL-C levels and the differences in contributions of rare large-effect and common small-effect variants.

Quality Improvement of Heart Failure Clinics: Defining and Developing Quality Indicators to Improve Health Care

Daniel Durocher, Stuart Smith.

Heart failure clinics have been developed with the rationale that they reduce hospital admissions, improve patient outcomes, reduce mortality and improve quality of life. Despite the existence of heart failure clinics there is a lack of standardization on what a heart failure clinic is, what role it should play in the community and what services it needs or should provide. We conducted quality improvement of heart failure in our centre. We reviewed the literature and best practice guidelines on heart failure clinics and set to establish quality indicators for our center with the idea that these would help better our institution and improve outcomes. We reviewed previous definitions and set to define a heart failure clinic. We determined a number of quality indicators based on existing evidence that should be targeted by heart failure clinics to improve patient outcomes.

What proportion of the published articles in critical care journals are valid and relevant

Atoosa Enzevaei, Janet Martin Davy Cheng.

Introduction:Despite randomized clinical trials and systematic reviews are the most valid type of researches, they are not commonly found in publications, and if exist they might not be relevant to clinical practice. we hypothesize, only small proportion of clinical trials in critical care journals are based on a highly valid research methodology and are relevant to clinical practice.Method:We reviewed published articles in critical care journals with highest impact factor between 2009-2014.Abstracts were screened based on their study design.We targeted randomized trial, systematic review and meta analysis, as the most valid evidence based methodology. Then we targeted the articles with a hard outcome as the most clinically relevant articles. At the end the proportion of the valid and relevant articles to total publications were calculated using quantitative analysis. Result: the number of valid and relevant articles published between 2009-2014 for American Journal of Respirology and Critical Care Medicine was 68 from 296 total articles (19%), for the journal of Critical Care Medicine 89 form 499 total published articles (15%) and for American Journal of Critical Care 68 from 185 published articles (36%).Conclusion: The number of both valid and clinically relevant articles published in critical care journals are less than 40% of all publications across the top 3 highest impact journals. That would emphasis the importance and the need of the methodologically valid research with the purpose of answering a clinically relevant question to make an impact on clinical practice and the patient care.

Cardiovascular Comorbidity in Systemic Lupus Erythematosus has a Large Care Gap

Faranak Esmaeilbeigi, Janet Pope.

Objectives: To determine current practices regarding cardiovascular disease (CVD) risk assessment in systemic lupus erythematosus (SLE) amongst rheumatologists and subspecialty trainees in Canada. Methods: A 36-item questionnaire assessing current preventative care strategies, risk assessment, and beliefs regarding SLE and CVD was sent electronically to members of the Canadian Rheumatology Association (N = 425). Questions were based on various Canadian recommendations including the Canadian Cardiovascular Society Dyslipidemia Guidelines and the Canadian Hypertension Education Program. Responses were stratified based on practitioner demographic data and chi-squared testing was performed where appropriate to assess for statistical

significance. Results: 99 physicians and trainees responded (22% response rate). 91% believed that SLE is a major risk factor for CVD, and 68% felt that rheumatologists should assess for CV risk. 42% were not comfortable with current cardiac guidelines. 97% felt that family physicians are not aware of the cardiac risk in SLE patients and 64% did not routinely inform family physicians about this risk in their communications. . For patients they followed with SLE, 15% did not check blood pressure at every visit, 32% did not order a lipid profile, regardless of patient risk factors and 34% did not screen for diabetes. Conclusion: There was little consistency in terms of CV risk assessment and preventative measures, indicating a care gap. Results also indicate a need for improved communication between family physicians and specialists as most respondents felt that general practitioners may not be aware of the elevated risk of CVD in SLE.

Reducing 30-Day Readmission Rates in the Elderly: A Systematic Review

Zhaowei Gong, Reza Naqvi, Raza Naqvi, Monidipa Dasgupta.

Background: Rehospitalisations impose significant costs on the healthcare system. The elderly are a particularly at-risk population. The 30-day readmission rates in Canadian acute care hospitals were approximately 8.5%, with costs estimated to be over $17 billion. Purpose: To evaluate existing studies that aimed to reduce rehospitalisations in the elderly, and determine which interventions are effective at reducing 30-day readmission rates. Data Sources: MEDLINE and EMBASE were searched for studies up to March 2016. Study Selection: English-language randomised controlled trials that investigated interventions which reduced 30-day rehospitalisations in patients ≥ 65 years. Data Extraction: Two investigators independently identified studies for review based on titles and abstracts. Articles were included for full-text review if at least one investigator deemed it relevant. Conflicts were resolved by reaching a consensus after full text review. Results: Initial search yielded 1712 abstracts. Full text review found 18 trials that satisfied the inclusion criteria. Only 5 studies showed that the interventions under investigation reduced 30-day readmission. These interventions all involved outpatient contact such as telephone follow-up or home visits. None of the studies with only inpatient interventions reduced 30-day readmission. Conclusion: Although the elderly are at an increased risk for rehospitalisations, there is a lack of literature on this population. Available trials suggested that outpatient follow-up and home visits could be useful interventions. Future research should verify intensive outpatient interventions as effective and economically feasible means to reduce rehospitalisations.

Does cell size matter?: Utilizing mean cell volume in hospitalized patients as a screen to determine common causes of anemia including iron deficiency anemia, vitamin B12 and folate deficiency

Manika Gupta, Kathy Copley, Mike Keeney, Ian Chin-Yee.

Background: The approach to anemia is traditionally based on the mean cell volume. Based on this approach anemia is subdivided into microcytic, normocytic and macrocytic causes. This approach may not accurately discern common causes of anemia in hospitalized patients. Previous studies suggest the MCV may not be a sensitive measurement to differentiate IDA and megaloblastic anemia due to vitamin B12 or folate deficiency. Method: We retrospectively reviewed all adult patients with confirmed IDA, vitamin B12 and folate deficiency to determine the sensitivity of MCV. One year's data of all patients at LHSC with IDA (hemoglobin less than 115 g/l, ferritin less then 30 (M) and 10 (F)) and vitamin B12 deficiency (less than 145) was reviewed. Results: Of the 894 patients with IDA, 564 patients had low MCV and 769 patients had low MCV or high RDW-SD with a sensitivity of 63.1% and 86.0% for IDA. Of the 96 patients with vitamin B12 deficiency, 12 patients had high MCV and 62 patients had high MCV or high RDW-SD with a sensitivity of 12.5% and 64.6% for vitamin B12 deficiency. Only one of 2244 patients had folate deficiency. Conclusion: A normal MCV does not exclude IDA or vitamin B12 deficiency. Clinicians need to be aware of the low

sensitivity of the MCV as a screen. Folate deficiency is rare in North America and should not be routinely ordered to determine cause of anemia. Further chart review is planned to look at confounding factors, which may influence MCV in nutritional anemia.

Changes in antibodies to extractable nuclear antigens, double stranded DNA and complement over time in systemic lupus erythematosus.

Carly Hewson, Janet Pope, Thomas Carlo-Raissi.

Objective: To examine the utility of repeat measurements of anti-extractable nuclear antigen antibodies (Sm, RNP, Ro/SSA, and La/SSB, Scl70), anti-double stranded DNA (DS-DNA), and complement during systemic lupus erythematosus (SLE) followup. Methods: One hundred and thirty seven patients from the 1000 Faces of Lupus Canadian cohort were retrospectively selected. Included patients had repeated testing of the ENA panel, DS-DNA or C3, C4 tests. We assessed the frequency of change in repeat measurements of ENA antibodies, DS-DNA, C3 and C4. Autoantibody patterns were classified as: always negative, negative at initial testing with positive seroconversion, positive at initial testing with negative seroconversion, and always positive. C3 and C4 were expressed as always normal, normal at initial testing with change to low, low at initial testing with normalization, and always low. Results: Overall, in 89.4% of patients the ENA autoantibodies did not change on repeat measurements. 3.3% of patients were initially negative and seroconverted to positive. 6.5% of patients were initially positive and converted to negative. Among patients initially negative for a given autoantibody, the frequency of the seroconversion to positive pattern was 1.6% for Ro, 1.6% for La, 0.8% for RNP, 0.8% for Sm. No patients were positive for Scl70 in this study. The average number of ENA measurements was 5.4. Higher rates of seroconversion were seen with antibodies to DSDNA and C3, C4. Conclusion: There is a low frequency of change in repeat measurements of ENA autoantibodies. This suggests that routine repeat testing is not necessary in most SLE patients.

Developing a resident-driven post-graduate academic half-day curriculum

Nicole Hugel, Dr. Sheri-Lynn Kane.

Background: One of the challenges Internal Medicine programs face is delivering an Academic Half-Day (AHD) that engages multiple levels of trainees. Using a resident-driven approach, we endeavored to redesign our AHD to make sessions more interactive, and to target content to expected competence at various stages of training. Methods: We formed an AHD planning committee that consisted of faculty, residents, and administrative staff. We assigned topics using the Royal College Objectives of Training, focusing on objectives that the residents felt were less frequently covered in other areas of the curriculum. Expected level of competence was taken into account when planning sessions. Presenters were encouraged to use a case-based approach to deliver content. Residents were surveyed at the beginning and end of the academic year to determine their satisfaction with AHD. Results: Our new AHD curriculum included both large group sessions with all residents, and small-group sessions divided by level of training. At the end of the first year, residents commented that AHD had improved over the past year and enjoyed the splitting of year levels. One of the drawbacks was the scheduling challenge associated with an increased number of speakers. Conclusion: By using a resident-driven approach, we planned an AHD curriculum that accounted for the expected competence and learning needs at different levels of training. Moving forward, we are using curriculum mapping to further assist our planning process.

ReCoM: The Development of the Resident Communication Manual

Rachel Kyle, Raza Naqvi.

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

Immune responses to homocitrulline and citrulline in patients with Rheumatoid Arthritis

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

Introduction: Rheumatoid arthritis (RA) is an autoimmune disorder characterized by joint inflammation and immune responses to citrullinated peptides. Citrulline is a non-standard amino acid resulting from post-translational modification of arginine. Anti-citrullinated protein antibodies (ACPA) are a specific biomarker for RA and are arthritogenic. Recently, anti-homocitrullinated protein antibodies (AHCPA) have been shown to be associated with RA. Homocitrulline arises from post-translational modification of lysine, is structurally similar to citrulline and therefore, AHCPA like ACPA could be involved in RA pathogenesis. Objective: Examine ACPA and AHCPA expression and cross-reactivity in RA using synthetic homocitrullinated and citrullinated peptides. Methodology: Serum samples were collected from 86 RA patients and 52 healthy volunteers. ACPA and AHCPA were screened by enzyme-linked immunosorbent assay (ELISA) using synthetic citrulline- and homocitrulline-rich peptides (JED and HJED respectively). Antibody cross-reactivity to JED and HJED was investigated by inhibition ELISA. Statistical analysis was performed using GraphPad Prism 6.0. Results: ACPA (JED-binding) and AHCPA (HJED-binding) were detected in RA but not in healthy controls. 54/86 (62.8%) and 38/86 (44.2%) of RA sera were positive for ACPA and AHCPA respectively. ACPA and AHCPA were inhibited by both JED and HJED. ACPA were inhibited significantly greater by JED compared to HJED ($p<0.0001$). AHCPA were inhibited significantly greater by HJED compared to JED ($p<0.0001$). Conclusions: ACPA and ACHPA are frequently expressed in RA, are able to bind both citrullinated and homocitrullinated antigens and therefore are cross-reactive. This suggests that AHCPA is associated with RA, are immunologically similar to ACPA, and may be arthritogenic.

Immune responses to homocitrulline and citrulline in a mouse model of Rheumatoid Arthritis

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

Introduction: Rheumatoid arthritis (RA) is an autoimmune disorder characterized by joint inflammation and immune responses to citrullinated peptides (post-translationally modified arginine). RA has been linked to the Shared Epitope (SE), a 5-amino acid motif in MHC class II molecules, which bind citrullinated peptides triggering T- and then B-cell activation.

Recently, immune responses to homocitrullinated (post-translationally modified lysine) proteins have been shown to be associated with RA. Homocitrulline is structurally similar to citrulline and predicted to bind the SE, however its role in RA pathogenesis is unknown. Objective: Examine immune response to homocitrulline and citrulline in a mouse model of RA. Methodology: DR4tg (SE+) mice were immunized with homocitrullinated peptide (HJED) or vehicle control and sacrificed on various days. Splenocytes were harvested and stimulated with homocitrullinated peptide, citrullinated peptide (JED) or unstimulated. T-cell proliferative responses were examined by 3H-thymidine incorporation assay and reported as a stimulation index (SI) (peptide-stimulated cell number/unstimulated cell number). Statistical analysis was performed using GraphPad Prism. Results: HJED-immunized DR4tg mice showed a significant splenocyte proliferative response to HJED at all days examined (day 30, 70, 100) (SI: 2.17-2.96) compared to control mice (SI: 0.73-1.17) ($p<0.05$). HJED-immunized mice did not respond to JED at days 30 and 70 (SI: 1.05-1.16) but developed a significant response to JED at day 100 (SI: 3.04) compared to control mice (SI: 0.61)($p<0.001$). Conclusions: The RA mouse model showed that an immune response to citrulline can develop from immunization with homocitrulline and may lead to RA development.

Improving Patient Flow: The Impact of an Emergency Department Consults Rotation in Two Canadian Teaching Hospitals

Simon Landman, David McCarty, Roman Shapiro.

<><>OBJECTIVE<><> - Evaluate the impact of a daily Internal Medicine consult service provided to the Emergency Department on patient flow. <><>APPROACH<><> - Patient flow parameters were obtained for all patients referred to Internal Medicine from ED between January 1 and November 30, 2015. A daily ED consult service (EDCR) was introduced July 1, 2015. Parameters from patients seen by this service were compared to patients seen before EDCR implementation. <><>RESULTS<><> - 6090 patients referred to IM; 5716 had complete data available. Mean intervals (minutes) for patients seen after EDCR introduction (n=2869) compared to those seen before EDCR introduction (n=2847) were as follows: -ED registration to Physician Initial Assessment (PIA): 64.72 vs. 81.31, ($P<0.001$) -ED registration to disposition decision : 408.11 vs. 427.86, ($P<0.001$) -ED registration to IP registration: 404.61 vs. 422.99, ($P=0.001$) -ED wait time for available bed: 485.55 vs. 595.90, ($P<0.001$) -Hospital length of stay (hrs): 184.65 vs. 235.76, ($P=0.003$) -Mean time to PIA: 73 minutes. -Disposition decisions (admit/discharge) were made after 418 minutes on average. -Average time in ED: 958 minutes. -Mean ED wait after disposition decision: 540 minutes. -Mean length of hospital stay: 227 hours. -EDCR was associated with 16.6 minutes faster time to PIA ($p<0.001$), 19.8 minutes faster time to disposition decision ($p<0.001$), 130 minute reduction in time spent in ED ($p<0.001$), and 51.1 hour reduction in length of hospital stay ($p=0.003$). <><>CONCLUSIONS<><> - The EDCR is associated with favourable changes in hospital metrics, including a significant 51.1 hour reduction in length of hospital stay.

Factors Associated with the Increasing Rates of Discharges Directly Home from Intensive Care Units (Directly from ICU Sent to Home: Changing Trends in Intensive Care Unit Discharges – DISH Study)

Vincent Issac Lau, Joyce NG Lam, Fran Priestap, Ian Ball.

Objectives: Evaluate relationship between rates of discharge directly to home (DDH) from the intensive care unit (ICU) and ward/ICU bed availability, and to identify characteristics that make them candidates for DDH. Methods: Retrospective cohort analysis of adults from intensive care unit observing DDH rates over time (April 2003 – March 2014). We describe demographics of 642 patients and the association between DDH and bed occupancy rates (January 2009 – December 2014). Results: DDH rates increased from 28 patients (3.1%) in 2003 to 120 (12.5%) in 2014. Mean age was 48.1 ± 17.2 years. Mean number of pre-existing co-

morbidities was 5.1 ± 3.8 diagnoses. Mean multiple organ dysfunction score (MODS) at admission was 4.2 ± 2.9. Mean number of discharge diagnoses was 1.4 ± 0.6 (most common were overdose (176 patients, 27.4%), pneumonia (70 patients, 10.9%) and seizures (44 patients, 6.9%)). Mean nine equivalents of nursing manpower score (NEMS) on admission was 27.8 ± 7.2, decreasing to 11.9 ± 9.1 by discharge. 62% of patients (n = 397) waited > 4 hours for a ward bed, with mean delay of 2.6 ± 2.1 days before DDH. Inverse correlation between ICU occupancy and DDH rates (rP = -0.55 (p <0.0001, R2 = 0.29) exists, but no correlation with ward occupancy (rP = -0.055 (p = 0.64)). Conclusions: DDH rates are increasing over time, and were inversely correlated with ICU bed occupancy, but not correlated with ward occupancy. DDH patients are younger, have fewer co-morbidities and discharge diagnoses (reversible single-system problems). Delay with ward transfers leads to increased length of stay in both ICU and hospital overall.

Improving the Quality of Care of Patients with Systemic Vasculitis using an Interdisciplinary Approach

Lebert JM, Clark W, Golverk D, Mandzia J, Pope J, Strong MD, Barra L.

Background/Objectives: Systemic vasculitis (SV) is a rare group of diseases characterized by inflammation in the blood vessels affecting multiple organ systems that can be difficult to diagnose and manage. The aim of this project was to determine whether an interdisciplinary approach to the management of SV improves the management of patients with SV. Methods/Results: Patients from the St. Joseph's Health Care Interdisciplinary Vasculitis Clinic (IVASC) were compared to historic controls. IVASC consists of joint clinics with Rheumatology, Nephrology and Neurology, as well, as a referral network with 5 other specialties relevant to the management of SV. A total of 131 patients were enrolled: 46 new diagnoses were included in the analyses and compared to 36 historic controls diagnosed with SV 2000-2013. Time to diagnosis for IVASC patients and historic controls was similar. At baseline and 6 month follow-up, vasculitis disease activity and damage scores were not significantly different between groups. Overall adherence to clinical practice guidelines was 84% for the control group versus 88% for IVASC patients (p = 0.03). In particular, maintenance therapy with steroid-sparing agents (p<0.007) and primary preventative measures, such as aspirin use in giant cell arteritis (p<0.003), PCP prophylaxis (p<0.003) and influenza vaccination (p=0.04), were less frequent in the control group. Conclusion: This study suggests that an interdisciplinary approach to vasculitis improves adherence to clinical practice guidelines; however, more research is needed to assess the benefit of long-term patient outcomes.

Comparison of vital sign documentation for pre-hospital lift-assist calls and non lift-assist calls.

Matthew Davis, **Lauren Leggatt**, Melanie Columbus, Jennifer McGuire, Amanda Spadafora.

Introduction: When an individual requires assistance with mobilization, emergency medical services (EMS) may be called. If treatment is not administered and the patient is not transported to hospital, it is referred to as a "Lift Assist" (LA) call. We have previously shown that LA are associated with morbidity and mortality. Given that LA calls result in no-transport, there may be a bias towards not upholding the same standards of care as patients who are transported to hospital. Objective: To determine if there is a difference in Ambulance Call Record (ACR) documentation of vitals signs between LA calls and non-LA calls. Methods: All LA calls from a single EMS agency were collected over a one-year period (Jan - Dec 2013). A control group of randomly selected calls of low acuity (Canadian Triage Acuity Scale 3,4,5) from the same time period was collected for comparison. ACRs from these calls were reviewed for missing vital sign documentation. Results: Of 42, 055 EMS calls, 808 (1.9%) were LA calls. A comparison of 784 randomly-selected non-LA control calls were reviewed. There were significantly more missing vitals (12.08% vs 6.64% p < 0.001) in the LA cohort. Conclusions: There is a significant

discrepancy in the complete documentation of vital signs in LA calls vs non-LA calls. Abnormal vital signs may be a clue to a subtle disease process that has resulted in a LA call, thus care should be taken to ensure that these patients are treated with the same standards of care and documentation.

Factors predicting morbidity and mortality associated with pre-hospital "lift assist" calls

Matthew Davis, **Lauren Leggatt**, Michelle Klingel, Shelley McLeod, Melanie Columbus , Kristine Van Aarsen, Adam Dukelow, Michael Lewell.

Introduction: When an individual requires assistance with mobilization, emergency medical services (EMS) may be called. If treatment is not administered and the patient is not transported to hospital , it is referred to as a "Lift Assist" (LA) call. We have previously shown that LA are associated with morbidity and mortality. What places patients at an increased risk for morbidity and mortality is not yet known. Objective: To determine factors that are associated with increased risk of 14 day morbidity, determined by an ED visit or hospital admission, and mortality in LA calls. Methods: All LA calls from a single EMS agency were collected over a one-year period (Jan - Dec 2013). Logistic regression analyses were run to predict ED visit or hospital admission within 14 days of the LA call from patients' age, gender, co-morbidities and vital signs at the initial LA call. Results: Patient age > 61 ($p < 0.001$) and history of cardiac disease ($p = 0.006$) significantly predicted ED visit, while patient age >61 ($p = 0.001$) and an Ambulance Call Record (ACR) missing at least 1 vital sign ($p = 0.017$) significantly predicted hospital admission. The sample size was too small to determine predictors for mortality. Conclusions: Patients at risk for morbidity are older than 61 years of age and have co-exisiting cardiac disease. Patients who are greater than 61 years of age and had at least one missing vital sign on the ACR were more at risk for hospital admission.

A case of Leprosy contracted in a North-American Extreme Tourist

Mary Lu, Peter Medline, Ian Toft, Michael Silverman.

An otherwise healthy, 69 year-old man from Ingersoll, Ontario, saw his family physician for an erythematous rash on his torso and extremities. A clinical diagnosis of pityriasis rosea was made, however he did not respond to two courses of oral prednisone. Additional history revealed 2 years of progressive loss of sensation of the lower extremities, with recent thickening of the ear lobes, and an extensive travel history all over Africa, Asia, Central and South America from the 1970s to 80s. On examination, he had greater than 100 symmetrically distributed, well-defined, erythematous, confluent papules and plaques on the torso and proximal extremities, which were hairless with decreased sensation to pinprick. Skin biopsies showed perivascular and interstitial mixed cell infiltrate of lymphocytes, histiocytes and a few plasma cells. A Fite's Acid Fast stain was strongly positive and compatible with borderline lepromatous leprosy (BLL), confirmed by DNA detection by PCR. Screening serologies for HIV, hepatitis B and C, vitamin B12 deficiency, and syphilis were negative. He was started on multi-drug therapy with dapsone, rifampin and clofazimine for 24 months and clinically improved. We present only the second known case of a Canadian tourist contracting leprosy abroad. This case illustrates the importance of maintaining a wide differential diagnosis for an avid traveller presenting with peripheral neuropathy and rash. Leprosy should be suspected in a tourist having traveled to endemic areas even after many decades, as treatment can prevent permanent disfiguration and disability.

Inpatient referrals from LHSC clinical teaching units to palliative care: A seamless transition?

Andre Maddison, Andrew Smaggus, Shiraz Malik.

Inpatient palliative care consultation has been demonstrated to improve quality of life, as well as decrease hospital readmissions, ICU transfers, and hospital costs, for people with a life limiting illness. The clinical teaching units (CTU) at LHSC routinely admit patients with non-curable cancer, as well as end stage heart, lung, liver, or kidney disease. However, the use of inpatient palliative care consultations for CTU patients remain unexamined. We conducted a descriptive study of all patients referred from LHSC CTU from both University and Victoria hospitals to inpatient palliative care over a 1-year period from August 2013 - July 2014. The purpose of this study was to characterize the population and identify possible areas for quality improvement. In a 1-year period 638 patients were referred from CTU to the inpatient palliative care consultation service. Of referrals, the mean age of patients was 75, and 55% died during their admission. Based on data collected, we conclude that many patients are referred to palliative care early in their admission to CTU and patients are referred for a variety of non-cancer diseases, suggesting knowledge and appreciation of the benefit of early palliative care consultation for malignant and non-malignant disease. However, when further analyzed there is indication that patients with non-cancer diagnoses are referred statistically significantly later than those with a cancer diagnosis. CTUs are sites of core medical training, and therefore, it is imperative that we model early integration of palliative care in order to continue to improve care of patients at end of life.

Utility of Biomarkers for the Diagnosis and Management of Takayasu's Arteritis: A Systematic Review

Malette J., Barra L.

BACKGROUND: Takayasu's arteritis (TAK) is a rare large vessel vasculitis predominantly affecting young females. Currently, there are no diagnostic criteria for TAK or guidelines to assess disease activity. This study presents a systematic literature review of studies examining various biomarkers and their utility in diagnosing and managing TAK. METHODS: A comprehensive literature search was performed using MEDLINE, PubMed, EMBASE, Cochrane Library, Web of Science, and BIOSIS Previews. After duplicates were removed, abstracts were analyzed independently by two authors to further exclude studies that were not relevant or analyzed fewer than 10 patients with disease. RESULTS: The literature review yielded 2131 citations. After duplicates were removed, 1445 publications were retrieved. 189 articles met inclusion criteria. All studies were observational and mostly of low to moderate methodologic quality. The majority of publications originated from the Middle East and Asia. Study sample size ranged from 10-216. Patients were female with an average age span of 30-36 years and disease duration ranging from 2.2-3.6 years. Most commonly evaluated biomarkers were ESR and CRP in relation to disease activity and diagnosis. However, there have also been promising results seen with assays measuring levels of IL-2, IL-6, IL-12, Pentraxin-3, and matrix metalloproteinases. CONCLUSIONS:Currently, there is no clinically available biomarker that is specific for diagnosing TAK. Studies suggest a relationship between several biomarkers and disease activity However, these studies have low sample size and lack a gold standard comparator. Larger, better designed studies are needed to determine the utility of biomarkers in managing TAK.

The role of metalloproteinases and TIMPs in regulation of pulmonary microvascular endothelial cell barrier function during sepsis

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

Sepsis, a systemic inflammatory response to infection, is a serious disease with significant mortality characterized by injury and dysfunction of microvascular endothelial cells (MVEC), especially in the lung. Mechanisms protecting against septic MVEC dysfunction are unclear; however, the tissue inhibitors of metalloproteinases (TIMPs), which regulate metalloproteinase activity, may be one such mechanism. Metalloproteinases, including the matrix metalloproteinase (MMP) and a disintegrin and metalloproteinase (ADAM) families, are

associated with inflammation and tissue damage. Based on this, my hypothesis is that murine septic pulmonary MVEC (PMVEC) barrier dysfunction is due to disruption of the balance between metalloproteinases and TIMPs leading to increased metalloproteinase activity. Analysis of metalloproteinase and TIMP expression by qRT-PCR revealed a significant increase in Timp1, Mmp2, Adam10, Icam, Vcam and Sele expression in PMVEC in vitro following stimulation with cytomix (equimolar TNF alpha, IL1 beta, and IFN gamma). Additionally, expression of these genes was also significantly increased in PMVEC lacking TIMP3 (Timp3-/-) under basal conditions. Ex vivo analysis of expression in PMVEC from naïve and septic (cecal ligation and perforation) mice revealed that expression of Timp1, -2, -3, Icam, Vcam and Sele was significantly expression; however, no differences in metalloproteinase expression were detected. My data demonstrates that PMVEC-dependent expression of metalloproteinases and TIMPs is altered under septic conditions; however, whether this disruption leads to altered metalloproteinase activity and PMVEC barrier dysfunction is currently unknown and will be addressed in future studies. Understanding these mechanisms may provide insight into potential therapeutic interventions in human sepsis.

The Impact of Ventilation Induced Lung Injury on the Intracellular Pulmonary Surfactant System

Scott Milos, Reza Khazaee, Lynda McCaig, Cory Yamashita, and Ruud Veldhuizen.

Pulmonary surfactant is a lipoprotein mixture stored in lamellar bodies within alveolar type II pneumocytes. As lamellar bodies exocytose into airspaces, their contents unravel and function to reduce surface tension. However, during lung injury such as ventilation induced lung injury (VILI), there are impairments of the extracellular surfactant, contributing to decreased oxygenation. Whether this impairment caused by VILI originates intracellularly through affecting lamellar bodies is unknown. Hypothesis: VILI will alter rat lung lamellar body morphology, numbers, phospholipid content, and function. Rats were randomized into experimental groups: naïve, control ventilation, and VILI. Following ventilation and oxygenation monitoring, rat lungs were fixed, stained, sliced, and imaged for lamellar body morphological and numerical analysis via electron microscopy. A separate cohort of rats had lamellar bodies isolated from lung tissue homogenate and surfactant phospholipid pool-sizes were quantified. Surface tension reduction during surface area cycling of unravelled lamellar bodies was assessed using a constrained sessile drop surfactometer. Results showed rats exposed to VILI had severely impaired arterial oxygenation compared to ventilation controls. While lamellar body morphology was no different between groups, VILI rats had reduced lamellar body numbers, staining intensity, and isolated phospholipid content compared to ventilation controls. Preliminary data suggests no difference between groups in the ability of lamellar body surfactant to reduce surface tension during compression. In conclusion, these experiments provide micrographic, quantitative, and functional insight into how intracellular surfactant is altered during VILI. Overall data suggest a reduction in cellular lamellar body number after VILI, potentially contributing to impaired lung function.

Safety of Weight-Adjusted Dosing of LMWH in Clinically Obese Patients with VTE

Gillian Mount MD, MSc, Martha Louzada MD, FRCP, MSc.

Obesity, as defined as a body mass index (BMI) greater than 30 kg/m2, is a well-known risk factor for venous thromboembolism (VTE). Despite this observation, obese patients are under-represented in anticoagulation safety trials. Current guidelines recommend patients with active malignancy and VTE be treated with long-term low molecular weight heparin (LMWH), but it is unclear whether this practice is safe in obese cancer patients. We hypothesized there would be an increased risk of major or clinically significant non-major bleeding in obese cancer patients receiving long-term, actual weight-adjusted LMWH compared to patients receiving capped doses. We conducted a single centre retrospective cohort study of obese cancer patients referred to thrombosis clinic from

January 2010 to present day. Of the sixty-nine patients who met eligibility criteria, 35 (44%) were male, median age 64 (24-89), median weight (kg) 96.4 (69.6-155.6), median BMI (kg/m2) 34.1 (27-51.4) and 60 (87%) had a solid tumour malignancy. Median dose of LMWH was 18,000u (11,000 – 30,000), with sixty (87%) prescribed dalteparin and nine (13%) tinzaparin. There were a total of nine (13%) bleeding episodes with five (7.2%) constituting major bleeding. Platelet counts were appropriate in all cases but one, where a non-major bleed occurred in a patient with a platelet count of 27. Recurrent VTE occurred in seven (8.7%). Overall, the incidence of total and major bleeding was similar to the published literature. Additional patient data is required to determine safety of long-term, actual weight-adjusted dosing of LMWH for VTE treatment in obese cancer patients.

Mentorship experience across specialties: Resident's perspective

Khoa Binh Nguyen, MD, Sheri-Lynn Kane, MD, FRCPC.

BACKGROUND: Literature has demonstrated the importance of mentoring during residency. However, previous studies have not examined mentoring relationship across many different specialties. OBJECTIVE: To survey the prevalence of mentored residents across different programs and to examine factors related to satisfaction of both mentored and non-mentored residents. METHODS: A survey was developed through literature review and Delphi process with IM residents. Program Directors from all programs at the Schulich School of Medicine and Dentistry were invited to participate. Residents from consenting programs were asked to complete the survey at the academic half-day. Programs were identified by size. Descriptive statistics were used to summarize the data. RESULTS: Overall response rate was 52%. Of the 173 responding residents, 81 (46.8%) endorsed having a mentor. Of those mentored, 87.7% report satisfaction with their mentoring. Top factors associated with identifying a mentor are specialty of interest and comfort interacting with mentor. Non-mentored residents preferred to have an elected mentor of their choice. All residents identified similar discussion topics focused on their training and career planning. Results were similar between programs. CONCLUSION: Of respondents, only half of the residents identified having a mentor. Amongst mentored residents, there was overall satisfaction with the mentoring relationship. Discussion of career and training issues are of significant importance to both mentored and non-mentored residents. Mentorship experience is similar across programs. Our results may help programs to improve methods for identifying resident mentors and providing guidance to faculty participating in mentorship.

A Novel Surfactant-Based Host-Defense Peptide for the Treatment of Bacterial Pneumonia

Michael Nicholson, B Banaschewski, L McCaig, E Veldhuizen, C Yamashita, and R Veldhuizen.

BACKGROUND: An increasing prevalence of antibiotic resistance, especially in chronic lung disease patients, have mandated the development of novel therapies. Host-defense peptides, such as a chicken-derived cathelicidin (CATH-2), exhibit excellent anti-microbial activity in vitro however in vivo efficacy has not been previously tested. It was hypothesized that a combination of CATH-2 and an intrapulmonary delivery vehicle, bovine lipid extract surfactant (BLES), would exhibit excellent bacterial killing and improved physiologic parameters in an in vivo model of Pseudomonas aeruginosa (PA) pneumonia. METHODS: Adult male Sprague-Dawley rats were intubated, mechanically ventilated for 30 minutes, followed by intratracheal inoculum of 8 x 10^8 CFU/mL of PA. After one hour, rats were randomized to receive an intratracheal administration of either: saline, BLES, CATH-2, or CATH-2/BLES. Peak inspiratory pressure (PIP) and arterial gases were recorded throughout. Bacterial burden was assessed using growth analysis of lung homogenate. RESULTS: CATH-2 group had significantly higher PIP values and lower PaO2 at multiple time points than the CATH-2/BLES group. Colony growth data demonstrated a significant difference between the CATH-2 and control groups; however the CATH-2/BLES group

was similarly lower, but not statistically significant from controls. CONCLUSION: CATH-2 had excellent anti-microbial activity in an in vivo pneumonia model and mechanical ventilation, although at the expense of significant reduction in lung function; possibly producing an overwhelming inflammatory response. Furthermore, CATH-2/BLES significantly improved physiological parameters compared to CATH-2 but at the expense of antimicrobial function. Further investigation includes optimal concentration combination of CATH-2 in BLES and inflammatory response initiated by CATH-2.

Successful treatment of steroid-resistant fibrosing organising pneumonia causing respiratory failure with mycophenolic acid

Christina Paul, Ammy Lin-Shaw, Mariamma Joseph, Keith Kwan, Gianluigi Sergiacomi, Marco Mura.

Organising pneumonia (OP) is characterised by alveolar injury, granulation tissue buds, deposition of fibroblasts and loose connective tissue within alveolar spaces. It is usually promptly responsive to corticosteroid treatment. We describe a series of 3 cases of severe, progressive, biopsy-proven fibrosing OP causing respiratory failure. All cases presented with peribronchial and subpleural consolidations, and only had a partial and unsatisfactory response to corticosteroids. However, they responded to mycophenolic acid (MPA) treatment evidenced by resolution of respiratory failure, and clinical and functional improvement. The efficacy of MPA in the treatment of interstitial lung disease (ILD) secondary to connective tissue disease is increasingly being recognised. Given the proven effectiveness in these 3 cases, MPA as a treatment option for aggressive forms of fibrosing OP and interstitial lung disease needs to be further explored.

Use of three dimensional rendering of point of care ultrasound images to assess static body structures in healthy volunteers and patients in the intensive care unit

Sanath Rao, Daniel Bainbridge David Tessier Aaron Fenster.

This is a feasibility study to evaluate the effectiveness of a 3D ultrasound apparatus. This project uses a computerized device attached to a point of care ultrasound probe to compile a set of ultrasound images and make a 3D rendering. A standard 2D image is compared to the 3D rendering by attending physicians and physicians in training using a questionnaire. The idea is to determine whether static structures that can be identified in a point of care setting are easier to identify from a traditional 2D image or from the 3D approach with the apparatus. Images of: Lower limb veins (possible visualization of thrombi); Thyroid (size and pickup of nodules and their size); Basal lung/Pleura (intraparenchymal fluid versus pleural fluid); Inferior Vena Cava visualization in inspiration and expiration (determination of distensibility for fluid responsiveness); Abdominal Fluid (from 4 abdominal views); Joint Space (evaluations in knee, hip, shoulder, wrists, fingers, and ankles) are obtained. Primary Outcome: Null hypothesis being tested is: 3D ultrasound imaging with the rendering apparatus is not inferior to traditional 2D images when attempting to identify static anatomical structures in a point of care setting. Secondary Outcomes: Null hypothesis being tested is: 3D ultrasound imaging with the rendering apparatus is not inferior to traditional 2D images when attempting to assess volume and shape of static anatomical structures in a point of care setting. A Wilcoxon test is performed on the questionnaire data for the 3D images vs the 2D images for each separate physical body part imaged.

Maternal Diabetes diet supplemented with or without olive oil differentially impacts pancreas development

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Maternal (T1DM), alters fetal development increasing the predisposition to glucose intolerance later in life. We have shown that dietary addition of 6% olive oil in pregnancy to mild diabetic rats increased the numbers of embryos and decreased neonatal malformations. This was related to the activation of PPARs, a family of nuclear receptors essential for placental development, embryonic stem cell proliferation and implantation. Oleic acid, a ligand of PPARs, lowers LDL and total cholesterol levels, controls blood sugar and reduces insulin resistance. Therefore, we examined the effects of maternal diabetes with or without olive oil on neonatal and adult pancreas development. Differences in body and pancreas weight between all groups were not statistically significant at day 2 and 4 months of age. Immunohistochemistry and morphometric analysis showed that the percentage of islet area, β and α cell area and β cell mass at day 2 postnatal was not statistically significant between all groups. However, at 4 months of age the addition of olive oil restored β-cell mass with a significant increase ($P < 0.05$). Expression of two PPARs, γ and δ were present at both type points and downstream target genes PDX-1, insulin and Glut-2. To establish that PPARs were specific of β cells their gene expression was examined in INS-1E cells. Overall, we conclude that maternal diabetes predisposes male offspring to an early onset of diabetes but the introduction of olive oil in the maternal diet prevented it, although the role of PPARs in this process was not clearly established.

Gaucher Disease Screening at a General Adult Hematology Referral, Single Canadian Tertiary Care Centre: A Prospective Study

Steve Russell, Cyrus Hsia.

Gaucher's Disease (GD) is the most common hereditary lysosomal storage disease where glucocerebrosidase deficiency leads to glycolipid accumulation in macrophages. Given its non-specific symptoms and lack of awareness, GD may be under-recognized by physicians. The goal of our study is to screen adults presenting to a single tertiary hematology outpatient centre with thrombocytopenia and/or splenomegaly for GD by using a high-throughput fluorescent assay in order to estimate the prevalence in this selected population. Sixty-two patients have been enrolled in this study to date and tested for β-glucosidase enzyme activity on dried blood spot (DBS). Forty-five percent of them are male with a mean age of 60.4 years. None tested had a positive screening test. Although no cases have been identified, this small sample size makes conclusions regarding the prevalence and screening of GD unreliable and further enrollment is needed to achieve an adequately powered study.

Kinematic measures of bilateral upper limb essential tremor personalize botulinum toxin type A therapy

Olivia Samotus, Hadi Moradi, Mandar Jog.

Essential tremor (ET) causes functionally and socially debilitating tremor in the upper limbs. Focal therapy can reduce severity though is frequently associated with adverse effects and lack of functional benefit. This study aims to demonstrate that sensor technology can quantitate tremor biomechanics and can be solely used to individualize botulinum toxin type A injection parameters. 21 ET participants attended 6 study visits and received treatment in both upper limbs every 12 weeks, totalling 3 injection cycles, and attended a follow-up visit 6 weeks post-treatment. Clinical rating scales and kinematics to assess tremor and functionality were completed at each visit. Participants performed scripted tasks to capture unique tremor compositions using goniometers and torsiometers placed over arm joints. A dosing algorithm was used to calculate dosing and to select muscles. Wrist tremor severity during scripted tasks following the first treatment at week 6 demonstrated a statistically significantly reduction by 64.0%; elbow and shoulder tremors

were significantly reduced by 58.2% and 33.6%, respectively. Relief of tremor was maintained 12 weeks following treatment at the time of re-injection. Handwriting and functional performance (FTM part B and C) were significantly improved following the third treatment. No significant adverse effects were reported though participants perceived mild weakness not functionally bothersome. Kinematic tremor assessments allow clinicians to standardize both multi-joint tremor assessments and injection parameter determinations.

Risk Factor Management in Vascular Surgery Patients

Sangha, Navjeet, Dresser, George.

A prospective cohort study of inpatients admitted to the vascular surgery service comparing best practises of risk management (adherence to ACE-inhibitor and statin therapy as well as smoking cessation) vs usual care with a composite endpoint of repeat vascular intervention and death. Data will be presented from vascular surgery inpatients with interventions performed in 2013 and 2014 with followup data as available over the successive years.

Use of Alkylating Chemotherapy in High Grade Neuroendocrine Tumours: Evaluation of real world data

Arani Sathiyapalan, Suzanne Richter, Michael Susmoy Sanatani, Stephen Welch, Walter Illarion Kocha.

High grade Neuroendocrine tumours (NETs) have some demonstrated activity to alkylating agents including streptozocin (STZ)and dacarbazine (DTIC). However, minimal data is available to describe response rates to alkylating therapy and vary between 6 – 69%. Real world data was evaluated to understand decision making around treatment initiation and discontinuation and impact on clinical outcome. We reviewed the medical records of 36 patients with metastatic NETs who received either a DTIC regimen (n=15) or STZ based regimen (n=21). Patient cases were evaluated for time to progression (TTP), overall survival (OS), time to treatment failure (TTF) and reason for treatment cessation. Among 36 patients treated, there was a similar observed TTF (STZ: 3 months and DTIC: 4 months), however there was prolonged TTF of 11 months with STZ compared to 5.3 months with DTIC. There was no significant difference in OS with a mean of 48.7 months (DTIC) versus 47.6 months (STZ). The predominant cause of treatment cessation in both groups was due to progressive disease, but this was increased in DTIC (71%) versus STZ (42%). The rate of treatment cessation due to toxicity was almost tripled in STZ (19%) versus DTIC (7%). STZ was associated with a prolonged PFS in comparison to DTIC, but there was no difference in OS. Despite STZ appearing to have an increased toxicity rate, the rate of cessation between the groups was similar. This real world evaluation demonstrated similar efficacies with improved tolerability of DTIC based chemotherapy as a potential alternative to an oral alkylating agent.

The BMi: A Novel Clinical Decision Tool to Guide Azacitidine Therapy in Myelodysplastic Syndrome patients

Roman Shapiro, Alejandro Lazo-Langner.

Objective: Development of a tool to predict treatment failure of myelodysplastic syndrome (MDS) patients treated with azacitidine who attain stable disease. Significance: MDS patients who attain stable disease on azacitidine continue the drug until disease progression. The development of a decision tool to predict treatment failure would guide the clinician as to whether the risk of continuing azacitidine outweighs the benefit. Methods: Retrospective chart review of MDS patients treated at LHSC in the period of 2010-2014 was done. The likelihood of treatment failure was evaluated with a novel tool called BMi, derived from mathematical modeling of clinical data. The statistical correlation of the BMi to time to treatment failure was determined.

Collaboration with a staff scientist is underway in order to determine whether the decision tool can be improved with a whole bone marrow genome methylation signature. Results: The BMi is able to categorize patients based on hematological parameters collected within the first 6 cycles of azacitidine therapy. The categorization results in two patient groups with a statistically significant difference in the mean time to treatment failure. The BMi had an 80% correlation with treatment failure within 3 cycles of azacitidine. Concurrent evaluation of MDS patient bone marrow genome methylation is currently in progress. Conclusions: The BMi has been developed with the goal of estimating the likelihood of treatment failure of azacitidine in the setting of stable disease. The genome methylation signature of MDS patient bone marrows may strengthen the ability of the decision tool in predicting azacitidine treatment failure.

Brain White Matter Integrity is Associated with Future Falls In Seniors With Mild Cognitive Impairment

Jonatan A. Snir, Robert Bartha and Manuel MonteroOdasso.

Background: Falls remain the leading cause of injury-related hospitalization among Canadian seniors. Both mild cognitive impairment (MCI) and gait disturbances are independent predictors of falls in community-dwelling older people. Recently, cross-sectional association between white-matter integrity (WMI) and fall risk has been established. However, the prospective association between white matter integrity and future falls is unknown. Methods: Longitudinal cohort study with 3 year follow up of bi-annual assessments and 3T MRI at baseline, 18 and 36 months. For this analysis, we included 10 participants who have full follow–up. Cognition was evaluated with a battery of neuropsychological tests, gait using an electronic walkway and falls using a fall calendar. Voxel-wise and region-specific image analysis were performed using FSL analysis tool. Partial correlation analysis was used for the associations between WMI and future falls controlling for age, years of education, sex, BMI and baseline cognition. Results: Lower WMI in the anterior region of the corpus callosum was associated with reduced gait performances ($R2=0.99$; $p<0.05$). Furthermore, voxel-wise analysis highlighted specific clusters along the right superior-longitudinal fasciculus and the left corticospinal tract correlating with prospective falls (family-wise corrected $p<0.05$). Discussion and Conclusions: Low WMI is associated with the development of gait disturbances and future falls. This preliminary results support the concept that low integrity in common brain networks which control gait and cognition may be a new risk factors for falls. Future results of our study including a larger sample can point a new modifiable factor in falls risk: white matter disease.

Polypharmacy increase risk of falls probably by affecting gait velocity and stability

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

Polypharmacy has been associated with many negative outcomes in older adults. However, associations with future gait and mobility decline is unknown. We aim at identify the effect of polypharmacy (> 4 medications) on the incidence of gait decline and its relation to falls in elderly patients, with particular attention to anti-hypertensives, sedatives, and Vitamin D. We performed a longitudinal study on 249 elderly patients (mean age of 76.7 with 63.7% female) from the Brain & Gait Cohort Study who were followed for a maximum of 5 years with biannual assessments. Based on baseline intake of chronic prescribed medications, participants were divided into the polypharmacy group (>4 medications) and non-polypharmacy, and we compared the gait parameters from these two groups. ANOVA was performed to assess the significance of difference between the two. Second part of the study perform the same analysis for the aforementioned medication classes. All analysis will be corrected for age, sex, depression and comorbidities. Polypharmacy increased risks of developing slow gait (defined as <1m/s) during follow up with an OR of 1.2(p <0.001), and increasing gait

instability (variability) (B= 0.2 P<0.001). Polypharmacy was associated with increased falls with a hazard ratio of 3.4, though not statistically significant. The known risk of falls in older adults taken more than 4 medications can be mediated by a reduction of gait velocity and by an increase in gait instability. These novel findings may point to interventions to improve gait by reviewing medications profiles before falls can occur in this population.

Safe utilization of Ibrutinib with or without steroids in patients with Chronic Lymphocytic Leukemia with Autoimmune Hemolytic Anemia

Rosanne St. Bernard, Alejandro Lazo-Langner, Anargyros Xenocostas, Joy Mangel, Kang Howson-Jan, Selay Lam, Leonard Minuk and Cyrus C. Hsia.

Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults in North America with autoimmune hemolytic anemia (AIHA) being a common associated complication. Furthermore, usual CLL therapies such as fludarabine have been associated with worsening of AIHA when used in isolation. Ibrutinib is a novel B-cell receptor signaling inhibitor therapy that inhibits Bruton tyrosine kinase (BTK). It has revolutionized the management of CLL, and is highly effective in relapsed CLL. However, ibrutinib can modulate cytokine levels and immune response directing vigilance in autoimmune processes. We report a case series of patients with CLL associated-AIHA that responded to ibrutinib. Eight of nine patients in our series had uncontrolled hemolytic anemia at the time of initiation of ibrutinib. All nine patients have had either complete resolution or improvement in their AIHA or hemolytic parameters, and there have been no AIHA relapses during follow-up. This is the largest case series to date and our findings are consistent with other isolated case reports that support the safe use of ibrutinib in CLL-associated AIHA. We are the first to demonstrate that even in the absence of recent prednisone use, ibrutinib is effective in improving AIHA. Ibrutinib may act as an immune stabilizer, and while more investigations are needed to understand the predictive factors and pathophysiology of ibrutinib in autoimmune cytopenias in CLL, these findings allude to the intriguing possibility of ibrutinib therapy in primary AIHA.

Polymicrobial bacteremia with Actinomyces odontolyticus, Fusobacterium and Atopobium parvulum secondary to septic thrombophlebitis in an immunocompetent patient

Cassandra Townsend MD, Sandra Wong BScPhm ACPR, Linda Wang MD, Raymond Kao MPH MD FRCPC.

A 25 year-old immunocompetent man was found to have polymicrobial bacteremia secondary to a right arm septic venous thrombus. His blood cultures grew Actinomyces odontolyticus, Fusobacterium and Atopobium parvulum. He was treated with intravenous piperacillin-tazobactam for 6 weeks, followed by oral amoxicillin-clavulanic acid for 6 months. Co-infections with Actinomyces odontolyticus, Fusobacterium and Atopobium parvulum are rarely documented and this is the first known reported case of thrombophlebitis associated with these bacteria. We explore several hypotheses to account for this rare presentation in an immunocompetent individual.

Pharmacologic Management of Takayasu's Arteritis: a Systematic Review

Grace Yang, Kevin Lee, Christian Pagnoux, Lillian Barra and CanVasc.

Objective: The mainstay of treatment for Takayasu's Arteritis (TAK) is glucocorticoids; however, a large proportion of this disease is glucocorticoid-resistant and relapse is common upon withdrawal of glucocorticoids. The purpose of this study is to review the evidence on other immunosuppressants and biologic therapies for the induction and maintenance treatment of TAK.

Methods: A systematic literature review was conducted using Embase, Medline, and Cochrane databases for articles published between 1947 to July 2015. Search terms for Takayasu's arteritis, treatment, drug therapy, and all possible immunosuppressive and biological agents were used. Case reports and small case series (< 4 cases) were excluded. Two authors independently reviewed the articles and discrepancies were resolved by consensus. Results: Of the 915 publications identified from the literature search, 35 publications met inclusion criteria. Studies included open-label prospective studies and retrospective studies. Study sample sizes ranged from 4 to 36, with mean age between 11 to 41 and the percentage female between 75-100%. Treatments studied included methotrexate, azathioprine, mycophenolate mofetil, leflunomide, cyclophosphamide, anti-TNF, and tocilizumab. Studies reported effectiveness with respect to reducing disease activity and inflammatory markers, halting angiographic progression, and glucocorticoid-sparing effect. Inclusion criteria and outcome measures were too heterogeneous to be pooled for meta-analysis. Conclusion: Observational studies suggest a role for immunosuppressants and biologics in TAK; however, conclusions cannot be made regarding their efficacy given the lack of controlled studies. There is a need for larger, better designed studies with uniform inclusion criteria, disease activity scoring systems, and outcome measures.

Reducing wait time for radiological investigations in Urgent Medical Clinic

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Objective: Urgent medicine clinic is designed to provide rapid assessment for patients referred by ER in-order to provide immediate care and avoid hospitalization. However, there is often delays in obtaining CT/MRI/US resulting in delay in management. The aim of the project was to reduce wait times by 50% for obtaining radiological investigations. Methods: Between June-September 2015, sample of 27 tests ordered showed mean wait time of 20.7 days. Current state and gap analysis showed lack of transparency and standardization in triage and booking process after order entry resulting in uncertainty as to when the test will be performed affecting provision of care. Also, the process of patient notification was sub-optimal. If test date was 4 days later after order entry, booking dates were communicated to physician's secretary and not to patient directly. Secretary's absence created miscommunication leading to no-shows, which is estimated around 5-7%. Meetings were held between Medicine, Radiology coordinators and physicians to develop new process. Entering E5-Urgent medicine in reason for test became important signal to radiology for priority consideration. Furthermore, nurse/MD called the facilitator to obtain date for the test and provided it to the patient before leaving the clinic. Results: Mean wait time after the intervention reduced from 20.7 to 9 days with most tests done within a week. Conclusion: Standardized process of order entry, prioritization and providing patients with appointment before they left clinic reduced wait times by 56%. Future step is to evaluate impact on no-show rate, hospitalizations and patient satisfaction.

Comanagement by Nephrologists is Associated with Increased Likelihood of Appropriately Dosed Prescriptions in Patients with Chronic Kidney Disease

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Background: Patients with chronic kidney disease (CKD) are commonly prescribed excessive drug doses for their kidney function. Objective: To determine whether care by both nephrologists and family physicians (i.e. comanagement) versus family physicians alone was associated with increased appropriately renally-dosed prescriptions in patients with stage 4/5 CKD. Methods: We performed a retrospective cross-sectional study of antibiotic prescriptions from family physicians in Ontarians aged ≥66 years, with estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m2 using linked healthcare databases from 2003-2014. Patients were categorized by comanagement, defined as having at least one outpatient visit with a nephrologist in the 1 year prior to prescription date. The outcome was antibiotic prescriptions

renally dosed appropriately for a given patient's eGFR. The groups were matched one to one via propensity score matching. Conditional logistic regression modelling was used to determine the independent association between comanagement and appropriate dosing. Results: After propensity score matching, 3937 patients were included in each group. The median age of these patients was 81 (IQR 76-86), and 63% were female. Patient comorbidities included: hypertension (92%), diabetes (51%), and congestive heart failure (40%). Comanagement was significantly associated with renally-dosed prescriptions with a conditional odds ratio of 1.20 (95%CI 1.09-1.32). Neither eGFR reporting nor degree of kidney dysfunction significantly modified the association between comanagement and appropriate dosing. Conclusion: In patients with stage 4 or 5 CKD prescribed an antibiotic, patients who were comanaged had 20% greater odds of having appropriately dosed prescriptions from their family physicians.