Western Association of Physicians
Western Society for Clinical Investigation
Plenary Session
Thursday, January 24, 2019
9:00 AM

1 MUC5B-OVEREXPRESSION PROMOTES INCREASED ER STRESS IN MOUSE MODELS OF PULMONARY FIBROSIS

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10.1136/jim-2018-000939.1

Purpose of study A common gain-of-function promoter variant in the *MUC5B* gene is the strongest risk factor for the development of idiopathic pulmonary fibrosis (IPF). Endoplasmic reticulum (ER) stress occurs with disruption to cellular proteostasis and is increased in human IPF lungs. The purpose of this study is to understand the relationship between ER stress and *MUC5B*-overexpression.

Methods used Two mouse lines for *Muc5b*-overexpression were used: *Scgb1a1-Muc5b* and *SFTPC-Muc5b*, which overexpress *Muc5b* in airway club cells and alveolar type 2 cells, respectively. These were compared to wildtype (WT) C57BL/6J littermates. Pulmonary fibrosis was induced using intratracheal bleomycin installation with saline treatment used as a control. Relative mRNA expression was assessed using qRT-PCR. Protein expression was assessed using immunofluorescence staining for CHOP (an ER stress marker) and *Muc5b*. Nuclear (activated) CHOP-positive and *Muc5b*-positive cells were counted and normalized to total cells in each field of view.

Summary of results While no differences in whole-lung mRNA expression of ER stress markers were found in saline-treated mice, increased CHOP-positive cells were observed in distal airways of *Scgb1a1-Muc5b* mice (2.3-fold increase; $p=0.0002$) and in alveoli of *SFTPC-Muc5b* mice (8.6-fold increase; $p<0.0001$) compared to WT mice. Preliminary analysis also shows intracellular co-expression of both CHOP and *Muc5b* in *Muc5b*-overexpressing mice. Notably, while bleomycin treatment caused no change in CHOP-positive cell counts in WT mice compared to saline, bleomycin treatment in *Muc5b*-overexpressing mice was associated with decreased CHOP-positive cells.

Conclusions These results indicate that although there is no apparent difference at the transcriptional level, there is a significant increase in baseline number of CHOP-positive cells in the lungs of *Muc5b*-overexpressing mice compared to WT. These data, along with evidence of *Muc5b* and CHOP co-expression, suggests a direct connection between ER stress and *Muc5b*-overexpression. The decrease in CHOP expression in *Muc5b*-overexpressing mice is potentially due to increased cell death of specifically CHOP-positive cells, which would suggest that ER stress plays an important role in lung injury and remodeling.

Adolescent Medicine and General Pediatrics I
Concurrent Session

12:45 PM

Thursday, January 24, 2019

2 AN INTERVENTION TO REDUCE UNNECESSARY CHEST RADIOGRAPHS (CXR) IN RESPIRATORY SYNCYTIAL VIRUS (RSV) BRONCHIOLITIS

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10.1136/jim-2018-000939.2

Purpose of study Studies have shown a limited value of performing CXRs in patients with RSV bronchiolitis. The objective of our study was to determine the effectiveness of an intervention to reduce the proportion of inappropriate CXRs.

Methods used We performed a retrospective chart review on pediatric patients less ≤ 2 years of age diagnosed with RSV at Children's Hospital of Orange County (CHOC) Emergency Department (ED) during the 2017–2018 RSV season. A total of 459 patients fulfilled our inclusion criteria. 52 patients were excluded because they were transferred from outside hospitals. Educational intervention regarding appropriate indications for CXR took place mainly in January of 2018. It included Quality Improvement Scoresheets, meetings with the ED leadership and communication with physicians as well as education of ED scribes. CXRs were considered appropriately ordered if the patient had a fever $>39^{\circ}\text{C}$, focal finding on physical exam, or was in severe respiratory distress. We compared the trends in use of CXR before and after the intervention.

Summary of results A total of 116 patients were diagnosed with RSV bronchiolitis during pre-intervention and 343 during the post-intervention period. CXRs were done on 55 (47%) and 144 (41%) patients during the pre-intervention and post-intervention, respectively. When the appropriateness of CXRs were reviewed, patients during the post-intervention were more likely to get appropriate CXRs (71% pre vs 88% post, $p=0.0122$). Comparing the pre and post-intervention CXRs that were ordered appropriately, 23% vs 43% were read by radiologist as having a local finding ($p=0.025$) during the pre and post-intervention periods, respectively.

Conclusions Our intervention was effective in decreasing the proportion of inappropriate CXRs in patients with RSV bronchiolitis. Our study was limited because we included patients

Abstract 2 Table 1 Impact of intervention on CXRs

	Pre-intervention CXR (n=55)	Post-intervention CXR (n=144)
Appropriate CXR	39 (71%)	125 (87%)
Focal Findings	9 (23%)	54 (43%)
Inappropriate CXR	16 (29%)	19 (13%)
Focal Findings	2 (13%)	7 (37%)

with complex medical conditions who may have required CXRs based on their underlying illnesses. Further studies are needed to evaluate the long-term effectiveness of this intervention for different subsets of patients in different hospital settings.

3 REPRODUCTIVE HEALTH OF FEMALES WITH CONGENITAL HEALTH DEFECTS

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10.1136/jim-2018-000939.3

Purpose of study According to the Center for Disease Control (CDC), congenital heart defects (CHD) are the most common birth defects in the United States. Approximately 40 000 newborns are affected annually. The availability of advanced surgical techniques with better procedure outcomes, as well as improved long-term management of CHDs, enable approximately 90% of CHD newborns to reach adulthood with good cardiac functionality. This population change manifests new healthcare challenges that must be addressed. Specifically, unique concerns for women of reproductive age arise. Their impaired cardiovascular and hemodynamic functionality creates greater challenges for safe pregnancies and deliveries. With their high-risk status necessitating defect-specific care, personalized medicine is key to their reproductive health.

With over 30 CHD types, this study stratifies factors affecting reproductive outcomes, based on CHD condition severity. Using the data collected in our multi-institutional CH-STRONG survey-based study, we examine CHD women's reproductive history, health concerns, and discussions with care providers; assess whether results differ from the general population or by CHD severity; and determine if previous pregnancies affect healthcare utilization.

Methods used Based on our study of 502 female patients, 157 reported a history of pregnancy. Using binary logistic regression, we investigate factors affecting pregnancy outcomes, including minority status, possessing multiple comorbidities, having at least a high school education, and regular cardiology visits.

Summary of results Regular visits significantly predict consistent access to healthcare for all CHDs and severe CHDs in particular at $p < 0.05$. Regular visits and education level are significant predictors for reproductive education overall, but not for severe CHDs alone.

Conclusions Our current findings elucidate the important elements contributing to good pregnancy outcomes, specifically education and regular care from an ACHD cardiologist. This study serves as a platform for creating new guidelines and recommendations for proper management of CHD patients of childbearing age, based on their specific heart defect.

4 COST AND RISK ANALYSIS OF PENICILLIN ALLERGY

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10.1136/jim-2018-000939.4

Purpose of study Penicillin allergy is the most common drug allergy. However, over 90% of children labeled as penicillin allergic are not truly allergic and are able to utilize penicillin.

We hypothesized that false penicillin allergy subjects patients to additional costs and adverse effects of alternative antibiotics.

Methods used We performed a retrospective chart review sampling of 1800 patients from a health care system's electronic medical record in 18 five-year age groups from 5 to ≥ 90 years. Each 5 year age group consisted of 50 penicillin allergic patients and 50 non-penicillin allergic patients. We calculated the cost of each order and prescription of each of the patients in our sample and then compared the mean and median differences between the two groups.

Summary of results There were 12 353 orders and prescriptions in the 1800 patients. Using the low end of the cost range for each antibiotic, the median cost difference in the 25 to <30 , 35 to <40 , 45 to <50 , and 75 to <80 year age groups were significantly greater by \$3, \$7, \$18, and \$15 in the penicillin-allergic group compared to the non-allergic group, respectively. The median cost difference in the 10 to <15 and 80 to <85 year-old age groups were both significantly greater by \$16 in the non-allergic group compared to the penicillin-allergic group. The rest of the 5 year age groups had no statistically significant difference between the two groups. Across the calculated accrued lifetime (summing all the age groups), mean penicillin allergic patient's antibiotic orders and prescriptions were found to be \$1895 greater than that of non-allergic patients. The penicillin-allergic group had a higher utilization of quinolones, macrolides, tetracyclines, sulfonamides, lincosamides, and glycopeptides. Since the cost spread is roughly 50-fold, the true cost difference between the two groups could be as high as 50 times these values.

Conclusions Across the lifetime, patients labeled as being penicillin allergic have antibiotic costs that are significantly greater than those of non-allergic patients. It also increases the utilization of quinolones and other broad-spectrum drugs. It would be cost effective and clinically beneficial to conduct allergy testing on low risk patients to reduce the number of individuals falsely-labeled with a penicillin allergy.

5 RETROSPECTIVE CHART REVIEW OF ADOLESCENT HEMATOLOGY CLINIC

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10.1136/jim-2018-000939.5

Purpose of study To investigate the causes of and treatments for heavy menstrual bleeding among adolescent females referred for hematologic evaluation. Some adolescent hematology literature emphasizes prevalence of underlying hemostatic disorders in such patients. We aim to add information about therapies offered to these young women.

Methods used A retrospective chart review was conducted of patients seen in Children Hospital Los Angeles' combined Hematology-Adolescent Medicine clinic between January, 1, 2015 and May, 22, 2018 for heavy menstrual bleeding and evaluation for underlying hemostatic disorders. Upon approval from institutional ethics committees, de-identified data was collected and analyzed on a password-protected spreadsheet.

Summary of results Of 115 patients referred for evaluation of heavy menstrual bleeding, 41 were diagnosed with underlying hemostatic disorders, 66 were found to be free of such disorders, and 8 patients had history of thrombosis or beta

thalassemia. Of the patients diagnosed with underlying hemostatic disorders, 21 had platelet dysfunctions, 19 had von Willebrand Disease, and 1 has Osler Weber Rendu syndrome. Of the 41 women diagnosed with hemostatic disorders, 21 were initially prescribed combined oral contraceptives; 12 (57%) had reduced blood loss, but all switched later to other methods. The 9 with persistent symptoms switched to different hormonal contraception (5) or antifibrinolytic agents (4). 17 women with hemostatic disorders were initially treated with antifibrinolytic agents; 12 (71%) responded to therapy although in some, hormonal contraception was later added to improve bleeding control. The 5 patients with persistent symptoms were prescribed new antifibrinolytic agents (2) or hormonal methods (3). Among the remaining patients with hemostatic disorders, 1 was started on a nonsteroidal anti-inflammatory drug and 2 did not receive treatment.

Conclusions Among 115 patients presenting with heavy menstrual bleeding, 41 (36%) were found to have underlying hemostatic disorders. The first line of treatment across both the underlying disorder subset and those without disorders was combined oral contraception with variable efficacy in reducing symptoms, supporting existing literature and its call for more formalized diagnosis and treatment of heavy menstrual bleeding.

6 RAMAN SPECTROSCOPIC CHARACTERISTICS OF PEDIATRIC NON-HODGKIN LYMPHOMA

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Purpose of study Raman-enhanced spectroscopy (RESpect) can be used to characterize molecular footprints of biological tissues. The focus was to characterize RESpect fingerprints of pediatric non-Hodgkin lymphoma (NHL) hypothesizing that a spectrum of pediatric NHL will have unique RESpect features. **Methods used** Frozen pediatric NHL control tissues (follicular hyperplasia, FH) from Cooperative Human Tissue Network, Pediatric Branch and normal B-cells (NBC) from volunteers were analyzed by RESpect via 40-point scan at 50x magnification. The data were analyzed and compared for molecular

similarities/differences. Specific chemical peaks were assessed to differentiate NHL subtypes (BL, BCL, large T-Cell, T-cell lymphoblastic, DLBCL), FH and NBC by unique chemical structures.

Summary of results 5–10 unique RESpect peaks and PCA were identified that differentiated NHL. Statistical differences were found using PCA analysis and Mahalanobis Distance for BL (blue) and NBC (red).

Conclusions RESpect of pediatric NHL provided evidence that unique characteristics could be leveraged. The data supported continued efforts to use RESpect in the setting of childhood NHL diagnosis. The work was supported by the St. Baldrick's and Chun Foundations, MD007584 and MD007601.

7 IMPLEMENTATION OF HIGH FLOW NASAL CANNULA AND INPATIENT CLINICAL PATHWAY OF ACUTE BRONCHIOLITIS AT COMMUNITY REGIONAL MEDICAL CENTER

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Purpose of study Bronchiolitis is a disorder characterized by inflammation, edema and increased mucous production in the small airways of the lung; resulting in tachypnea, hypoxia and respiratory distress in children <2 years of age. Treatment of bronchiolitis is usually supportive with IV fluids and supplemental oxygen. High flow nasal cannula (HFNC) is commonly used to prevent respiratory failure and reduce intubations. Prior to 2018, all patients with acute bronchiolitis admitted to Community medical Center (CRMC) who needed HFNC were admitted to the pediatric ICU (PICU). We introduced a new inpatient clinical pathway for acute bronchiolitis with hopes to reduce admissions to the PICU and the cost related to admissions.

Methods used We started a quality improvement project to implement the use of HFNC and the new clinical inpatient pathway for acute bronchiolitis. Multiple educational sessions were setup to educate medical staff including nurses, respiratory therapist, and other staff regarding the new clinical pathway. An anonymous pre and post questionnaire was distributed to medical personal regarding the new implemented clinical pathway for acute bronchiolitis. We also tracked the number of patients admitted for bronchiolitis to the acute pediatrics floor, PICU and those that required transferred to the PICU and compared these numbers to the previous year. **Summary of results** Reduction of PICU admissions by 26%.

94% responded moderately or extremely comfortable with treatment of acute bronchiolitis; an increase of 12%; 0% responded 'neither comfortable or uncomfortable' or lower; down from 15%; 25% responded they were 'never' unsure with the management of acute bronchiolitis; up from 0%. 22% were not familiar with the clinical pathway, down from 64% on pre. 44% thought that at least 1/2 of the patient's were unnecessarily transferred to PICU.

Conclusions Successful and safe implementation of HFNC with a novel clinical pathway for treatment of bronchiolitis. Significant decrease in PICU admission, Increased confidence of staffs in treatment of acute bronchiolitis, Need for continued training and education of medical staff/personnel

Abstract 6 Table 1 Chart

Tissue	Site	Diagnosis	% Tumor
1	Lymph Node	Diffuse, Large T-Cell	100
2	Lymph Node	T-Cell Lymphoblastic Lymphoma	100
3	Lymph Node Left	T-Cell Lymphoblastic Lymphoma	100
4	Abdomen	Burkitt Lymphoma (BL)	100
5	Soft Tissue, Retroperitoneum	Burkitt Lymphoma (BL)	100
6	Ileum	Burkitt Lymphoma (BL)	100
7	Retroperitoneum	B-Cell Lymphoma (BCL)	100
8	Lymph Node-Left	Diffuse Large B-Cell (DLBCL)	100
9	Lymph Node	Follicular Hyperplasia	0
10	Lymph Node	Follicular Hyperplasia	0
11	Lymph Node	Follicular Hyperplasia	0

8 ASSOCIATION OF OBSTRUCTIVE SLEEP APNEA (OSA) AND DEPRESSION IN THE PEDIATRIC POPULATION

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Purpose of study The relationship between OSA and depression in pediatric population remains unclear. The purpose of this study was to investigate whether OSA is associated with an increased risk of depression in children.

Methods used A literature review through PubMed and Google Scholar was conducted to find studies in which patients under 18 years of age were diagnosed with OSA through a sleep study underwent an assessment for depression. Studies were excluded if the sample size was less than 10 patients, there was no control group, or if the study was published before the year 2000.

Summary of results Nine studies satisfied our inclusion criteria (see table 1). All studies suggested an association between OSA and depression. Although in most studies parental income and body mass index were accounted as possible contributing factors to depression, other factors such as family history, comorbidities or social factors were not included in the analysis. In addition, severity of depression was not measured. The studies that involved adenotonsillectomy (AT), showed improvement in depressive symptoms but compared to control, the effect was not as significant. Limitations of the studies evaluating the effect of AT included either a small sample size and/or lack of a true control group: children with OSA who did not undergo AT.

Conclusions Our review demonstrated an association between OSA and depression in children. However, studies with larger sample size that take into account different variables contributing to depression as well as more intensive follow-up are warranted. Pediatricians and psychiatrists should consider OSA when they evaluate depression in

children. In addition, behavioral measures such as depression may be useful to justify treatment in patients with OSA.

9 COMPARISON OF 2-DAY DEXAMETHASONE VERSUS 5-DAY PREDNISONE FOR TREATMENT OF PEDIATRIC PATIENTS WITH ACUTE ASTHMA EXACERBATION

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10.1136/jim-2018-000939.9

Purpose of study The objective of this study was to compare the efficacy and tolerance of oral dexamethasone with oral prednisone in management of acute asthma in pediatric patients.

Methods used A literature review was conducted using Pubmed, Google Scholar, and Cochrane to find articles related to the topic. Only pediatric studies that compared the efficacy and relapse rates of a 2 day regimen of dexamethasone (0.6 mg/kg/day versus a 5 day regimen of prednisone (2 mg/kg/day)mg/kg were included. Studies in which patients were hospitalized or received intravenous steroids were excluded.

Summary of results We found 5 studies that met our inclusion criterion. The sample included patients from the age 2–18 years old. Patients with moderate to severe exacerbation were excluded from these studies. Results are summarized in table 1 below. All studies were conducted prospectively. Our review shows that there were no significant differences in relapse rates of the 2 day treatment of dexamethasone compared to a 5 day prednisone treatment. However, a couple of the studies indicated that there were more side effects, such as vomiting and lower compliance in the 5 day prednisone group.

Abstract 8 Table 1 Association of OSA and depression

1st Author and Year Published	Subjects w/Sleep Apnea (n) vs Controls (n)	Measure of Depression in Subjects	Measure of Depression in Controls	P-value
Beebe, 2004	13 vs 16	Mild OSA: BASC=58 Moderate to Severe OSA: BASC=62	BASC=49	0.016
Beebe, 2010	100 vs 37	Mild OSA: BASC=51.4 Severe OSA: BASC=54.4	BASC=46.9	0.025
Bourke, 2011	42 vs 35	Mild OSA: BASC=51.4 Severe OSA: BASC=54.4	CBCL=51.4	0.001 (Mild OSA) 0.05 (Moderate to Severe OSA)
Carotenuto, 2012	94 vs 107	CDI=21.94	CDI=17.59	0.001
Chang, 2017	567 vs 5670	14 (2.46%) by DSM-IV criteria	63 (1.11%) by DSM-IV criteria	0.006
Crabtree, 2004	85 vs 35	CDI=51	CDI=43	0.001
Dillon, 2007	79 vs 27	Change in CPRS=-0.187	Change in CPRS=-0.27	0.041
Lewin, 2002	28 vs 10	Untreated OSA: Change in CBCL=0.2 Treated OSA: Change in CBCL=3.7	Change in CBCL=0.2	0.001 (Baseline OSA vs Control) Not significant (Follow-up Treated vs Control)
Mitchell, 2007	23 vs 17 (w/mild sleep-disordered breathing)	Change in BASC T score=7.2	Change in BASC T score=9.9	0.001 (pre- to post-operative change in both groups);

BASC: Behavior Assessment System for Children; CDI: Children Depression Inventory; CPRS: Children's Psychiatric Rating Scale; CBCL: Child Behavior Checklist

Abstract 9 Table 1 Studies comparing 2-day oral dexamethasone to 5-day oral prednisone

Author	Sample Size (ages 2–18)	Outcome	Dexamethasone	Prednisone	P values
Qureshi/ 2001	533 (272 dex 271 pred)	Relapse rate% Admit after Relapse% med not given% vomit at home%	20 (7.4) 4 (20) 1 (0.4)	18 (6.9) 3 (17) 10 (4)	0.84 0.81 0.004
Paniagua/ 2017	557 (294 dex 296 pred)	Admit after Relapse% adherence% vomit at home%	6 (2) 1 (0.4) 279 (99.3)	11(4) 2 (0.7) 265 (96)	0.17 ns ns <0.05
Greenberg/ 2008	89 (38 pred dex 51)	Admit after Relapse% vomit at home%	6 (2.1) 3 (8) 5 (10)	12 (4.4) 8 (16) 7 (18)	0.27 0.24
Seghezzi/ 2018	762 (263 dex 499 pred)	30 day readmission 30 day relapse 7 day readmission 7 day relapse	5 (1.) 14 (5.3) 2 (0.8) 4 (1.5)	11 (2.2) 26 (5.2) 4 (0.8) 7 (1.4)	0.78 0.95 0.95 0.90
Rose/ 2001	533 (272 dex 261 pred)	Relapse% vomit at home%	7.4 5 (10)	6.9% 7 (18)	ns 0.24

Conclusions Our literature review suggests that 2 day regimen of oral dexamethasone is as effective as 5 day regimen of prednisone in outpatient management of acute asthma exacerbation.

Cardiovascular I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

10 THE ROLE OF GLUCOSE AS A PROMOTER FOR CARDIAC REGENERATION

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Purpose of study Heart failure is the leading cause of death worldwide. Our focus is on non-genetic mechanisms by which cardiac regeneration can be lengthened or enhanced. Specifically, we are interested in the cyto-protective effects of glucose in cardiomyocyte growth, differentiation and proliferation and how this knowledge can be applied to regeneration therapies. Our preliminary data showed that glucose induces cardiomyocyte proliferation and inhibits cardiomyocyte maturation in human embryonic stem cells derived cardiomyocytes (hESC-CM) via the Pentose Phosphate Pathway in a dose dependent manner. Whether this pathway can be a therapeutic target for heart regeneration is unknown. **Our hypothesis is that glucose promotes neonatal heart regeneration in a murine model.**

Methods used Non-Transmural cryoinjury was performed to the apex of the left ventricle in wild-type pups and cardiac specific overexpression of Glucose Transporter 1 Transgenic

pups. In the acute phase (P1-P7), the level of cardiomyocyte cell proliferation was measured via flow cytometry analysis and immunostaining with PH3 and cTnnt. Glucose uptake by cardiomyocytes was measured by 18F-FDG assay and Glut1 immunostaining. In the chronic phase (P14, P21, P40), we quantified the level of fibrosis by histology (H and E and Picrosirius Red) and neovascularization by immunostaining with PECAM.

Summary of results Increased cardiomyocyte proliferation was observed in the Transgenic Glut1 pups. Myocardial glucose uptake declines from the muscular layer towards the trabecular layer, corresponding with maturation of the heart. We observed that Glut1 cardiomyocyte-specific overexpression resulted in improved cardiac repair compared to wild type (WT) mice at 21 days postnatally. Compared to wild-type, Glut1 hearts showed increased angiogenesis around the site of injury. We believe that increased in blood vessel formation is secondary to an increase in cardiomyocyte proliferation.

Conclusions This study would be the first to demonstrate the potential role of glucose as a promoter for cardiac regeneration and reveal a potential mechanism for congenital cardiomyopathy associated with diabetic pregnancy.

11 THE ROLE OF THE UNIVERSITY OF COLORADO HUMAN CARDIAC TISSUE BANK (UC-HCTB) IN THE TRANSOMICS FOR PRECISION MEDICINE (TOPMED) PROGRAM

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10.1136/jim-2018-000939.11

Purpose of study Tissue specific biorespositories are expensive yet valuable entities that enable critical biological studies of human diseased tissue. The University of Colorado Human Cardiac Tissue Bank (UC-HCTB) was established over 30 years ago to collect human cardiac samples. The extensive UC-HCTB has joined the Transomics for Precision Medicine (TOPMed) study sponsored by the NIH-NHLBI. TOPMed aims to sequence the entire

genome, transcriptome, and proteome of human samples to establish a robust, publicly-available dataset for biological discovery and hypothesis testing of NHLBI focused diseases, akin to the established Cancer Genome Atlas (<https://cancergenome.nih.gov/>). Here, we present the study design of the HC-HCTB TOPMed collaboration and present early 'omic' data related to human heart failure genomics.

Methods used 1078 human heart samples from the IRB-approved UC-HCTB are approved for submission. Tissue selection is from left ventricle samples harvested at the time of orthotopic heart transplantation or implantation of a left ventricular assist device (LVAD). Whole genome and transcriptome sequencing will be done in phase one of the project.

Summary of results The UC-HCTB contains tissue from 1343 unique patients. Of these patients, 860 have complete clinical and demographic data on age, sex, race, year of transplant, and diagnosis. The 860 samples include 591 (69.7%) failing and 269 (31.3%) non-failing hearts. Common diagnoses include: ischemic cardiomyopathy (26.7%), idiopathic dilated cardiomyopathy (22.7%), familial cardiomyopathy (4.3%), and retransplant (3.8%). The failing and non-failing samples are 21.7% and 52.8% female respectively. The racial distribution among the failing hearts is 77.5% White, 9.6% Black, 9.1% Hispanic, and 2.4% Asian.

Conclusions Initial studies include DNA and RNA sequencing; subsequent, planned studies include metabolomic and proteomic analysis. We present data on the analyses of disease versus control states and within-disease, subgroup analyses. Additional, planned analyses will include studying gender and racial differences in gene expression.

12 PREDICTION OF MORTALITY AND HOSPITAL READMISSION FOR HEART FAILURE: A SIMPLIFIED RISK SCORE

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10.1136/jim-2018-000939.12

Purpose of study The goal of this paper is to identify factors that can predict the risk for heart failure (HF) mortality and hospitalization within 180 days in patients with moderate to severe HF. Those factors are used to develop a simplified risk score using parsimonious variables that can be reliably used in the outpatient setting.

Methods used A secondary analysis of data collected on 210 unique participants from two prospective cohort studies conducted by a single team of HF investigators from 2010–2013. A one-tailed bivariate correlation of 30 candidate variables based on prior models and clinical significance followed by a backward logistic regression was first conducted, then, a Cox regression was performed for the final list of variables. Patients were risk stratified based on their risk score (equation 1).

Equation 1: RISK SCORE=[0.943 * (1 if pt is NYHAF III, or 0 if N/A)] + [2.079 * (1 if pt is NYHAF IV, or 0 if N/A)] – [0.922 * (1 if pt is on ACEi/ARB or 0 if N/A)] – [0.903 * (1 if pt is on BB or 0 if N/A)] – [0.028 * PTSBP] – [0.034 * LVEF]+9

Summary of results Patients in the index cohort (n=210) had a mean (±SD) age of 56.20 (13.47), 48.1% were females. Mean left ventricular ejection fraction 28.41 (12.34)%. During the 180 days, 3 patients died, 6 had at least one HF related ER visit, 46 had at least one HF related hospitalization, and 155 had no events. The final model included five variables; NYHA Class, beta blocker (BB) usage, ACEi or ARB usage, LVEF, and systolic blood pressure (SBP). Odds ratio and 95% confidence interval were as following NYHA class III 2.57 (1.27–5.21), NYHA class IV 7.99 (3.11–20.54), ACEi/ARB usage 0.398 (0.208–0.760), BB usage 0.41 (0.21–0.79), Systolic BP 0.97 (0.95–0.99), and LVEF 0.97 (0.94–0.99) all at p<0.05. Cox regression yielded a Chi square of 53.09. Discrimination was assessed by Receiver operator characteristic which yielded an Area under the Curve of 0.773. Raw C statistic was 0.731.

Conclusions HF is a significant burden for patients and the healthcare system with a high risk for hospitalization and mortality. A simple and convenient scoring system based on 5 clinically-relevant parsimonious variants (NYHAF class, LVEF, SBP, BB usage, ACEi/ARB usage) can be used to risk stratify HF patients in the outpatient setting.

13 CHARACTERIZATION OF MACROPHAGES DERIVED FROM THE HEMOGENIC ENDOCARDIUM

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10.1136/jim-2018-000939.13

Purpose of study During mammalian embryogenesis, *de novo* hematopoiesis occurs transiently in multiple anatomical sites including yolk sac, dorsal aorta, and heart tube. Whether these local transient hematopoietic mechanisms are essential for embryonic growth is unknown. Here, we identify and characterize endocardium-derived macrophages.

Methods used Tissues from Nfatc1^{Cre/+};R26^{YFPReporter/+} embryos were harvested at various timepoints. Hearts from wild type and Nfatc1^{Cre/+}; R26^{TomatoReporter/+} mice were harvested at embryonic (E10.5, E15.5), post-natal neonate (P1), P28, and adult stages. Flow cytometry with hematopoietic and macrophage-specific markers were performed to quantify macrophages derived from the endocardium and proliferation assessed with EdU incorporation.

Summary of results Colony formation assays from explanted heart tubes and genetic lineage tracing with the endocardial specific Nfatc1-Cre mouse revealed that hemogenic endocardium is a *de novo* source of tissue macrophages in the endocardial cushion, the primordium of cardiac valves. Macrophages in Nfatc1-Cre and wild-type adult mice macrophages represented a small percentage of total cardiac cells and a small percentage of cardiac cells were EdU positive. Nfatc1-derived macrophages were a minority in the developing heart.

Conclusions The resident macrophage population is a small population within the adult murine heart which at steady-state is not proliferative. Further analysis at different embryonic and post-natal stages will give insight into emergence of cardiac tissue macrophages, with a potential role for transient hemogenic activity in cardiac valve formation.

14 ADENOVIRUS DETECTION CONFOUNDING INCOMPLETE KAWASAKI DISEASE

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10.1136/jim-2018-000939.14

Case report A 4-year-old male with history of constipation presented with 3 days of fever and intermittent abdominal pain with non-bilious vomiting. He also had decreased po and constipation. ROS was negative for sore throat, limb swelling and rash. One exam, he was febrile with mild left lower quadrant tenderness without rebound or guarding. Initial CBC showed WBC 8.3 K/mm³, Hb 11.4 g/dl and PLT 188 K/mm³. CMP showed elevated AST 112 U/L and ALT 75 U/L. CRP was elevated at 43.5 mg/L. UA and rapid strep were unremarkable. KUB showed constipation and abdominal ultrasound was unremarkable. He passed stools with transient relief of abdominal pain after two enemas and miralax. He continued to spike daily fevers up to 103 F for the next 3 days. He also developed nasal congestion, unilateral non-exudative conjunctivitis and right cervical lymphadenopathy during the hospital course. Repeat WBC dropped to 4 K/mm³, PLT increased to 217 K/mm³ and transaminitis resolved.

Human adenovirus (HAdV) infection was considered given conjunctivitis, congestion, gastrointestinal symptoms, leukopenia and transaminitis. A respiratory PCR was positive for adenovirus. However, incomplete Kawasaki disease (KD) was another possibility given 6 days of persistent fever, conjunctivitis and lymphadenopathy with elevated CRP. Subsequently, Echocardiogram (Echo) revealed dilated coronary arteries (Z scores=+4.4, LAD and +3.8, LMCA). He was treated with high dose aspirin and IVIG. Fever resolved for the next 36 hours and patient was safely discharged with cardiology follow up.

Discussion This is a case demonstrating Kawasaki Disease presentation to be concurrent with adenovirus activation. A high index of suspicion, elevated CRP and abnormal cardiac echo lead to correct diagnosis and treatment. KD has a higher incidence in the winter-spring when many respiratory viruses circulate. Further confusing the situation, HAdV results in a clinical illness similar to KD. It has been well known for certain species of HAdV to establish latent infection in the throat and reactivate with inflammatory stimuli. The consequences of untreated KD include substantial morbidity and mortality. Our case clearly indicates that it is important not to dismiss the diagnosis of KD in a child with incomplete features of KD because of HAdV detection.

15 CA REGULATION IN A NOVEL TAMOXIFEN-INDUCIBLE CARDIAC-SPECIFIC SODIUM-CALCIUM EXCHANGE KNOCKOUT MOUSE

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10.1136/jim-2018-000939.15

Purpose of study To test the hypothesis that sodium-calcium exchange (NCX) is a critical component of intracellular calcium (Ca) regulation and excitation-contraction (EC) coupling in ventricular myocytes.

Methods used We generated a tamoxifen-inducible cardiac-specific knockout (KO) of NCX using Cre-Lox technology and the α MHC-MerCreMer promoter. We injected the mouse with tamoxifen (40 mg/kg/day IP) for 5 consecutive days to activate the promoter and excise exon 11 of NCX, rendering the protein inert.

Summary of results Surprisingly, NCX KO mice were viable with preserved cardiac function despite >90% reduction in NCX protein expression by western blot. We also found a two-fold increase of SERCA2 ($p<0.01$), which pumps cytosolic Ca back into the sarcoplasmic reticulum (SR), and a two-fold increase of PMCA ($p<0.05$), which is an alternative but less efficient Ca efflux mechanism than NCX. We also measured a reduction in expression of Ca_v1.2, the l-type Ca channel. Ca current (I_{Ca}) generated by the l-type Ca channel is the major route of Ca influx into the cell, responsible for triggering Ca release from the SR to generate Ca transients and cell contraction. We confirmed that I_{Ca} was reduced by 37% ($p<0.001$) in live cells using the patch clamp technique. Ca transients were preserved, indicating increased EC coupling gain, suggesting improved EC coupling efficiency to maintain normal Ca transients despite reduced I_{Ca}.

Conclusions We conclude that tamoxifen-induced NCX KO mice survive by upregulating alternative mechanisms to promote Ca uptake (SERCA2) and efflux (PMCA), while reducing Ca influx (I_{Ca}) and increasing EC coupling efficiency. Comprehensive understanding of how cells can survive without NCX is needed to develop manipulation of NCX as a therapeutic approach to maximize contractility in heart failure without provoking arrhythmias or Ca overload and cell death, which occurs with traditional inotropes such as β -adrenergic agonists and digoxin.

16 DONOR LEFT VENTRICULAR HYPERTROPHY: DOES DONOR HISTORY OF HYPERTENSION MAKE A DIFFERENCE?

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10.1136/jim-2018-000939.16

Purpose of study Donor left ventricular hypertrophy (LVH) >1.2 cm has been a relative contraindication for donor heart acceptance for transplantation. Cardio-pulmonary resuscitation (CPR) with chest compressions may also cause edema within the interventricular septum (IVS) and posterior wall (PW). It is not clear whether LVH due to a history of hypertension (HTN) in the donor or LVH due to edema from CPR have the same outcome after heart transplantation.

Methods used Between 2014 and 2017, we assessed 86 heart donors with LVH >1.2 cm. We divided these donor hearts into those with a history of HTN (n=27) and those without (n=59). Post-operatively, we assessed for the presence of primary graft dysfunction (PGD), 1 year freedom from any-treated rejection, acute cellular rejection, antibody-mediated rejection, 1 year freedom from cardiac allograft vasculopathy (CAV) as defined by stenosis $\geq 30\%$ by angiography, and 1 year survival. We also assessed for the persistence of LVH at 6 and 12 months post-transplantation.

Summary of results LVH in donors with and without a history of HTN resulted in similar rates of LVH persistence at 6 and 12 months after transplantation. The rate of resolution of

Abstract 16 Table 1

Endpoints	Donor Left Ventricular Hypertrophy >1.2 cm (n=86)		P-Value
	Hypertension (n=27)	No Hypertension (n=59)	
Incidence of Primary Graft Dysfunction (%)	3.7%	5.1%	1.000
1 Year Survival	81.5%	98.3%	0.003
1 Year Freedom from Any-Treated Rejection	85.2%	81.4%	0.647
1 Year Freedom from Acute Cellular Rejection	96.3%	98.3%	0.532
1 Year Freedom from Antibody-Mediated Rejection	92.6%	88.1%	0.531
1 Year Freedom from CAV	92.6%	94.9%	0.552
LVH >1.2 cm at 6 Months Post-Transplantation, %	40.7%	40.7%	1.000
LVH >1.2 cm at 12 Months Post-Transplantation, %	38.9%	43.2%	0.785

LVH was similar between the groups. LVH donors with HTN did have significantly reduced 1 year survival (see table 1). There is no significant difference in PGD, first-year rejection, or first-year CAV.

Conclusions LVH and HTN in donors appear to increase the risk of mortality after heart transplantation. The poor outcome of donor hearts with LVH and HTN may have something to do with the longevity of the LVH but this is not clear. Larger studies will be needed to confirm these findings.

17 SHORT AND STOUT DONORS IN HEART TRANSPLANTATION: DO THEY MAKE A DIFFERENCE?

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10.1136/jim-2018-000939.17

Purpose of study Certain donor characteristics after heart transplantation (HTx) are known to have less optimal outcome post-HTx. One of the major factors leading to worse outcome is female donors to male recipient possibly due to size (height and weight) mismatch relative to male donors. We try to compensate for this size mismatch by using obese female donors into male recipients. However, there have been recent concerns with obese donors, in the sense that there are commonly large fat deposits on the donor heart. It is not known whether short and obese female donors (oversizing) results in acceptable outcome after HTx. We sought to assess for this possibility in our large single center.

Methods used Between 2010 and 2017 we assessed 799 donors and divided them into female donors (n=246) that were short (≤ 66 inches) and obese (BMI ≥ 30) (n=61) and short and non-obese (BMI < 30) (n=128). In addition, we compared both groups to a male donor cohort inclusive of similar heights and weights. All patients were reviewed for 1 year outcomes including survival, freedom from CAV (as defined by stenosis $\geq 30\%$ by angiography), freedom from

Abstract 17 Table 1

Endpoints	Female Donors		Male Donors		P-Value
	Short and Obese (n=61)	Short and Non-Obese (n=128)	Short and Obese (n=24)	Short and Non-Obese (n=68)	
1 Year Survival	86.9%	92.1%	91.7%	94.1%	0.453
1 Year Freedom from CAV	96.7%	96.9%	91.7%	91.2%	0.290
1-Freedom from NF-MACE	80.3%	85.0%	87.5%	85.3%	0.742
1-Freedom from Any-Treated Rejection	83.6%	83.5%	79.2%	86.8%	0.851
1 Year Freedom from Acute Cellular Rejection	91.8%	92.1%	91.7%	94.1%	0.938
1 Year Freedom from Antibody-Mediated Rejection	95.1%	92.9%	95.8%	95.6%	0.825

non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke), and freedom from any-treated rejection, acute cellular rejection, and antibody-mediated rejection.

Summary of results There is no significant difference in 1 year outcomes between short and obese female donors, short and non-obese female donors, and male donors of similar heights and weights (see table 1).

Conclusions Short and stout female donors appear to be acceptable for HTx which increases the donor pool. Larger numbers are needed to confirm these findings.

18 A CASE OF INFECTIVE ENDOCARDITIS, POSTPARTUM CARDIOMYOPATHY AND INTRAVENOUS DRUG USE CAUSING HEART FAILURE IN A PREVIOUSLY HEALTHY 26-YEAR-OLD FEMALE

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10.1136/jim-2018-000939.18

Purpose of study Heart failure is an uncommon diagnosis in healthy young adults, particularly that of new and rapid onset. We present a case of a young female with multiple possible etiologies of worsening heart failure, with one likely exacerbating another.

Method Retrospective Case Report.

Case presentation 27-year-old female with history of IV drug use presented to an outside hospital at 35 weeks gestation with pelvic pain. She had an emergent C-section, but was found to bacteremic with MSSA. TTE showed mobile vegetation on TV suggestive of endocarditis, tricuspid regurgitation, and hypokinesis of LV with EF of 35%. Patient was treated with IV Nafcillin. Two weeks later, she experienced worsening dyspnea with a repeat TTE revealing an echodensity suggestive of ruptured chordae tendinae, and EF of 20%. Lisinopril, Carvedilol, and Digoxin were started for HF management. Left heart catheterization ruled out ischemic causes leading to primary diagnosis of postpartum cardiomyopathy. She left against medical advice, but presented to our institution 2 days later dyspneic at rest with diffuse

anasarca. Physical exam revealed a holosystolic murmur, bibasilar lung crackles, and 3+ pitting edema of lower extremities. Labs indicated BNP of 1793, and positive toxicology for amphetamines and opiates. Patient was restarted on IV Nafcillin, Lisinopril, Carvedilol, with aggressive diuresis. New findings of TEE revealed dilated cardiomyopathy, EF of 10%–15%, and a 0.6 cm vegetation on TV. Patient was not a candidate for valve replacement, thus managed medically. Upon clinical improvement and completed endocarditis treatment, patient was discharged, however, lost to follow up.

Conclusion Postpartum cardiomyopathy is a diagnosis of exclusion, and known to develop rapidly in the third trimester or within 6 months of delivery. Patient likely had an underlying non-ischemic methamphetamine induced cardiomyopathy with a component of PPCM. Patient's acute TV endocarditis and subsequent rupture of chordae tendinae further exacerbated her symptoms and led to acute decompensated heart failure. Optimal management included IV antibiotics, Beta blockers, Ace-inhibitors, and diuresis which resulted in clinical improvement.

Endocrinology and Metabolism I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

19 EXAMINING THE ROLE OF FRUCTOSE INTAKE ON THE EPISODIC MEMORY OF CHILDREN

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10.1136/jim-2018-000939.19

Purpose of study Overconsumption of added sugars is a possible contributor to rising childhood obesity rates in the United States. Beyond known metabolic health risks, research in rat models show that high dietary fructose intake impairs hippocampal function, which is pertinent to sensitive periods of neurocognitive development such as childhood. We examined the association between dietary fructose intake and performance on an episodic memory task in children 7–11 years old. We hypothesized that increased dietary fructose intake would impair memory task performance.

Methods used As part of a larger study, children underwent two 24 hour dietary recalls, anthropometric measurements, and the NIH Toolbox Picture Sequence Memory Test (PSMT), which is a measure of episodic memory. Total caloric energy, total fructose consumption, and sources of dietary fructose were calculated using Nutritional Data System for Research. We used a Pearson Correlation to measure the association between % of total calories consumed from fructose and age-standardized PSMT scores.

Summary of results Seventy-six children (33 M; 43 F; mean ($\pm$ SD) age 8.4 ± 0.9 years) with a mean BMI of 18.7 ± 4.2 kg/m² were included in the analyses. Average BMI percentile was $65.7\% \pm 30.1\%$. Average PSMT age-standardized score was

100.8 ± 12.9 . Average total caloric energy was 1788 ± 428 kcals/day. Dietary fructose consumption accounted for $4.6\% \pm 2.1\%$ of daily calories. Dietary fructose consumption was negatively correlated with PSMT age-standardized scores ($r = -0.23$, $p = 0.042$), and results remained after adjusting for sex and BMI. The largest dietary contributors to fructose consumption were beverages (17%), followed by desserts (12%) and fruit (12%).

Conclusions This study is the first to our knowledge to examine the role of fructose consumption and memory performance in a human-based study in children. In line with data in animal models, we observed that dietary fructose consumption was negatively associated with memory performance in children, a population vulnerable to dietary factors on neurocognitive development.

20 ANALYSIS OF INFLAMMATORY SIGNALING IN REPRO-METABOLIC SYNDROME

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10.1136/jim-2018-000939.20

Purpose of study Obesity in women is characterized by elevated lipids, insulin resistance and relative hypogonadotropic hypogonadism; decreased LH, FSH, ovarian steroids and reduced pituitary response to GnRH, which we define as Repro-Metabolic syndrome. We have previously shown that this phenotype can be induced in normal weight women by infusion of free fatty acids and insulin. Obesity is also a state of chronic inflammation. To identify potential mediators of insulin and lipid-related reproductive endocrine dysfunction, we examined serum levels of inflammatory markers.

Methods used 11 normally cycling reproductive aged women of normal BMI (< 25 kg/m²) were recruited with IRB approval. All were studied in the early follicular phase of the menstrual cycle. Each participant underwent infusion of either saline or insulin plus free fatty acid (Intralipid), for 6 hours, in sequential cycles in random order. Euglycemia was maintained by glucose infusion. Frequent blood sampling (q10 min) was performed to measure gonadotropin pulsatility.

Serum samples from 180–230 min (at which time steady state lipid/insulin levels were achieved) were pooled and analyzed using ELISA for 32 inflammatory signaling molecules (cytokines, interleukins, adipokines and growth factors: table 1) and markers of endoplasmic reticulum stress (CHOP and GRP78). Mean levels in saline controls were compared to insulin/lipid infusions by paired t-test.

Abstract 20 Table 1 Inflammatory markers

IL-10	IL-6	IL-16	VEGF	MDC
IL12p40/p70	IL-8	IL-17	Eotaxin	MIP-1 α/β
IL-13	IFN- γ	IL-1 α	Eotaxin-3	TARC
IL-1 β	TNF- α	IL-5	IP-10	Adiponectin
IL-2	GM-CSF	IL-7	MCP-1	FGF21
IL-4	IL-15	TNF- β	MCP-4	Leptin

Summary of results Acute induction of the Repro-Metabolic syndrome was confirmed by a decrease in LH and FSH and the development of insulin resistance. No significant differences were observed in any of the inflammatory signaling or ER stress markers tested.

Conclusions Infusion of lipid and insulin to mimic the metabolic syndrome of obesity was not associated with an increase in inflammatory markers. Our results imply that the endocrine disruption and adverse reproductive outcomes of obesity are not a consequence of the inflammatory environment, but may be mediated by direct lipotoxic effects on the hypothalamic-pituitary-gonadal axis.

21 EXERCISE CAPACITY AND CARDIOMETABOLIC HEALTH IN ADOLESCENT GIRLS WITH TURNER SYNDROME

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10.1136/jim-2018-000939.21

Purpose of study Turner syndrome (TS) is characterized by an abnormal or missing X chromosome in females. Women with TS have low exercise capacity, a four times increased risk for type 2 diabetes, and premature mortality from cardiovascular disease. Research on cardiometabolic health in adolescents is limited. Our objective was to compare exercise capacity and other cardiometabolic risk markers between adolescent females with TS to that of healthy female controls matched for age, body mass index percentile (BMI%), and habitual physical activity level.

Methods used This is a matched case-control cross-sectional study of cardiometabolic health assessments in pubertal females, 13–21 years, with and without TS. Exclusions included current growth hormone treatment, diabetes, and exercise limitations. All participants completed a fasting blood draw, dual energy x-ray absorptiometry, and graded bicycle ergometry to peak oxygen consumption (VO₂peak). Cases and controls were matched 1:1 by age, BMI%, and self-reported habitual physical activity level. Cardiometabolic outcomes were compared between cases and controls using the paired t-test or non-parametric equivalent.

Summary of results Participants with TS (n=21) were well matched to controls (n=21) for age (17.3±2.1 vs 16.7±1.4 years), BMI% (82±15 vs 79±20), and self-reported physical activity level (sedentary range). Total body adiposity was significantly higher in TS (40.0±6.6 v. 35.9%±7.0%, p=0.025). However, VO₂ peak, systolic and diastolic blood pressure, HbA1C, LDL, and triglycerides were not different in TS (p>0.1), and HDL was actually higher in TS (p<0.001).

Conclusions Although adult women with TS have lower exercise capacity, in this sample of adolescent girls matched for BMI and habitual activity level, girls with TS had no difference in VO₂ peak by bicycle ergometry. Adiposity was higher in TS; however, many other cardiometabolic risk factors were not different between girls with and without TS. This highlights that obesity and physical activity level may be primarily responsible for the high cardiovascular morbidity and mortality in this population in adulthood. Therefore, targeting a healthy BMI and daily physical activity in childhood and adolescence may help prevent cardiovascular disease in TS.

22 IMPROVED ADIPOSE BROWNING AND METABOLIC FUNCTIONS IN MUSCLE-SPECIFIC FOLLISTATIN TRANSGENIC MICE MAY RESULT FROM MUSCLE-ADIPOSE CROSS-TALK

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10.1136/jim-2018-000939.22

Purpose of study Increased energy expenditure resulting from promoting adipose browning has proved beneficial for targeting several metabolic diseases. We have recently reported that muscle-specific follistatin (Fst) transgenic (Fst-Tg) mice show significant upregulation of key adipose browning characteristics and improved metabolic functions compared to the age and gender-matched wild-type (WT) mice (1–3). The purpose of this study was to identify key myokines that are differentially expressed in Fst-Tg mice compared to the WT that may play an important role in promoting adipose browning and improved metabolic functions.

Methods used 8 weeks old male mice overexpressing Fst from a skeletal muscle-specific promoter (Fst-Tg) and age-matched wild-type (WT) mice were used in our studies. Gastrocnemius (Gastroc) and levator-ani (LA) muscle tissue samples from Fst-Tg and WT groups were harvested and analyzed for key genes and protein involved in the regulation of mitochondrial biogenesis, fatty acid oxidation (FAO), energy metabolism and insulin signaling pathways by quantitative real-time PCR and western blot analysis respectively. Serum levels of key myokines were also analyzed by enzyme-linked immunosorbent assay (ELISA).

Summary of results Muscle tissues isolated from Fst-Tg mice show significantly increased expression of key myokines including fibroblast growth factor 21 (FGF21), irisin, interleukin 6 (IL-6) and peroxisome proliferator-activator receptor gamma coactivator 1-alpha (PGC1a) compared to the WT mice. Muscle tissues from Fst-Tg mice also show significant upregulation of SirT1/AMPK/PGC1a and insulin signaling (IRS/IR-β/AKT) pathways implicated in adipose browning and improved metabolic functions. Serum FGF21 levels were significantly increased in the Fst-Tg mice compared to the WT mice.

Conclusions Our results provide novel evidence of muscle-adipose cross-talk and its possible implication for the therapeutic use of Fst in the regulation of obesity and related metabolic diseases.

23 GLUCAGON-LIKE PEPTIDE-1 RESPONSE TO GLUCOSE CHALLENGE IS NOT DIFFERENT IN OBESE ADOLESCENTS WITH PCOS, BUT GIRLS WITH PCOS RESPOND TO ACUTE GLUCAGON-LIKE PEPTIDE-1 AGONIST THERAPY

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10.1136/jim-2018-000939.23

Purpose of study Obese girls with polycystic ovarian syndrome (PCOS) have high risk for metabolic disease and 40% prevalence of impaired glucose tolerance (IGT). Decreased glucagon-like peptide-1 (GLP-1) secretion, seen in type 2 diabetes

and adults with PCOS, reduces first phase insulin release, contributing to hyperglycemia. Therapy with GLP-1 agonists lowers post-prandial glucose in those with diabetes. Post-prandial GLP-1 and GLP-1 agonist responses were unknown in youth with PCOS. We predicted lower GLP-1 secretion in girls with PCOS that would be improved with acute GLP-1 agonist treatment.

Methods used 72 obese adolescent girls were enrolled in a cross-sectional study (BMI 35.0 ± 6.1 kg/m², age 15.6 ± 1.8 years; 24 controls, 48 PCOS). All girls underwent a 6 hour oral sugar (75 g glucose +25 g fructose) tolerance test (OSTT) with frequent sampling of serum glucose, insulin, GLP-1, c-peptide, and glucagon. A GLP-1 agonist, exenatide, was given the evening prior to the OSTT in 10 of the girls with PCOS. Three sets of analyses using two-way ANOVA with repeated measures were performed: 1) PCOS status, 2) IGT status (n=23) or 3) PCOS untreated vs. GLP-1 agonist treated.

Summary of results Girls with PCOS, despite higher glucose and insulin concentrations, showed no differences in GLP-1, glucagon or c-peptide. Insulin curves were significantly higher, with no differences in GLP-1, glucagon or c-peptide in those with IGT, compared to girls with normal glucose tolerance. In the PCOS group and the IGT group, insulin curves were biphasic, indicating an inadequate initial insulin peak. In the GLP-1 treated PCOS group, glucose was significantly lower. Whereas the insulin curves were not statistically different, there was a shifted early first phase peak.

Conclusions Despite early glucose and insulin abnormalities, obese girls with PCOS or IGT do not have lower GLP-1 secretion compared to obese controls. In obese girls with PCOS, post-prandial glucose was significantly decreased and the first-phase insulin peak was more robust in response to agonist. Due to observed GLP-1 resistance, obese youth with PCOS may benefit from GLP-1 therapy.

24 HEALTH COACHING WITH MONETARY INCENTIVES: FIVE YEAR FOLLOW-UP OF GLYCEMIC CONTROL AND LIPIDS

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10.1136/jim-2018-000939.24

Purpose of study To compare HbA_{1c} and other biometrics in wellness participants (WP) of 2 companies: Co A provided health coaching and reduced health care premiums. Co B did not.

Methods used We measured HbA_{1c} and lipids in 617 WP of Co A and 82 WP of Co B, and estimated 10 year cardiovascular risk (CVR) by the method of Goff et al. Face-to-face coaching by Advanced Care Practitioners of Co A WP with HbA_{1c} >5.6 emphasized exercise, healthy weight, and optimal diet. Results were provided to all WP, to be shared with primary clinicians.

Summary of results HbA_{1c} rose in Co B WP and fell in Co A WP (table 1) in whom prediabetes (PD) fell from 268 to 163 (P=0.001). PD rose in Co B WP from 11 to 23 (chi squared=8.944, P=0.003). Incident diabetes (DM) was found in 24 Co A WP vs. 74 expected (Zhang et al., P=0.001). DM developed in 4 Co B WP vs. 2 expected (P=0.40). Cholesterol, low-density lipoprotein and high-density lipoprotein

Abstract 24 Table 1 Five-year follow-up of HbA_{1c} and lipids in wellness participants with (Company A) and without (Company B) health coaching and monetary incentives

	Company A			Company B		
	Initial	Follow-up	P	Initial	Follow-up	P
HbA _{1c} , %	5.58±0.36	5.52±0.60	0.003	5.29±0.36	5.62±0.58	0.0001
Cholesterol, mg/dL	190±38	187±36	0.015	197±41	183±37	0.034
LDL, mg/dL	125±36	111±33	0.0001	130±38	111±31	0.001
HDL, mg/dL	43±12	47±13	0.0001	47±12	52±14	0.001
Triglycerides, mg/dL	136±75	139±80	0.375	102±65	102±58	0.992
BMI, kg/sq m	29.9±6.1	30.6±5.5	0.0001	28.7±5.7	29.5±6.1	0.42
Waist, inches	38.5±5.4	39.3±5.5	0.0001	36.9±5.1	37.9±5.9	0.27
CVR, %	4.9±4.3	7.0±7.2	0.0001	2.4±2.2	3.8±3.2	0.001

Abbreviations: BMI, Body Mass Index, kilograms per square meter; CVR, ten-year risk of cardiovascular event, per cent; HDL, high-density lipoproteins; LDL, low-density lipoproteins.

levels improved in both Co A and Co B. Triglycerides were unchanged in both groups, as was blood pressure (BP). CVR increased in both groups (table 1) due to aging and unimproved BP.

Conclusions Glycemic control improved in Co A, associated with health coaching and monetary incentives. In Co B, HbA_{1c} with the expected secular trend, and prediabetes rose from 13 to 28 per cent. Lipids improved in both groups. BP was unchanged, so more emphasis on this metric is needed.

25 EFFECT OF AN UP-REGULATOR OF NITRIC OXIDE ON THE PREVENTION OF OSTEOPOROSIS IN THE RAT

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10.1136/jim-2018-000939.25

Purpose of study Osteoporosis is a common disorder in the elderly. It is characterized by an imbalance in the osteoblast/osteoclast turnover making bones susceptible to fractures. Osteoblast/osteoclast balance depends on the presence of estradiol thus by stimulating the production of nitric oxide (NO) prevents bone resorption. It has been shown that a new nutraceutical combination, COMB-4, accelerates fracture healing by stimulating the production of NO, prompted us to study whether treatment with COMB-4 could play a role in the prevention of osteoporosis.

Methods used Nine-month female Sprague Dawley rats were placed into four groups (n=8 per group): sham (Non-OVX), ovariectomized control (OVX), estradiol (OVX +Estradiol), and COMB-4 (OVX +COMB-4). Rats in the OVX and Sham groups received vehicle by retrolingual administration (RLA). COMB-4 comprised of Paullinia cupana (45 mg/kg BW), Muira puama (45 mg/kg BW), ginger (45 mg/kg BW) and l-citrulline (133 mg/kg BW) by RLA. OVX +Estradiol group received estradiol valerate (0.8 mg/kg BW) by RLA. After 100 days of treatment, bone mineral density (BMD) and bone mineral content (BMC) were measured by DXA Scan. Tartrate acid resistant phosphatase (TRAP) staining in lumbar vertebrae, as well as serum TRAP and osteocalcin, were measured.

Summary of results As expected compared to the sham group, OVX rats showed a decrease in BMD, BMC as well as an increase in TRAP serum by 20% ($p < 0.05$). Serum osteocalcin was decreased in OVX by 80% with respect to control. Estradiol reverted all bone and serum markers to the levels seen in the sham group. Treatment with COMB-4 in OVX rats resulted in similar outcomes as seen in the estradiol and control groups. COMB-4 significantly decreased the number of TRAP + cells by five-fold with respect to OVX ($p < 0.05$) in the lumbar vertebra.

Conclusions COMB-4 is capable of restoring the abnormal BMD, BMC and bone markers associated with OVX presumably by its ability to stimulate NO production by the osteoblast. Based on these results, COMB-4 may prove to be a potential non-hormonal alternative therapy to prevent or possibly delay the onset of osteoporosis.

Health Care Research I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

26 DETERMINING THE ACCEPTABLE OPIOID PRESCRIPTION RATE AMONG EMERGENCY DEPARTMENT PHYSICIANS AND RESIDENTS AT AN ACADEMIC TEACHING HOSPITAL

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10.1136/jim-2018-000939.26

Purpose of study The purpose of this study is to assess the variability in the opioid prescribing frequency of emergency physicians among some of the most common discharge diagnoses seen in the emergency department. This study will also explore the various physician-, patient-, and institutional-specific factors that influence opioid prescribing and the extent to which these factors are considered by emergency physicians.

Methods used We plan to administer a two-part survey to emergency department attending physicians and residents at the University of California Irvine Medical Center (UCIMC) in Orange, California. The first part of the survey consists of a list of 19 discharge diagnoses common to the emergency department and asks physicians to specify what percent of cases prescribing an opioid seems medically indicated for each diagnosis. The second part of the survey consists of a list of possible factors that a physician might consider when prescribing an opioid and asks physicians to rank, using a Likert scale, how much each factor weighs into their decision to prescribe an opioid. The mean, median, interquartile range will be calculated from the data collected.

Summary of results Recent studies have shown that emergency physicians working in the same department demonstrate wide variation in their rates of opioid prescribing. A

large study of 2 15 678 medical beneficiaries found that rates of opioid prescribing varied widely between low-intensity and high-intensity prescribers by 7.3% and 24.1% respectively. Furthermore, another recent study found that 65% of emergency physicians underestimate their opioid prescribing practice. These findings raise the question as to whether or not physicians agree on the need to prescribe an opioid for a given diagnosis and what factors influence the decision to prescribe, both of which we plan to explore in this study.

Conclusions Wide variation in the opioid prescribing practice of emergency physicians would suggest a need to standardize and improve adherence to treatment guidelines and evidence suggesting alternatives to opioids.

27 EXPLORING THE NICHE OF STUDENT RUN CLINICS IN COMMUNITY CARE

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10.1136/jim-2018-000939.27

Purpose of study UC Davis, like most medical schools, is proud of its Student Run Clinics (SRCs), but some believe that these clinics ultimately do more for students than patients. We asked, what motivates patients to utilize SRCs in the context of other perceived options? We hoped that answering this question would provide insight to medical school administrators and also to policy makers who are concerned about gaps in the health care delivery system.

Methods used

- 41 undergraduate researchers contributed, following two half day trainings in qualitative research techniques.
- Interview questions were created in consultation with coauthoring experts in qualitative research design and public health.
- 104 individual interviews were conducted with patients at 8 clinics in Fall, 2017.
- Interviews were translated from six languages by native speakers.
- Two lead authors utilized a grounded theory approach to identify themes from all interviews across clinics.

Summary of results We identified four major themes in the interviews, with selected quotes:

Preference:

'They give us more attention, they listen to us here... They inspire my trust to say what I feel.'

'I don't trust going into the emergency rooms or hospitals anymore... They called CPS on me and I got my son taken for trying to get medical care.'

Community:

'I see it as a good thing for [students] and us at the same time because one day they will be the ones helping us.'

'Thank you for the respect you have for us.'

Accessibility:

'Obamacare didn't help at all... premiums were going to be just as high or higher than what we were paying with Covered California.'

'I just applied and got MediCal. There's a language barrier and I don't really know how to use it.'

'I don't have any insurance I'm signed up with yet... I was kinda falling through the cracks on a lot of things.'

Room for Improvement:

'If you had a larger place where you could take in more people, that's what I would say I would want for this clinic.'

'The stethoscopes and blood pressure cuffs do not work a lot of the times.'

'Just, like, let more people know it's there.'

Conclusions Our exploration of themes that arose in our standardized interviews revealed that SRCs, across all communities, have a robust role. Even as patients recognize limitations of the clinics, they experience significant advantages unique to the SRCs which continue to bring them back, even when other options exist.

28 COMMUNITY-BASED INNOVATIONS IN MATERNAL HEALTH AIMED TO REDUCE MATERNAL AND NEONATAL MORTALITY IN SOUTH EAST ASIA

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10.1136/jim-2018-000939.28

Purpose of study Maternal health innovations address the issue of maternal mortality and offer solutions to improve maternal health. Maternal and child deaths can be prevented with the implementation of innovative, low-cost programs that increase the utilization of maternal health care services. This study identified effective community-based innovations improving maternal and neonatal mortality outcomes in South East Asia.

Methods used The following research question guided the search: 'What has been the effectiveness of community-based innovations to reduce maternal and neonatal mortality in South East Asia?'. MEDLINE, Global Health, EMBASE and CINAHL databases were searched and English articles between 2000–2015 were filtered. A title, abstract and full-text review was then completed. The Center for Disease Control and Prevention's Program Evaluation Framework was used to evaluate each program. This involved evaluating for utility, feasibility, propriety and accuracy. Each study was then thematically categorized into 4 categories based on the nature of the program: 1) maternal health services (MHS) programs, 2) access to MHS programs, 3) community development programs and 4) financial incentive programs. The structure, process and outcome of each program was also investigated.

Summary of results The initial search yielded 756 articles. After conducting a title, abstract and full text review, a total of 15 studies were analyzed in this study. The majority of articles were multi-thematic. Overall, there were 4 studies with financial incentives, 2 studies using community development initiatives, 6 studies targeting access to MHS and 8 studies involving the presence of MHS programs.

Conclusions Financial health programs aimed to change health-seeking behaviours and eliminate financial barriers to care. However, structural barriers such as lack of transportation reduced utilization rates of services. Community development programs facilitated participatory women's groups and instituted training of traditional birth attendants in bag-valve-mask resuscitation of neonates. Increased transportation between home and hospital was one of the most common interventions used to increase access to medical services. Lastly, introducing maternal health resources in rural communities improved access to information.

29 STATUS OF MATERNAL CHILD HEALTH IN RURAL NEPAL: A SITUATION ANALYSIS IN HUMLA DISTRICT

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10.1136/jim-2018-000939.29

Purpose of study The majority of Nepal's births take place in remote, rural and resource poor areas, and adverse outcomes are common. Little information exists about available health resources and care practices for maternal-child health (MCH) in these areas. The intent of this study was to evaluate MCH resources and care practices in Humla district, one of the most remote regions in the world, and to identify areas of intervention for antepartum, intrapartum, and postpartum care.

Methods used In November 2017, our team surveyed 53 women in 16 locations who had delivered in the preceding 24 months. Women were identified from government birth records or by the local health workers. We completed a previously validated, standardized MCH household survey, based on WHO maternal-newborn practice guidelines with a primary focus on ante-, intra- and post-partum care processes and outcomes after delivery. We also surveyed 11 health posts and the only hospital with MCH care capacity using a standardized, validated health facility assessment tool. Reporting is descriptive.

Summary of results

Health facilities 1/11 health posts had a health worker trained as skilled birth attendant (SBA) and all facilities lacked basic equipment/supplies needed for safe delivery. The district hospital in Simikot is well staffed with trained personnel, however due to a lack of roads the majority of people living in this area have to walk for several days to reach it.

MCH care 47% of pregnant women had their blood pressure checked and 34% were screened for anemia. Most women delivered at home (66%) and only 18% delivered with a SBA trained health worker. Health worker follow-up after delivery was uncommon for most women (3%). Community members identified concerns about distance/time to travel, and lack of facilities/trained staff as reasons why they choose to deliver at home. A mortality estimate revealed a NMR of 45/1,000 and MMR of 400/10,000.

Conclusions The majority of pregnant women do not receive appropriate MCH services due to a lack of access to trained personnel, facilities and equipment. Mortality rates are above the national average. Interventions to strengthen MCH services in Humla are urgently needed.

30 IMPROVING HEALTH LITERACY IN A PEDIATRIC INFECTIOUS DISEASE CLINIC

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10.1136/jim-2018-000939.30

Purpose of study Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. Inadequate health literacy contributes to poor health outcomes and increases healthcare costs. Healthcare information can overwhelm even persons with advanced literacy skill especially when stressed by healthcare issues. Best outcomes are produced by health literacy-

competent healthcare providers who ensure communication is easy to understand and verify comprehension. Improving communication with patients and their families increases understanding and participation in the plan of care. The purpose of this project was to improve the health literacy of a Pediatric Infectious Diseases outpatient clinic's patients and families using the Agency for Healthcare Research and Quality (AHRQ) universal precautions toolkit.

Methods used The project involved inter-professional collaboration by physicians, clinic nurses, patient services staff, and pediatric patients with their families. The site for the project was a pediatric infectious diseases clinic in an academic-based practice located in the Southwest region of the United States. The Plan-Do-Study-Act framework was used and outcomes measured included the clinic staff's perception of the clinic's health literacy practices compared to evidence-based practice and the patients/families' perception of health literacy support in a subspecialty clinic.

Summary of results There was an improvement in how patients and families rated the health literacy practices of the healthcare team. After focusing on improving written and spoken communication, the healthcare team rated their health literacy practices as improved based on a pre-post comparison of best health literacy practice.

Conclusions Implementing health literacy improvement activities as a means of improving communication with patients and families is feasible and serves patients' needs by improving health literate care in a Pediatric Infectious Disease outpatient clinic. Ongoing efforts to improve means of communication like encouraging multidisciplinary team involvement, evidence-based toolkits, easy-to-read illness specific handouts and using technology are in process.

31 EVALUATION OF HEALTHCARE OF GENDER-DYSPHORIC VETERANS IN THE VA NORTHERN CALIFORNIA HEALTH CARE SYSTEM (VANCHCS)

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10.1136/jim-2018-000939.31

Purpose of study The Department of Veterans Affairs has a policy of welcoming LGBTQ Veterans, and has established working groups to coordinate care for Veterans in this population. We wished to evaluate the care provided to gender-dysphoric Veterans in VANCHCS.

Methods used Using ICD-10 criteria, we identified a population of 148 Veterans as of May 31, 2018. We stratified these individuals by preferred gender, regardless of 'official' records, and further evaluated their medical records for cross-sex hormone therapy and access to mental health, endocrine, speech pathology, and dermatology resources.

Summary of results Of the 148 Veterans, 10 were non-binary, 43 were transmen, and 95 were transwomen. Because of small numbers, we excluded non-binary Veterans from further analysis. The transmen were significantly younger than transwomen (42±13.7 vs 51.5±15.9 years., $p<0.001$ by t-test). Transwomen were more likely to be Air Force Veterans than transmen (21.1% vs 17.1%), and less likely to be Army Veterans (38.9% vs 43.9%). Transwomen were more likely to see an Endocrinologist (83.2% vs 72.1%), and Speech Therapy (44.2% vs. 25.6%) than transmen. Cross-sex hormone

therapy for transwomen included multiple combinations, whereas for transmen, testosterone was the sole therapy. Both groups were followed comparably in Mental Health Clinics (87.4% for transwomen, 90.7% for transmen). Only 35 transwomen (36.8%) were seen in Dermatology clinics for gender identity issues. In summary, our populations represented diverse backgrounds and received a variety of treatments.

Conclusions We conclude that care for these Veterans could be enhanced by a more consistent, team-based approach to therapy.

32 QUANTIFYING INSTITUTIONAL DIFFERENCES IN PEDIATRIC RENAL SONOGRAPHY TECHNIQUES AND INTERPRETATION

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10.1136/jim-2018-000939.32

Purpose of study Identifying opportunities to receive medical imaging closer to home may reduce financial and temporal costs for patients and families. We wondered if there were differences in imaging methods and/or quality of radiographic interpretation among studies performed at freestanding children's hospitals and other institutions. We undertook this study to describe differences in renal bladder ultrasound (RBUS) image and report quality associated with the obtaining type of institution.

Methods used We identified all new patients with RBUS seen in the urology clinic of a free standing, university affiliated children's hospital (FCH) between January 1 and December 31, 2017 with a RBUS ordered at or before the initial visit with available radiographic interpretation. We recorded the number of longitudinal and transverse views of each kidney, bladder and the number of cine loops in each study and whether the interpreting radiologist commented on renal parenchymal echogenicity (RPE) and upper tract dilatation (UTD).

Summary of results 637 patients met inclusion criteria with 388 (61.1%) having RBUS at FCH. Children undergoing RBUS at FCH and NFCH were similar in age (median 5.6 vs. 5.4 years) and gender (51.7% male vs 43.0% female). RBUS from FCH had similar renal imaging, but more bladder imaging and were less likely to have cine loops (OR=0.85, 95% CI: 0.61 to 1.19) than NFCH. When present, NFCH recorded more cine loops than FCH (median 4 vs 2). FCH reports more often described RPE (OR=101.8, 95% CI: 24.8 to 418.7) and commented on UTD (OR=2.87, 95% CI: 0.95 to 8.67). For patients with UTD, FCH reports used formal nomenclature more often than NFCH (OR=69.3, 95% CI: 34.6 to 138.5) and FCH utilized the newer nomenclature system more than NFCH (98.4% vs 69.2%).

Conclusions RBUS from FCH were quantitatively similar to those from NFCH having a similar amount of static images of the kidneys but more bladder images and fewer cine loops. Radiology reports were more detailed at FCH than at NFCH, particularly regarding assessment of RPE and utilization of standardized nomenclature to describe UTD in the pediatric population. Although RBUS are widely available and may offer cost and time savings for families, these findings should be considered by providers ordering RBUS locally.

33 FEASIBILITY OF A LOW-COST LOW-FIDELITY TRAINER FOR ULTRASOUND-GUIDED INJECTION AND ASPIRATION

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10.1136/jim-2018-000939.33

Purpose of study To determine the feasibility of using a low-cost vegetable-based task trainer for teaching medical trainees techniques for US guided injection and aspiration.

Methods used Firm-texture tofu commercially available at a local grocery store was fashioned into a block of appropriate size for simulation of neck soft tissue. Several materials, including olives, fluid-filled balloons, and fluid-filled gloves were embedded in the tofu to simulate subcutaneous pathology, and the simulated tissue blocks were evaluated for realism by experts using ultrasonography. The optimal iterations were then made available to trainees as an ultrasonography task trainer at an annual residency training bootcamp for emergency neck procedures. Volunteer medical trainees were asked to compare the novel model to two models previously used with regards to realism and pre- and post-training comfort with procedures involving neck ultrasonography. Course faculty were also asked to compare the realism and value of the novel task trainer compared with the previous models for teaching neck ultrasonography procedures.

Summary of results 6 Course faculty and 15 Trainees completed the surveys. All instructors felt that the task trainer had comparable or better soft-tissue characteristics compared with the commercially-purchased phantom silicone-based task trainer and the olive-embedded chicken breast trainers used previously. Prior to incorporation of the tofu trainer, the US module in the otolaryngology emergencies bootcamp showed one of the lowest gains in trainee comfort before and after training. After incorporation of the model, this station showed one of the highest gains. Free-text survey responses identified additional advantages over the previous models including superior simulated tissue qualities over the previous non-biological model, and lower concerns about disease transmission risks than the previous chicken-based model.

Conclusions This pilot study demonstrates feasibility and utility of a low-cost easily-accessible tofu-based trainer for improving medical trainee comfort with ultrasonography and ultrasound-assisted procedures with reduced disease transmission risk than models previously used. Further study could expand the evaluation to a larger cohort of experts and novices in a randomized head-to-head comparison.

34 SLEEPWEAR-RELATED INJURIES IN OLDER ADULTS: ESTIMATES FROM THE NATIONAL ELECTRONIC INJURY SURVEILLANCE SYSTEM

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10.1136/jim-2018-000939.34

Purpose of study Falls are a leading cause of injury in adults aged 65 years and older. Previous studies have focused on risk factor assessment and environmental modifications to decrease falls; our study expands the knowledge base by identifying sleepwear as a contributing factor to falls and related injuries.

Methods used We undertook a retrospective analysis of data obtained from the National Electronic Injury Surveillance System (NEISS). We extracted data concerning sleepwear-related injuries occurring in adults age 65 and older between 1998 and 2017. We report descriptive statistics as well as multivariate logistic regression analysis identifying contributing variables to sleepwear-related injuries.

Summary of results One thousand thirty six (1036) cases were identified and 1013 ultimately included for analysis. The median age was 82 (range 65–104), and 83% of the cases were female. The highest proportion of injuries occurred between the ages of 80 and 89 (39%). Pajamas were the most frequently implicated sleepwear (40%), followed by robes/housecoats (34%), and nightgowns/nightshirts (24%). Injuries that could be classified as falls represented 72% of the sample, and pajamas were responsible for 44% of these injuries. Age (both the 80–89 age group and the 90–99 age group) and wearing pajamas were associated with a statistically significant increased risk of falls. The most common injury types were fractures (35%), contusions/abrasions (15%), and internal organ injuries (11%). The head and the hip were the body parts most frequently affected at 20% and 18%, respectively. The NEISS data estimates a 266% increase in sleepwear-related injuries occurring in the United States over our 20 year study period.

Conclusions The number of sleepwear-related injuries in those age 65 and older has increased over the past 20 years and is likely to continue to increase as this segment of the population grows. Education, awareness, and targeted interventions for patients/caregivers in the home and professionals in clinical and residential care settings may represent high yield opportunities to prevent injuries, decrease morbidity, and enhance the health of older adults.

Immunology and Rheumatology I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

35 AUTOANTIBODY ISOTYPE CHANGES POST RHEUMATOID ARTHRITIS DIAGNOSIS

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10.1136/jim-2018-000939.35

Purpose of study Rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) are known to be elevated in Rheumatoid Arthritis (RA). Less is known about the ways in which the specific isotypes of these antibodies change after RA diagnosis. Evaluating these changes may enhance our understanding of the ongoing inflammatory response following disease onset. We tested post RA diagnosis serum samples from the Department of Defense Serum Repository (DoDSR) and a Colorado-based RA cohort called 'Studies of the Etiology of RA' (SERA) to better understand these changes.

Methods used From the DoDSR we obtained a single post-RA diagnosis serum sample from 214 RA cases. The samples were

divided into 2 groups: <2 years post RA diagnosis, and ≥ 2 years. We evaluated serum RF and ACPA immunoglobulin (Ig) IgA, IgG, and IgM isotypes, and then evaluated the rates of positivity for isotypes of both antibodies between samples <2 and ≥ 2 years post diagnosis. In a similar fashion we evaluated single samples from 1469 subjects with RA from SERA with the exception that only RF isotypes were tested.

Summary of results In DoDSR, there were significantly higher rates of positivity for IgA RF and IgA ACPA in subject samples from ≥ 2 years compared to <2 years. In SERA, all 3 RF isotypes were significantly increased in patients assessed ≥ 2 years from RA diagnosis compared to <2 years. In contrast, there were no significant differences autoantibody positivity based on age (<vs. ≥ 40 years) in either DoDSR or SERA at time of testing.

Conclusions Rates of autoantibody positivity continue to rise after a diagnosis of RA, and this does not appear to be age-dependent. This suggests an evolving autoimmune inflammatory response early in the course of disease despite therapy. In particular, the predominant change in IgA autoantibodies in DoDSR suggests that there may be a degree of mucosal involvement in the early period following RA onset. Further evaluation, including studying single individuals over time, is necessary to help clarify the nature of evolving autoimmunity in RA.

36 FACTORS INFLUENCING PARTICIPATION IN RHEUMATOID ARTHRITIS PREVENTION

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10.1136/jim-2018-000939.36

Purpose of study Recruitment of subjects for clinical prevention studies is complicated by the need for otherwise healthy individuals to assume the inherent risks within clinical research in absence of an active disease. The rheumatoid arthritis (RA) field has begun trials in prevention. One trial is StopRA that is evaluating hydroxychloroquine (HCQ) as a preventative treatment for those at high risk of developing RA. The goal of this current study is to evaluate the factors that influence an individual's decision to participate in StopRA to improve future study design and enrollment.

Abstract 36 Table 1

	Agree to trial?		
	Yes (n=30)	No (n=16)	P-value
Gender, N (% Female)	22 (73%)	13 (81%)	0.72
Age, mean (SD)	52 (15)	58 (17)	0.78
First Degree Relatives with RA, N (% Yes)	17 (57%)	2 (13%)	<0.01*
Education, N (% Some College or Greater)	27 (90%)	15 (94%)	1.00
Benefit to Me, median (range)	4 (2,4)	1.5 (0,4)	<0.01*
Benefit to my Family	4 (0,4)	1 (0,4)	0.01*
Benefit to Others	4 (2,4)	1 (0,4)	<0.01*
Risk of developing RA	4 (0,4)	2.5 (0,4)	0.03*
Potential Positive Side Effects	3 (1,4)	1 (0,4)	0.02*
Potential Negative Side Effects	2 (0,4)	4 (0,4)	<0.01*

0=no opinion; 1=not at all; 2=a little; 3=somewhat; 4=very much;

Time, Compensation, Moral Obligation, to Learn About RA and the Potential for Receiving a Placebo were not statistically different between groups.

Methods used After they had made their decision to participate, or not, in StopRA, individuals who were eligible for enrollment were surveyed about factors that influenced their decision.

Summary of results The characteristics of the participants and questionnaire responses are included in the table 1. In particular, subjects who agreed to participate in StopRA were significantly more likely to have First Degree Relatives (FDRs) with RA, less likely to be fearful of the medication, and perceive benefits to themselves and family from participation.

Conclusions These findings indicate that individuals who have FDRs with RA may be more likely to participate in RA prevention. Furthermore, wanting benefit to self, family and others were significant factors in the decision to enroll in preventative research. This approach provides an opportunity to optimize future study design and recruitment approaches. In addition, we will explore why FDRs status is a powerful motivator while surveying other factors including symptoms and perceived risk of developing RA.

37 UTILITY OF A VIRTUAL RHEUMATOLOGY CLINIC FOR COMMUNITY BASED INTERNAL MEDICINE RESIDENCY PROGRAM

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10.1136/jim-2018-000939.37

Purpose of study At our mid-sized community hospital, internal medicine residents have little routine access to subspecialty rheumatology faculty clinical and didactic teaching. We needed an active learning resource to disseminate practical aspects of rheumatologic diagnoses and management. Hence, we partnered with the University of Rochester, and collaborated to further develop the 'Virtual Rheumatology Clinic' Tool. Our primary outcome was to improve confidence in diagnosis and treatment of rheumatologic conditions. Our secondary outcomes were to improve knowledge base in rheumatology and obtain user feedback.

Methods used We had 58 participants (19 PGY 1, 20 PGY 2, 19 students) using the tool. Login instructions were sent via email. 6 modules (lupus, lower back pain, gout, myositis, giant cell arteritis and osteoporosis) were completed over 3 months. Knowledge was assessed by a pretest and posttest covering a broad range of rheumatology topics. Confidence and usefulness of the tool was determined by pre and post surveys. Data was analyzed by T test and Chi square test.

Summary of results Self-reported confidence in diagnosis and treatment of rheumatologic diseases was below average to average among students and residents before using the

Abstract 37 Figure 1

modules ($p=0.560$). Students gained more confidence compared to residents after completing the modules ($p=0.04$). There was no difference in pretest and posttest scores across the board ($p=0.08$). Residents had a greater mean increase in scores compared to students ($p=0.001$). Perceived usefulness of modules is shown in figure 1.

Conclusions The modules seem to be more appropriate for residents than students, based on overall improvement in objective test scores. Students and residents both acknowledged the usefulness of the modules. Improvement in global post-tests were not detected, likely in part because these were not limited to topics covered; sub scores on covered diagnoses did improve.

38 ADDITION OF OBLIQUE RADIOGRAPHS IN THE EVALUATION OF SACROILIITIS

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10.1136/jim-2018-000939.38

Purpose of study Traditional radiography is used to evaluate sacroiliitis in patients with suspected ankylosing spondylitis (AS). However, inconsistency in plain film techniques is well documented; as current dogma advocates against oblique images despite preliminary data suggesting better correlation with MRI. This study determined if the addition of oblique radiographs improves reliability in the scoring of radiographic sacroiliitis using the modified the New York criteria (mNY). This study also evaluated if oblique views altered assessment of sacroiliitis severity, diagnosis of AS, or reader confidence in scoring.

Methods used Radiographs of veterans enrolled in the Program to Understand Long-term Outcomes of Spondyloarthritis (PULSAR) cohort were evaluated by three readers using the mNY criteria. Inter-reader reliability was compared between Ferguson-views alone and Ferguson-views supplemented with oblique views. Mean mNY score and the proportion of patients meeting diagnostic criteria for AS were also compared between one- and three-view radiographs. Finally, patient characteristics were evaluated for association with severity of sacroiliac disease.

Summary of results The addition of oblique radiographs did not improve inter-reader reliability in mNY scoring compared to Ferguson views alone (Kappa 0.305 vs 0.298, $p>0.05$). However, the use of oblique views increased the mean mNY score compared to single view radiographs (3.06 vs 2.82, $p<0.001$ by t-test), improved reader confidence ($p<0.001$), and resulted in an increase in AS diagnoses (83% vs 73%). The mean mNY score with three views was also more predictive of patient functional assessments compared to one view.

Conclusions While the addition of oblique radiographs did not improve inter-rater reliability in scoring sacroiliitis, the increase in severity scoring and AS diagnoses associated with these additional views may influence the management of a disease where early treatment can improve future functional status. The use of oblique radiographs also correlated better with patient functional indices. This is a critical consideration in AS, as there is no definitive diagnostic test and diagnosis is frequently delayed.

39

COEXISTENCE OF LIMITED SYSTEMIC SCLEROSIS AND LUPUS ERYTHEMATOSUS TUMIDUS

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Case report Lupus erythematosus tumidus (LET) is a rare entity of cutaneous lupus erythematosus, which has not been associated with other collagen diseases. A 68 year old man developed LET 10 years after the diagnosis of systemic sclerosis (SS) in 2005, when he presented with progressive sclerodactyly, palmar and face telangiectasias, pitting scars on multiple digits, tightness of lips and skin around the neck, nailfold capillary drop-out seen with capillaroscopy, antinuclear antibody (ANA) titer of 1:1280, and positive nucleolar antigen (fibrillarin). He subsequently developed pulmonary fibrosis leading to pulmonary hypertension. In 2015, he developed photosensitive, diffuse erythematous thin papules coalescing into widespread bright salmon red plaques over the chest, back, face, arms, legs, and buttocks with no palmar scaling. Another rash on the upper part of his trunk and neck was described as succulent, elevated plaques showed a pattern of surface-color change reminiscent of Wickham's striae. In addition, sclerotic purple hued infiltrative plaques were noted over the posterior neck. Biopsies of the lesions showed spongiform, edematous dermatitis in the hands and perivascular and periadnexal lymphocytic infiltrations and interstitial mucin deposition consistent with LET in the hands. He died from complications of pulmonary fibrosis in 2017. Current view of autoimmunity clustering involves common genetic susceptibility or environmental factors. Yet, despite intense genetic and population studies on autoimmunity, the patterns of autoimmune clustering across the spectrum of these diseases remain elusive: inheritance of an 'at risk' genotype, environment-susceptible phenotype, and random-chance have all been suggested, but not proven. To our knowledge, this is the first case of LET in a patient with SS. Cutaneous lupus has been tied to risk for coexisting autoimmune conditions, but in our case the SS manifestations preceded the development of LET by several years. Accumulation of similar cases may clarify if onset of LET in a patient with full-blown SS has prognostic significance.

40

DNASE1L3 RELATED AUTOIMMUNE SYNDROME: A CASE REPORT AND REVIEW OF THE LITERATURE

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Case report The *DNASE1L3* gene is a member of the deoxyribonuclease I family. The encoded protein hydrolyzes DNA and mediates the breakdown of chromatin during cell apoptosis and necrosis. Several case reports describe homozygous variants in *DNASE1L3* as a cause of hypocomplementemic urticarial vasculitis syndrome (HUVS) and systemic lupus erythematosus (SLE). A homozygous c.289_290delCA

deletion is described in three sisters with juvenile onset HUVS (PMID 23666765). A homozygous c.643delT variant is described in 6 consanguineous families with pediatric SLE (PMID 22019780). Here we present a 17-year-old female with a juvenile form of HUVS who has compound heterozygous variants in *DNASE1L3* including a novel missense change. We describe the clinical characteristics of this case and review the literature on *DNASE1L3* associated autoimmune syndromes.

The patient is a 17-year-old female with an autoimmune disorder since the age of three. She was initially diagnosed with juvenile idiopathic arthritis but later developed features of urticarial vasculitis, episcleritis, lymphadenopathy, abdominal pain with bowel wall edema, antiphospholipid antibodies and hypocomplementemia. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, and anti-double stranded DNA antibodies were negative.

Whole exome sequencing identified compound heterozygous variants in the *DNASE1L3* gene. Variants identified include the previously described c.290_291delCA (p.T97Ifs*2) variant and a novel p.I60S (c.179T>G) variant. The novel p.I60S variant was not seen in healthy population databases, was predicted to be damaging by *in silico* analysis, and located in a codon highly conserved across species. Functional studies including RNA sequencing and *in vitro* enzyme assay are being pursued. HUVS typically presents in the 3rd and 4th decades of life. Our case helps to better define the phenotypic features of *DNASE1L3* related autoimmune disease and supports the hypothesis that autosomal recessive changes in *DNASE1L3* contribute to pediatric onset HUVS.

41

INTRAMUSCULAR STIMULATION THERAPY FOR CHRONIC PAIN CONDITIONS: A SYSTEMATIC REVIEW

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Purpose of study Intramuscular Stimulation (IMS) is a therapeutic needling technique, using acupuncture needles to treat myofascial pain syndromes (MFPS). While the term is internationally recognized there are few adequate randomized controlled trials (RCTs) to date. This review collected and evaluated the quality of the evidence for all English language RCTs for a particular technique of IMS. Only studies which used paraspinal and peripheral needle placement were included.

Methods used A search for RCTs published from several databases was conducted. Six RCTs evaluating IMS in patients with chronic back, neck, and headache pain were evaluated for quality of evidence for treatment efficacy.

Summary of results In two well-designed studies, IMS showed statistically significant improvement of myofascial pain syndrome (MFPS) symptoms compared to active comparator. In two other studies, IMS showed non-inferiority compared to established standard treatments of MFPS, and greater trochanteric pain syndrome. In two studies, IMS showed non-inferiority to superficial dry needling (SDN) in trigger point-associated headache.

Conclusions Evaluation of RCTs suggests that IMS which included paraspinal needling is likely superior to or as beneficial as existing treatments for patients suffering from chronic

Abstract 41 Table 1 Studies, outcomes measures, summary of results, level and quality of evidence, and design limitations

Study	Outcome Measure	Results		Interpretation	Evidence (S/E/I) ^a	Quality of Evidence (Jadad Score) -study design limitations
		Difference in Change Scores bet. Tx & Control	P-value			
Neck/back/hip						
Cuoto et al. (2013)	VAS	1	p<0.001	Over 4 weeks of being followed IMS and lidocaine injection showed statistically significant improvement in pain scores over placebo sham. IMS had VAS score 1 point lower than lidocaine injection. The difference between groups was statistically significant.	S	5
	PPT	0.89	P<0.001	Over 4 weeks of being followed both IMS and lidocaine injection showed improved PPT over placebo sham. The efficacy of IMS was statistically superior to lidocaine.	S	
	Sleep Quality	0.86 - 1.1	P <0.01	Both IMS and lidocaine injection showed improved sleep quality compared to placebo sham. The difference between IMS and lidocaine was statistically significant.	S	
Cerezo- tellez et al. (2016)	VAS	2.5	P< 0.000001	IMS + Stretching showed statistically significant improvement in pain at 3 weeks to 6 months follow-up compared to active control (stretching only).	S	4 –Single-blinded: assessor was blinded but the subjects were not blinded.
	PPT	1.1 - 1.2	p< 0.0003	Statistically significant improvements in PPT in all but one muscle group. (trapezius values reported)	S	
	Neck ROM	8.6 - 14.3	p< 0.000001	Statistically significant improvements in neck ROM	S	
Ga et al. (2007)	VAS	0.71	p=.238	After 28 days both IMS and peripheral needling showed decreased pain scores. There was no statistically significant difference between groups.	E	2- patient withdrawals and process of randomization NR, group differences were not statistically evaluated for all outcome measures. Single-blinded: assessor was blinded but the subjects were not blinded
	PPT	0.06	p=.402	Both groups showed improved PPT. There was no statistically significant difference between groups.	E	
Brennan et al. (2017)	Pain rating	-1.1	p=.81	Both IMS and cortisone injection showed improvement in pain scores. IMS was shown to be statistically non-inferior to cortisone injection.	E	3- Evaluator blinding was NR, Non-inferiority model. Patients could identify their group allocation despite not being told, therefore not blinded.
	PSFS	1.2	p=.63	Both groups showed functional improvement. IMS was shown to be statistically non-inferior to cortisone injection.	E	
Headaches						
Karakarum et al. (2001)	Headache Index	2.1	p=.s	Both IMS and control (subcutaneous needling) had improvements in headache index but the difference between groups was not significant.	E	3- patient withdrawals and process of randomization NR.
	TPT	.87	p<0.001	IMS had statistically significant improvements in muscle tenderness compared to control.	S	
	Neck ROM	0.4 - 0.44	p=.s	IMS had improvements in ROM but the difference between groups was not significant.	E	
Sedighi et al. (2016)	Headache Index	-0.07	p=.s	At 1 week improvement in headache index in both IMS and SDN groups but the difference between groups was not statistically significant.	E	1- Process of randomization, blinding, and patient withdrawals NR.
	TPT	0.2	p=.s	Improvement in TPT in both groups, but no significant difference between groups was reported.	E	
	Neck ROM	Friedman's test results on ordinal variables. (see Sedighi table 2)		Statistically significant improvement in Neck-ROM in all directions except extension in IMS group, but only statistically significant improvement in one direction in the SDN group.		

^a S=IMS was superior to control, E=IMS was equivalent to control

**PPT=pressure pain threshold using algometry PSFS=patient specific functional scale TPT=TrP tenderness

neck and back pain conditions associated with trigger points. This suggests that further studies should be done to evaluate the long-term effect of IMS in chronic pain conditions especially MFPS of the neck, back, and hip. Existing evidence does not suggest IMS is effective for patients suffering from chronic headaches.

Infectious Diseases I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

42 HEPATITIS C TREATMENT OUTCOMES AMONG PATIENTS TREATED IN PRIMARY CARE AND ADDICTION TREATMENT SETTINGS

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Purpose of study People who inject drugs are at highest risk for HCV infection but have the lowest treatment rates. Barriers include practices/policies which exclude patients who actively use drugs and restrict prescribing authorization to specialists. To counter-act such barriers, there is a need for evidence to show that patients with opioid use disorders (OUD) treated in primary care settings have equivalent treatment outcomes. This study evaluates HCV treatment outcomes of patients treated by primary care providers at Harborview Medical Center's Adult Medicine Clinic (HMC AMC) or at Evergreen Treatment Services (HMC ETS).

Methods used A retrospective electronic medical record (EMR) review was conducted for all patients receiving HCV direct-acting antiviral (DAA) treatment at HMC AMC or HMC ETS from 2016 to 2018. Patients were divided into 3 groups by OUD treatment status: buprenorphine maintenance, methadone maintenance, or neither. Patient demographic and clinical characteristics were extracted from the EMR and used to create descriptive analyses for study participants overall and for each OUD treatment group. The primary outcome was SVR12, defined as an undetectable HCV viral load at least 12 weeks after completing treatment.

Summary of results The overall sample was comprised of 97 patients with HCV who either completed treatment or are still undergoing treatment. A majority were >40 years old, male, single, unemployed, or current users of tobacco, and 79/97 (81%) received treatment for OUD. Eleven of thirteen (84.6%) patients treated with buprenorphine, 31/44 (70.5%) patients treated with methadone, and 12/16 (75%) patients receiving no OUD treatment fully completed HCV DAA treatment without interruptions or missed doses ($p=0.77$). Excluding patients with missing SVR12 data ($n=10$), 11/12 (91.7%) patients treated with buprenorphine, 34/36 (94.4%) patients treated with methadone, and 14/15 (93.3%) patients receiving no OUD treatment achieved SVR12 ($p=0.94$). Those with and without SVR12 data appear to have similar demographic and clinical characteristics.

Conclusions Patients treated with DAAs for HCV in primary care and addiction treatment settings appear to have high

rates of cure. Offering treatment in such settings can expand access to care for vulnerable populations.

43 PARAPNEUMONIC EMPYEMA IN CRITICALLY ILL CHILDREN

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Purpose of study Parapneumonic empyema (PPE) is a serious complication of community-acquired pneumonia (CAP) in children. Pleural fluid drainage is a key part of treatment and can be achieved by chest tube, video-assisted thoracostomy (VATS) or thoracotomy. Patients undergoing early VATS have lower rates of intensive care unit (ICU) admission and shorter hospital length of stay (LOS). This study describes patients with PPE admitted to Primary Children's Hospital (PCH) and compares clinical characteristics and outcomes between pleural fluid drainage strategies.

Methods used We conducted a retrospective cohort review of children with PPE undergoing one or more drainage procedure admitted to PCH between 2005–2016. Data was extracted from the electronic medical record for analyses.

Summary of results Of the 684 patients identified, only 5% of patients underwent VATS or thoracotomy. These procedures were significantly more common among ICU patients (0.1% vs 0.03%, $p=0.001$). ICU patients (33%) were similar to non-ICU patients in gender (58% vs 55% male), mean age (5 vs 4.9 years) and ethnicity. ICU patients had longer median LOS (13 vs 8 days, $p<0.001$) and were more likely to have complex chronic conditions ($p<0.05$). In patients who underwent VATS, ICU LOS (3.2 vs 2.8 days, $p=0.07$) was not significantly shorter. Most ICU patients (55.7%) required invasive mechanical ventilation. Patients who underwent VATS or thoracotomy had shorter duration of invasive mechanical ventilation than those who underwent chest tube placement (7.5 vs 14.5 days, $p=0.02$).

Conclusions Most patients underwent chest tube placement only, yet at PCH, ICU patients were more likely to undergo VATS. While LOS was similar in patients who underwent VATS, duration of mechanical ventilation was shorter. However, this study did not distinguish between the use of VATS as early therapy vs. rescue therapy, as previous studies have shown favorable outcomes for early VATS. As this is less well understood in the critically ill population, we can use a large cohort at a single institution to further understand the timing and type of interventions best suited for management of empyema in critically ill children.

44 STUDIES OF THE ANTIBIOTIC SPECTRUM OF NOVEL METHIONYL-TRNA SYNTHETASE INHIBITORS

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Purpose of study Novel antibiotics are needed to combat antibiotic resistant organisms. The bacterial methionyl-tRNA synthetase (MetRS) is a new target for antibiotic drug development. MetRS is an essential enzyme involved in protein synthesis, and inhibition by MetRS inhibitors has been

Abstract 44 Table 1

Compound Tested	S. aureus (ATCC 29213)	E. faecalis (ATCC 29212)	N. brasiliensis (ATCC 19296)	Bacillus sp. (Patient Strain)	L. monocytogenes (Patient Strain)	H. influenzae (ATCC 10211)
1717	0.125	0.0625	>16	0.125	0.03125	>8
1986	0.5	0.5	4	0.5	1	>8
2067	0.5	-	16	0.5	0.125	>8
2093	0.125	0.125	8	0.25	0.125	>8
2144	0.0625	0.0625	>16	0.5	0.25	>8
2205	1	-	>16	1	1	>8
2309	1	0.5	4	0.5	1	>8
Linezolid	2	2	2	-	-	-
TMP-SMX	-	-	0.5/9.5	-	0.0313/0.594	-
Vancomycin	1	4	-	0.125	-	-
Ampicillin	-	-	-	-	0.5	0.25

shown to halt growth of *Staphylococcus*, *Streptococcus*, and *Enterococcus* species. This work tested the hypothesis that Type 1 MetRS inhibitors have broad activity against Gram-positive bacteria and no activity against Gram-negative bacteria.

Methods used Minimum inhibitory concentrations (MIC) of test compounds against the selected bacterial strains followed standardized methods from the Clinical Laboratory Standards Institute. Organisms in the table 1 were tested by microbroth dilution assay and were performed twice in triplicate to verify results. Each assay included a control antibiotic with MICs documented to be in the range of published values.

Summary of results MIC values ($\mu\text{g/mL}$) of representative bacterial strains and compounds are presented in the table 1 below. MetRS inhibitors have number designations. MIC results on additional strains and compounds will be presented at the meeting.

Conclusions Novel MetRS inhibitors are effective against many types of Gram-positive bacteria *in vitro*, with MICs similar to or lower than commonly used antibiotics. New activities were most notable against *Bacillus* sp. and *Listeria monocytogenes*. MetRS inhibitors have little effect on Gram-negative bacteria, including *Haemophilus influenzae* (shown), *Burkholderia cepacia*, and *Serratia marcescens*, due to structural differences of the MetRS enzyme. These experiments further validate the MetRS as a drug target for combating Gram-positive infections and expand the known activity of these compounds.

45 STRATEGIES OF GRAM-POSITIVE BACTERIA TO OVERCOME THE ABSENCE OF AN ESSENTIAL SIGNAL TRANSDUCTION PROTEIN

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Purpose of study With antibiotic resistant bacteria on the rise, it has become increasingly important to study pathways unique to bacteria and discover novel antimicrobial drug targets. One promising target is the WalRK system of Gram-positives, a two component system (TCS) exclusive to bacteria, highly conserved structurally, and essential to

viability. We investigated compensatory mechanisms of mutation contributing to bacterial survival when WalR dependent gene expression is misregulated, with the expectation that new molecular pathways and connections are revealed.

Methods used We engineered strains, where the native *walRK* genes can be inducibly removed from the genome and where growth relies on ectopic expression of different WalRK constructs. Strains without WalK readily accumulated second site suppressor mutations that allowed for growth. To identify the mechanism of suppression we employed Sanger sequencing, Illumina sequencing, and Western blotting to detect WalR protein levels.

Summary of results Strains lacking WalR did not grow under any conditions, whereas a strain lacking WalK readily accumulated suppressors. Sequencing of *walR* in 40 suppressor strains revealed one with a WalR E207K mutation, a likely constitutively active allele. This strain initially grew poorly and accumulated additional mutations, which were revealed by whole genome sequencing to be in central carbon metabolism genes *ackA* and *citZ*. 20 suppressors without a WalR mutation revealed significantly elevated WalR levels in western blots. A strain overexpressing *walR* from an inducible promoter was engineered and validated that *walR* overexpression is sufficient to overcome the absence of WalK. Genetic mutations that lead to *walR* overexpression were identified by sequencing revealing mutations in *yviE*, *pksL*, *ymzD*, and *S611* genes.

Conclusions Our studies revealed that bacteria can readily overcome the absence of the WalK kinase by either overproducing WalR or by mutating it to a constitutively active form. The former is achieved by mutations in genes *yviE*, *pksL*, *ymzD* and *S611*. The latter results in poor growth that can be overcome by altering the central carbon metabolism. These findings reveal compensatory survival mechanisms and advance our understanding of the crucial WalRK system.

46 LEADING RISK FACTORS FOR DECOLONIZATION FAILURE OF METHICILLIN RESISTANT STAPHYLOCCUS AUREUS (MRSA): A COMPREHENSIVE LITERATURE REVIEW

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10.1136/jim-2018-000939.46

Purpose of study While several studies have assessed various decolonization methods for MRSA, studies evaluating reasons for decolonization failure are scant. The objective of this study was to identify leading risk factors for failed decolonization of MRSA.

Methods used We conducted a systematic literature review using Pubmed, Cochrane data base, and Google Scholar. We focused on studies published after the year 2000 that used MRSA decolonization method of nasal mupirocin with or without chlorhexidine body wash. Only studies that evaluated risk factors associated with failure were included.

Summary of results Five studies fulfilled our inclusion criteria (see table 1 below) and the majority focused on adult patients. All but one study (Mody et al) used both nasal mupirocin and chlorhexidine body wash. Culture after treatment to determine success was performed at different time points

Abstract 46 Table 1 MRSA decolonization-failure risk factors

Author and Year	Number of Patients	Their Definition of Decolonization Failure	Failure Rate	Risk Factors for Failure
Harbarth, 2000	51 decolonization treatment and 51 placebo	Isolation of MRSA at any body site at 1 month	75% failure in treatment group; 82% failure in placebo group	More than 2 distinct MRSA sites $p=0.035$; Previous fluoroquinolone $p=0.048$
Kolher, 2012	51 decolonization treatment and 27 no treatment	Isolation of MRSA at 12 months	Treatment group 35% failure; No treatment group 78% failure	Old age $p=0.056$; MRSA subtype 21 $p=0.021$
Mody, 2003	64 decolonization treatment and 63 placebo	Isolation of MRSA up to 6 months	At 3 months, 39% failure in treatment group; 80% failure in no treatment group At 6 months, 60% failure in treatment group; 75% failure in no treatment group	75% Mupirocin resistant; 67% recent hospitalization
Singh, 2017	32 successful decolonization with treatment and 18 unsuccessful decolonization	3 consecutive swabs negative for decolonization after 48 hours	64% (32) successfully decolonized; 36% (18) failure to decolonize	Asthmatic Patients $p=0.031$; Usage of post-operative antibiotics $p=0.032$
Sai, 2015	104 successful decolonized with treatment and 164 unsuccessful decolonization	3 consecutive swabs negative for MRSA, with 48 hours in between each	61% (164) failure to decolonize	Presence of wounds $p=0.00001$; More than 2 colonization sites $p=0.003$; Mupirocin resistance $p=0.001$

during the studies. Decolonization failure ranged from 35% to 75% in the treatment group. Different risk factors that were associated with decolonization failure included having >2 MRSA colonized sites, old age, presence of MRSA subtype 21, mupirocin resistance, recent hospitalization, post-operative antibiotic use, and underlying conditions.

Conclusions Our literature review identifies some of the risk factors that interfere with successful decolonization of MRSA. Limitations of these studies include small sample size to take into account potential risk factors, different decolonization methods, and non-uniform definitions of success. Despite these limitations, common risk factors that were found among multiple studies included MRSA colonization at multiple body sites, presence of specific subtypes of MRSA, recent hospitalization, and mupirocin resistance. Large prospective studies are warranted to identify potential risk factors that may help with more efficient decolonization strategies among various subgroups of patients.

47 HIV TRANSMITTED DRUG RESISTANCE IN LIMA, PERU

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Purpose of study Transmitted drug resistance (TDR) mutations threaten the efficacy of first-line antiretroviral therapy (ART) in those initiating treatment. In Peru, genotypic resistance profiling is not routinely performed at ART initiation, and administration of a partially effective regimen can lead to virologic failure. Previously reported TDR prevalence in Peru ranged from 1.0%–4.7% as last reported before 2012.

Methods used We obtained HIV sequence data from 3 parent studies conducted in 2013–2017 of ART naïve cisgender men who have sex with men (cis-MSM; $n=332$) and transgender women (TW; $n=144$) in Lima, Peru. Consensus gene sequences of HIV *pol* were interrogated for TDR using the Stanford HIVdb and scored for resistance to NRTIs and NNRTIs. We calculated binomial proportions and confidence intervals; χ^2

and Fisher's exact tests or generalized linear models examined possible predictors of TDR.

Summary of results Eighty (16.8%) of 476 individuals had TDR (95% CI: 13.6, 20.5). Twenty-two unique base changes totaling 94 mutations were present. Mutations conferring resistance to NNRTIs represented 88% of total TDR, and prevalence of a singular mutation (15.1%) was more common than 2+ (1.7%) mutations. TDR conferring high-level resistance to any ART was found in 44 (9.2%) individuals (95% CI: 6.8, 12.2). Cis-MSM were not more likely than TW to have acquired TDR (16.9% vs 16.7%, $p=1.00$). Year of diagnosis, age, diagnosis as incident or prevalent infection, or residence district were likewise not associated with risk of TDR.

Conclusions TDR prevalence within these cohorts was nearly 4-fold the highest previously reported prevalence in any population in Peru. Over half of observed TDR conferred high level resistance to first-line ART, and was largely to NNRTIs. Our findings support the WHO recommendation to consider integrase strand transfer inhibitors in first-line regimens, since empiric use of NNRTIs may fail. This study also represents the first differentiated evaluation of TDR in cis-MSM vs TW in Peru and demonstrates that although TW are at higher risk of HIV acquisition, they are at similar risk of transmitted resistance.

48 SCREENING FOR HUMAN IMMUNODEFICIENCY VIRUS AND HEPATITIS C IN SAN BERNARDINO COUNTY

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10.1136/jim-2018-000939.48

Purpose of study Currently, 15% infected with HIV and 50% infected with HCV are unaware of diagnoses. This is an important health concern because of implications for patient health and health of those at risk to be infected. This program is designed to assess if screening patients that come to the emergency department in the San Bernardino community is an effective way to diagnose new patients and link them to proper medical care.

Methods used Starting in 02/2017, patients seen in the emergency department at Arrowhead Regional Medical Center were screened for both HIV and HCV. Patients were given the option to opt out of the testing. Demographic data including ethnicity, age, and sex for patients whose screening tests were positive was collected as well as relevant laboratory values.

Confirmatory tests were run for patients who were positive for their screening tests. Confirmatory test ran for HIV was the Geenius™ HIV 1/2 confirmatory assay, and confirmatory test for HCV was the HCV RNA and PCR test.

Patients who had positive confirmatory tests were called and notified of the result. Follow up care was scheduled at this time for their condition. At this point, patients were deidentified and given a unique identifier for further analysis.

Summary of results From 02/2017 to 06/2018 18,109 HIV tests were performed and 18,605 HCV antibody tests were performed. Of the HIV tests, 163 new patients were confirmed to be HIV positive and of these patients, 120 were linked to care (prevalence 0.9%). This prevalence is statistically higher ($p < 0.05$) than the estimated general prevalence of the United States (95% CI 0.4116% to 0.4259%). Of the HCV tests, 719 new patients were confirmed to have an active form of the disease, and 376 were linked to appropriate care (prevalence 3.86%). This value is significantly higher than the national average prevalence reported as 2%.

Conclusions Screening in the emergency department is an effective method for diagnosing and linking new patients to appropriate follow up care. Furthermore, our data shows this community is statistically higher than the national average for HIV and HCV infection. This suggests a possible need for further testing and additional care to prevent the spread of these infectious diseases in this area.

49

THE ELIMINATION OF CANCER HEALTH DISPARITIES: ACCELERATION OF HPV VACCINATIONS

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10.1136/jim-2018-000939.49

Purpose of study The human papillomavirus (HPV) is associated with cervical, head and neck cancers, affecting both females and males. About 99% of all cervical cancers are related to HPV; of these; about 70% are caused by HPV types 16 or 18. The recognition of the virus, specifically HPV Types 16 and 18 and their association with cervical cancer, first led to the development of HPV vaccines, Gardasil and Cervarix. Gardasil is available for use in both females and males aged 9 to 26 years old, while Cervarix is available for females aged 9 to 25 years old. In 2014, a third vaccine, Gardasil 9, was approved by the FDA for prevention against additional HPV types. Despite the availability of this preventative measure against cervical cancer, the rate of HPV vaccination in the United States remains lower than that of other industrialized nations. The purpose of this study is to elucidate mechanisms to help increase the HPV vaccination rate.

Methods used Through the quantitative examination of the data from the states with the lowest and highest vaccination

rates, using SPSS statistical analysis; we analyzed several factors involved with the low up-take of the vaccines.

Summary of results The results collected show that socioeconomic status, misconceptions about HPV, and misconceptions about the safety of the vaccines have been identified as possible obstacles to the effective uptake of HPV vaccinations: The proposals made by the President's Cancer Panel to accelerate the uptake of the vaccines included increasing coverage of the vaccines through government-sponsored programs and the Affordable Care Act; increasing accessibility to the vaccines through pharmacies, schools, and clinics; and disseminating more information on HPV to healthcare providers, parents, caregivers and patients.

Conclusions Allowing greater accessibility to the vaccines for all populations regardless of income, education level, and eliminating misconceptions of the vaccines would play a significant role in eliminating cancer health disparities.

50

PERSISTENT METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS BACTEREMIA, SUCCESSFULLY TREATED WITH CEFTAROLINE PLUS DAPTOMYCIN

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Introduction Persistent bacteremia with Methicillin-resistant *Staphylococcus aureus* (MRSA) could be fatal with propensity for metastatic infection. Combination of anti-MRSA antibiotics have been utilized as salvage therapy. We are presenting a case of persistent bacteremia sterilized with combination of daptomycin and ceftaroline.

Case report A 40-year-old Hispanic male with untreated Hepatitis C, T2DM, hypertension, and active injection drug use, presented in DKA with fever, rigors, back pain and progressively worsening bilateral lower extremity weakness. He was started on empiric vancomycin and piperacillin/tazobactam (pip/tazo). CT chest/abdomen/pelvis revealed numerous pulmonary nodules, likely pulmonary septic emboli, as well as abscesses in the right iliac fossa, and right gluteus. A transesophageal echocardiography (TEE) revealed probable tricuspid valve endocarditis with septal and anterior leaflet thickening.

Blood and urine cultures on admission grew MRSA, and pip/tazo was discontinued and rifampin started. MRSA bacteremia persisted despite various antibiotic combinations, including 9 days of vancomycin plus rifampin, 7 days of televancin plus rifampin, and 4 days of televancin plus nafcillin. Patient also underwent multiple procedures to achieve source control, include drainage of the right iliopsoas abscess, aspiration of the right sacroiliac (SI) joint, and incision and drainage of the right gluteal abscess. Intraoperative cultures grew MRSA. Cultures from SI joint grew *Parabacteroides distasonis* and *Bacteroides thetaiotaomicron*.

With persistently positive blood cultures at day 21 of admission, salvage therapy with daptomycin plus ceftazoline was started. Clearance of bacteremia was achieved 2 days after the start of combination daptomycin plus ceftaroline. All further blood cultures have shown no growth. Metronidazole was added for coverage of *P. distasonis* and *B. thetaiotaomicron*. This combination was continued for 6 weeks from the

first negative blood culture. Patient has been asymptomatic at follow up appointments.

Conclusion Clinicians should be aware of synergistic combination therapy in treatment of serious and persistent infections with MRSA with bacteremia.

Neonatology General I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

51 CLINICAL DETERIORATION DURING NEONATAL TRANSPORT

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10.1136/jim-2018-000939.51

Purpose of study Identify clinical factors and transport timing variables associated with risk of clinical deterioration during neonatal transport in California.

Methods used This study included infants born 2007–2016 who were transported before 7 days after birth and were part of the linked California Perinatal Quality Care Collaborative (CPQCC) and the California Perinatal Transport System (CPeTS). The Canadian Transport Risk Index of Physiologic Stability (TRIPS) score is a physiology-based assessment used as a marker of stability during transport. Clinical deterioration (CD) was defined as an increase in TRIPS score during transport. Infants who experienced CD were compared to those who remained stable or improved. Log binomial regression estimated risk ratios and 95% confidence intervals for the association between covariates and the outcome.

Summary of results From 2007–2016, 47 794 infants were transported before 7 days after birth. 14 722 (30.8%) had CD. Early gestational age (GA) was associated with increased risk of CD with the highest risk at the earliest GA, RR 1.71 (95% CI 1.47–1.99) for ≤ 23 weeks, 1.61 (1.51–1.71) for 24–27 weeks, 1.31 (1.24–1.38) for 28–31 weeks compared to ≥ 37 weeks. This pattern was similar for birthweight. Other clinical variables associated with increased risk of CD were birth defects and delivery room resuscitation. Longer total transport times (time from referral call to arrival at accepting hospital) were also associated with increased risk of CD, RR 1.27 (1.17–1.38) for transports ≥ 6 hours compared to those < 2 hours. However, the main component of the transport process that was associated with increased risk was the time required for evaluation by the transport team, RR 1.42 (1.35–1.50) for evaluation times ≥ 2 hours compared to those < 1 hour.

Conclusions In a large and diverse population of infants undergoing transport in California, prematurity, birth defects, and delivery room resuscitation are associated with increased risk of CD. The risk of CD also appears to be associated with longer evaluation periods by the transport team, suggesting that higher risk infants likely require more time for stabilization prior to leaving a referring hospital. The study findings suggest that mothers who are anticipated to have high-risk deliveries should be transferred directly to more specialized centers when feasible to avoid any delay in care for those neonates.

52 THE EFFECT OF CONCOMITANT PRENATAL MATERNAL MARIJUANA USE ON HEALTH OUTCOMES FOR OPIOID EXPOSED NEWBORNS IN MASSACHUSETTS, 2002–2010

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10.1136/jim-2018-000939.52

Purpose of study To determine if health outcomes among opioid exposed neonates vary by concomitant maternal marijuana (MJ) use during pregnancy.

Methods used We analyzed 2 linked statewide datasets from 2000 to 2010: the Massachusetts (MA) Pregnancy to Early Life Longitudinal data system, which links birth certificates and fetal death records to maternal and infant delivery hospital discharge records; and the MA Bureau of Substance Addiction Services, which contains treatment records for reproductive-aged women in publicly-funded MA substance abuse treatment centers. General estimating equations determined the association between maternal MJ use and neonatal outcomes on opioid exposed neonates, controlling for maternal and infant characteristics.

Summary of results Of 4584 infants exposed to opioids during pregnancy, 430 were also exposed to MJ. In the MJ exposed group, mothers were more likely to be younger than 25, non-Hispanic Black race, unmarried, smokers, and have chronic medical and psychiatric conditions. In the adjusted analyses, neonates exposed to both opioids and MJ were more likely to be preterm (AOR 1.72; 95% CI 1.33–2.22) and have low birthweight (AOR 1.46; 95% CI 1.13–1.87) compared to opioid exposed neonates without MJ exposure. Infants exposed to both opioids and MJ had a decreased incidence of NAS (AOR 0.67; 95% CI 0.54–0.83) and prolonged hospital stay (AOR 0.66; 95% CI 0.53–0.83). There was no difference in the risk of cardiac, respiratory, neurologic, infectious, hematologic, gastrointestinal and feeding-related adverse outcomes.

Conclusions Maternal opioid plus MJ use during pregnancy was associated with increased preterm birth and low birthweight infants. Newborns exposed to both opioids and MJ had decreased NAS and prolonged hospital stay compared to infants exposed to opioids without MJ. These results should be interpreted with caution, as the long term neurologic effects of prenatal MJ exposure are unclear. Further research is needed to elucidate the biologic mechanisms that underlie the relationship between MJ and opioid exposure with infant health outcomes, and should account for dose and timing of substance exposure, the effect of polypharmacy, and include long-term developmental outcomes.

53 CORD BLOOD MAGNESIUM LEVELS AND NON-NEUROLOGIC OUTCOMES IN NEONATES LESS THAN 27 WEEKS GESTATIONAL AGE

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10.1136/jim-2018-000939.53

Purpose of study Randomized trials show decreased cerebral palsy (CP) and improved neurodevelopmental outcomes (NDO) with intrapartum MgSO₄ in preterm infants, and is standard of care for women at risk of delivery < 32 weeks. Concerns for an increased risk of necrotizing enterocolitis (NEC), especially in neonates < 27 weeks, have been raised (Kamaryar M et al. *AmJPerinatol* 2016). It is unclear if this is

Abstract 53 Table 1 Primary outcomes by initial cord magnesium sulfate levels

Characteristics (n=236)	MgSO ₄ ≤1.7 (%)	1.7	MgSO ₄ >2.5 (%)	p-value
NEC stage II/III	8/95 (8)	8/66 (12)	6/75 (8)	0.97
Death by 15 months*	18/88 (21)	11/63 (18)	15/75 (20)	0.92
Bayley-II physical<70**	20/95 (21)	21/66 (32)	19/75 (25)	0.66
Bayley-II mental<70†	23/95 (24)	11/66 (17)	14/75 (19)	0.69
Moderate-severe CP*	6/88 (7)	6/63 (10)	5/75 (7)	0.99
Death or Bayley-II<70*	24/88 (27)	17/63 (27)	20/75 (27)	0.93

*n=226 **n=172 †n=164

dose-dependent. We hypothesized that elevated cord blood Mg levels are associated with increased risk of NEC and/or death but improved NDO at 24 months among survivors born at <27 weeks with antenatal MgSO₄ exposure.

Methods used We performed a secondary analysis of neonates born at <27 weeks that participated in the BEAM Trial; a prospective, multicenter, randomized trial of antenatal MgSO₄ to women at risk of birth <32 weeks gestation to prevent death and cerebral palsy. The relationship between cord blood Mg level and development of Bell criteria stage II/III NEC was evaluated, as well as Bayley Scale of Infant Development-II at 24 months and/or death.

Summary of results 484 neonates (19.8% of original population) were included in the 23w4d to 26w6d cohort, with 236 initial cord blood Mg levels (48.8% of <27 weeks). The incidence of severe NEC, death by age 15 months or neurodevelopmental impairment was not associated with Mg levels. Hypotension during resuscitation was associated with Mg >2.5 mg/dL compared to a level <1.8 mg/dL (11% vs 3%; p=0.044). Other neonatal morbidities were not associated with Mg level.

Conclusions Severe NEC was not associated with cord blood Mg among infants born at <27 weeks, nor was survival at 15 months and NDO at 24 months. Risks versus benefits of antenatal MgSO₄ therapy must be judiciously weighed considering the potential risk of neonatal hypotension at resuscitation with higher levels.

54 A CASE SERIES ASSESSING NEONATAL CSF FLOWS IN HYDROCEPHALUS VERSUS CONTROL PATIENTS

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10.1136/jim-2018-000939.54

Purpose of study Management of neonatal CSF disorders including post-hemorrhagic hydrocephalus (nPHH) may benefit from MRI techniques that assess CSF flow such as TimeSTAMP and PC-MRI (2018 Borzage et al). Pediatric studies have reported CSF velocity estimates via PC-MRI of 5.28 ±2.88 cm/s in a study of 21 infants 1–12 months old (2016, Ozturk et. al); however these values may not apply to neonates.

We present a case series where we visualized and quantified the peak CSF velocity and flow rates in neonates with communicating and non-communicating hydrocephalus compared to neonates without CSF abnormalities.

Methods used Using a Phillips 3T scanner, we acquired images in patients and controls (7d–10 mo). Regions were imaged with TimeSTAMP and PC-MRI and included the cerebral aqueduct, interventricular foramen and foramen of Magendie.

With TimeSTAMP, we assessed communication of CSF flow and measured the distance of flow during the 2500 ms delay.

For PC-MRI, retrospective cardiac synchronization with pulse-oximetry was used with slices placed perpendicular to CSF flow. We acquired 20 phases with variable encoding velocities (VENC). We computed peak velocity and tested static parenchyma to determine the error in our measurements.

Summary of results Four nPHH patients and four controls were recruited. The nPHH patients (17 d–10 mo) had imaging performed either pre- or post-surgical intervention. The control patients' (7d–42d) indications for imaging included facial weakness, HIE, arachnoid cyst and poor feeding. The peak velocities at the cerebral aqueduct were 0.6 IQR (0.3, 0.8) cm/s via TimeSTAMP PC-MRI and 0.2 (0.2, 0.4) cm/s via PC-MRI with measurement error of 0.4 cm/s.

Conclusions In our case series, we found that neonatal CSF flows were 90% slower than values previously reported in infants. Neonatal CSF velocities may be too low to reliably measure with current PC-MRI and we will test the techniques via phantom studies to understand the limitations of PC-MRI and TimeSTAMP in low flow settings. We noted a lack of inter-ventricular CSF flow in some nPHH patients via TimeSTAMP, but not in control patients indicating potential clinical importance of this work.

55 OUTCOMES OF INFANTS SUSCEPTIBLE TO HYPOXIC ISCHEMIC ENCEPHALOPATHY WHO DID NOT RECEIVE THERAPEUTIC HYPOTHERMIA

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10.1136/jim-2018-000939.55

Purpose of study There are neonates with evidence of hypoxic ischemia (HI) who are judged not or only with mild encephalopathy and thus are not cooled, yet suffer consequences of cerebral HI. The goal of this study is to better characterize outcomes of infants susceptible to hypoxic ischemic encephalopathy (HIE) who did not receive therapeutic hypothermia (TH).

Methods used This retrospective study examined almost exclusively inborn infants at a level III neonatal intensive care unit (NICU) between 2012–2015. Targeted international classification of disease codes were used to identify infants at risk of HIE who did not receive TH. Exclusion criteria included gestational age <35 weeks, birth weight <1800 g, presence of known chromosomal abnormality, major congenital anomaly, or any infant that underwent TH.

Summary of results 26 infants met inclusion criteria. Outcomes were defined by at least one of the following: 1) brain magnetic resonance imaging (MRI) within ten days of birth suggestive of HIE 2) electroencephalogram (EEG) showing seizures 3) abnormal neurologic discharge examination or 4) adverse neurodevelopmental (ND) outcome following NICU discharge. 18 infants had no evidence of impairment. 8 infants had evidence of impairment as defined by an abnormality in at least one of the four above-mentioned categories.

Abstract 55 Table 1 Characteristics of 8/26 infants with at least 1 abnormal primary outcome

Infant	MRI DOL	MRI NICHD-NRN Score	EEG with Seizures	Abnormal Discharge Exam	Adverse ND Outcome*
1	6	1a	-	No	Autism
2	6	1a	-	No	No
3	7	2a	-	Yes	No
4	-	-	-	Yes	No
5	4	1a	Yes	No	No
6	3	1a	Yes	Yes	No
7	4	1b	Yes	Yes	Developmental Delay
8	10	1a	-	No	No

*For infants in 'No' category, ND outcomes either 1) negative or 2) not available

Conclusions 31% of infants had evidence of an abnormal primary outcome. Our results add to the growing literature that suggests infants with evidence of HI but no or mild encephalopathy might benefit from TH; further clinical trials will be needed to investigate these findings.

56 ASSOCIATION OF BRONCHOPULMONARY DYSPLASIA AND WHITE MATTER INJURY IN PRETERM INFANTS

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10.1136/jim-2018-000939.56

Purpose of study Previous studies have shown that bronchopulmonary dysplasia (BPD) is associated with white matter abnormalities in preterm infants. We aimed to evaluate the relationship between BPD, cumulative oxygen (CSO) and cumulative mean airway pressure (CMAP) exposure over the first 28d of life, and white matter injury (WMI) on magnetic resonance imaging (MRI).

Methods used We studied a retrospective cohort of preterm infants <32 weeks gestational age (GA) examined with 3T-MRI at 34–44 wks postmenstrual age (PMA). A blinded pediatric neuroradiologist scored WMI severity on T1-weighted MRI images per published criteria (Miller SP, 2003). We classified BPD by a consensus, severity-based definition, which was then grouped into none-mild (supplemental O₂ <28 d or supplemental O₂ ≥28 d but room air at 36 wks PMA) and moderate-severe (supplemental O₂ ≥28 d and supplemental O₂ or positive pressure ventilation at 36 wks PMA). CSO and CMAP were averaged for 3 daily time points and summed over the first 28d. ROC curves were used to evaluate the relationship between BPD, CSO, CMAP, and WMI.

Summary of results Among 72 infants, 25 (34.7%) had moderate-severe BPD. Infants with moderate-severe BPD had lower GA (26.9±2.1 wks vs. 29.3±1.7 wks, p<0.00001) and higher rates of PDA (72.0% vs. 38.3%, p=0.006) and NEC (12.0% vs. 0%, p=0.02). BPD was associated with higher CSO and CMAP (both p<0.001). BPD was associated with WMI (RR 5.64, 95% CI 1.23 to 25.92, p=0.01) with a trend toward higher CSO (p=0.059) and CMAP (p=0.052) in infants with WMI. Unadjusted area under the curve

(AUC) for prediction of WMI was 0.73 (95% CI 0.56–0.90) for BPD, 0.70 (95% CI 0.49–0.91) for CSO, and 0.71 (95% CI 0.51–0.91) for CMAP. AUC for a model including BPD, CSO, and MAP was 0.76 (95% CI 0.56–0.96). There was no significant difference in the AUC between all models (p=0.5).

Conclusions CSO and CMAP in the first 28d may influence risk of WMI in preterm infants. BPD at 36 wks PMA was not significantly more discriminatory and accounting with BPD for these early measures did not improve prediction of WMI.

57 LONG ACTING OPIOIDS AND ANTIEPILEPTIC MEDICATIONS PROLONG INPATIENT LENGTH OF STAY AND PHARMACOLOGIC TREATMENT OF INFANTS WITH NEONATAL OPIOID WITHDRAWAL SYNDROME (NOWS)

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10.1136/jim-2018-000939.57

Purpose of study Infants with opioid exposure commonly have polysubstance exposure. Our objective was to evaluate the impact of these exposures on neonatal withdrawal treatment-related outcomes.

Methods used We conducted a retrospective chart review of infants who received NWI scoring between 4/2015– 5/2018 in our NICU or newborn nursery. Outcome variables included length of stay (LOS), length of treatment (LOT), and need for pharmacologic treatment including adjunctive medications. A univariate analysis of individual exposure (short or long acting opioids, nicotine, stimulants, sedatives, cannabinoids, antidepressants, antiepileptics, antipsychotics) on outcome variables was tested using the Wilcoxon or Chi-Square test. Multivariable regression models were used to estimate the same outcome variables adjusting for breastfeeding at discharge, gestational age, SGA, and other medical circumstances delaying discharge. Significance was declared at p<0.05.

Summary of results Of the 248 infants with substance exposure who received NWI scoring, 81% had polysubstance exposure. Median LOS for all exposed infants was 9 days, with 37% requiring pharmacological treatment. Median LOT was 15 days. We detected no difference in all outcome variables between opioids alone and opioids+additional substances. When analyzed by individual exposure, the univariate analysis revealed long acting opioid (LAO) exposure increased the need for pharmacological treatment (p=0.012) including adjunctive medications (p=0.013), whereas antiepileptics increased LOS (p=0.014) and need for pharmacologic treatment (p=0.027). Adjusting for confounding variables, LAO additionally predicted an increased LOT by 29% (p=0.018), whereas antiepileptics additionally predicted an increased LOT by 39% (p=0.015). Short acting opioids decreased LOT by 33% and need for adjunctive medication by 71% (p<0.005).

Conclusions LAO and antiepileptics greatly prolonged hospitalization and need for pharmacological therapy. Specific knowledge of polysubstance exposures may help obstetricians and neonatal providers improve expectant management of polysubstance exposed newborns.

58

PRETERM INFANTS' CARDIAC RESPONSE TO MATERNAL VOICEC Gao, HM Feldman, KE Travis. *Stanford, CA*

10.1136/jim-2018-000939.58

Purpose of study *In utero* exposure to maternal speech benefits brain and language development. Heart rate increases in response to maternal speech in fetuses and term born infants. Preterm infants mature in the hospital nursery, an environment often deprived of maternal speech. Studies have yet to characterize how immediate cardiac activity varies in response to maternal speech in preterm infants. Here, we measure preterm infants' cardiac responses to mother's speech and identify factors that explain variability in these responses.

Methods used Preterm infants (n=24) were born 24–32 weeks gestational age (mean GA=29.70±2.08 weeks and mean postmenstrual age (PMA) at testing=33.73±0.72 weeks). Bedside monitors recorded each infant's heart rate before, during and after exposure to an audio recording of the infant's mother reading *Paddington Bear* in her native language. Cardiac response was defined as average heart rate in the first 2 min after speech onset, minus the 2 min before onset. T-tests and Pearson correlations explored if state, GA, PMA at testing, and maternal education were related to cardiac response.

Abstract 58 Figure 1 Mean difference in cardiac response at onset vs maternal education

Abstract 59 Figure 1 Tasks observed correctly

Summary of results As a group, heart rate increased in response to mother's speech among awake but not sleeping infants. Individual variability in cardiac responses was significantly associated with maternal education ($r=0.61$, $p<0.05$) but not with GA or PMA at testing ($p>0.05$).

Conclusions Heart rate in awake preterm infants responds to maternal speech. Findings suggested maternal education contributed to variability in infants' cardiac responses. Future analyses will explore why maternal education affects heart rate and how repeated maternal speech exposure affects variability in cardiac responses.

59

IMPACT OF REPEAT SIMULATED NEONATAL RESUSCITATION TRAINING ON NRP ALGORITHM ADHERENCE IN A COMMUNITY HOSPITALR Mamidi, T Huynh, W Lapcharoensap. *Oregon Health and Science University, Portland, OR*

10.1136/jim-2018-000939.59

Purpose of study To investigate the improvement of NRP algorithm adherence after repeat simulated neonatal resuscitation training with nurses, respiratory therapists, and licensed independent practitioners in a community hospital.

Methods used 62 non-standardized audiovisual recordings of simulated neonatal resuscitation were obtained between April 2017 and February 2018. Videos were analyzed for adherence to the NRP algorithm and scored using a classification tool based on the validated NRP Megacode Checklist. Tasks not visualized were not included in the analysis.

Summary of results Over time, there was a trend towards improvement in tasks performed correctly and concurrent reduction of omission errors. These tasks include: equipment checks, evaluation of heart rate and respirations, assessment with positive pressure ventilation (PPV), assessment within the first 5–10 breaths of PPV, corrective ventilation steps (MR SOPA), and 30 s of PPV prior to chest compressions (figures 1 and 2). Performance decreased in all categories between April 2017 and July 2017, after one simulated resuscitation.

Conclusions Repeat simulated neonatal resuscitation exercises with community hospital trainees is associated with increased tasks observed correctly and decreased errors of omission of the NRP algorithm. This suggests repeat

Abstract 59 Figure 2 Errors of omission

resuscitation training can improve adherence to the NRP algorithm. Performance decreased after a single simulated resuscitation, supporting that retention of skills is poor without repetition, consistent with previously published studies. Suggestions for future research include measuring real neonatal resuscitation outcomes in community hospitals that underwent such training.

Neonatology Pulmonary I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

60

PREVENTION OF PERINATAL NICOTINE-INDUCED BONE MARROW MESENCHYMAL STEM CELL DIFFERENTIATION TO MYOFIBROBLAST: A POSSIBLE APPROACH TO PREVENT CHRONIC LUNG DISEASE

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10.1136/jim-2018-000939.60

Purpose of study Alveolar lipofibroblasts (LIFs) are critical for lung homeostasis and injury/repair. Perinatal nicotine exposure drives the differentiation of LIFs to myofibroblasts (MYFs). Under appropriate conditions, bone marrow-derived mesenchymal stem cells (BMSCs) can differentiate into a wide variety of cell lineages, and are important players in lung injury repair. However, whether BMSCs can be preferentially driven to a lipofibroblastic phenotype is not known. We hypothesized that perinatal nicotine exposure would block offspring BMSCs lipogenic differentiation, driving these cells towards a MYF phenotype. Since PPAR γ agonists can prevent nicotine-induced MYF differentiation of LIFs, we further hypothesized that modulation of PPAR γ expression would inhibit nicotine's myogenic effect on BMSCs.

Methods used Pregnant Sprague Dawley rat dams received either placebo, nicotine (1 mg/kg body weight (BW)), or nicotine +the potent PPAR γ agonist rosiglitazone (RGZ) (3 mg/kg BW), once daily from embryonic day 6 until postnatal day 21, when pups were sacrificed. At postnatal day 21,

BMSCs were isolated and characterized morphologically, molecularly, and functionally for their lipogenic and myogenic potentials.

Summary of results Perinatal nicotine exposure resulted in decreased oil red O staining, triolein uptake, expression of PPAR γ and its down target gene ADRP by BMSCs, but enhanced α SMA and fibronectin expression, and activated Wnt signaling in mRNA and protein levels, all features indicative of their inhibited lipogenic, but enhanced myogenic potential. Importantly, concomitant treatment with RGZ virtually blocked all of these nicotine-induced morphologic, molecular, and functional changes.

Conclusions Based on these data, we conclude that BMSCs can be directionally induced to differentiate into the lipofibroblastic phenotype, and PPAR γ agonists can effectively block perinatal nicotine-induced MYF transdifferentiation, suggesting a possible molecular therapeutic approach to augment BMSC's lung injury/repair potential.

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61

CELLULAR RESPONSES TO HYPEROXIA IN THE DEVELOPING LUNG

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10.1136/jim-2018-000939.61

Purpose of study Exposure of the immature lung to high levels of oxygen (hyperoxia) is an important factor contributing to bronchopulmonary dysplasia (BPD). While supplemental oxygen is life-saving, it can induce inflammation and lead to permanent disruption of normal lung development. However, the immune mechanisms contributing to oxygen-induced injury are incompletely understood. The purpose of this study is to determine the changes in cellular composition of the lung after neonatal hyperoxia exposure with focus on myeloid cells.

Methods used Newborn C57BL/6 mice were exposed to 75% oxygen for 2 weeks. Lungs were harvested immediately after the hyperoxia exposure or at 2 months of age following recovery in room air. To assess myeloid cell subsets, lungs were homogenized and analyzed by multicolor flow cytometry. We identified alveolar macrophages (AM), interstitial macrophages (IM), Ly6clow patrolling monocytes (pMo), Ly6chigh

inflammatory monocytes (iMo) and neutrophils. Data was analyzed using FloJo.

Summary of results Exposure of the developing lung to hyperoxia resulted in significant changes in the composition of the myeloid cell population. After 2 weeks of hyperoxia we found a decrease in the proportion of AM and an increase of neutrophils and iMo. The proportion of pMo did not change. When analyzing the lung of adult mice previously exposed to hyperoxia in the neonatal period we observed a moderate increase in the proportion of AM, while the other analyzed myeloid cell subsets were comparable to normoxic controls.

Conclusions Hyperoxia induces an inflammatory response in the developing lung with differential effects on subsets of myeloid cells. This is initially characterized by a decrease in the proportion of AM accompanied by neutrophilic and monocytic infiltration of the lung. Contrary to the acute phase, adult mice previously exposed to hyperoxia in the neonatal period had an increase in the proportion of AM. These results reveal lasting changes in cellular composition of the lung myeloid compartment after neonatal hyperoxia exposure with important implications for the design of targeted cell therapy.

62 HUMAN PRETERM UMBILICAL CORD MESENCHYMAL STEM CELLS FOR NEONATAL CHRONIC LUNG DISEASE

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10.1136/jim-2018-000939.62

Purpose of study Neonatal chronic lung disease, also known as, Bronchopulmonary dysplasia (BPD), is a debilitating disease of preterm infants with high morbidity and mortality. Mesenchymal stem cells (MSCs) have shown therapeutic benefits in animal models of lung injury and repair.

Human preterm MSCs will have superior therapeutic efficacy in protection of lung injury in murine BPD. Our aims are: (1) To generate commercial grade human preterm MSCs and their cell free conditioned media; and (2) Determine *in vitro* properties and *in vivo* therapeutic efficacy of human preterm MSCs.

Methods used Human umbilical cord Wharton's jelly MSCs from preterm infants (Gestational age (GA) <28 weeks) and term infants (GA >37 weeks) were isolated and cultured according to our modified protocols and *in vitro* growth, differentiation, and secreted factors were analyzed utilizing duplication time, Western immunoblot, and proteomics analysis. *In vivo* therapeutic potential assessed in hyperoxia exposed murine BPD model measuring lung inflammation, lung injury, and pulmonary hypertension; and was compared to murine pups kept in a normoxic environment.

Summary of results in Human preterm MSCs had shorter duplication and differentiation time as well as a higher concentration of cardiopulmonary protective secreted factors compared to term MSCs. Intravenous administration of preterm MSC conditioned media protected from lung inflammation, alveolar loss, and pulmonary hypertension compared with term MSC conditioned media; and was comparable to pups kept in normoxic environment.

Conclusions Human preterm umbilical cord MSC conditioned media has superior cardiopulmonary protection in murine BPD and can serve as a therapeutic candidate for BPD.

63 L-CITRULLINE INDUCES ARGINASE EXPRESSION AND ACTIVITY IN HYPOXIC PIGLET PULMONARY ARTERIAL ENDOTHELIAL CELLS (PAEC)

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10.1136/jim-2018-000939.63

Purpose of study Impaired nitric oxide (NO) signalling contributes to chronic hypoxia-induced pulmonary hypertension (PH). L-arginine is the substrate for the NO producing enzyme, nitric oxide synthase (NOS), as well as for the enzymes arginase I and II, which can contribute to vascular remodelling. Due to its role as an arginine-NO precursor, L-citrulline has been identified as a potential therapy for chronic hypoxia-induced PH. Arginase expression and activity are regulated by L-arginine but the impact of L-citrulline on the induction of arginase expression and activity is unclear. We tested the hypothesis that supplemental L-citrulline will increase arginase expression and activity in piglet PAEC cultured under hypoxic conditions. **Methods used** Piglet PAEC were cultured under hypoxic conditions with different concentrations of L-citrulline (0.1–3.0 mM). Arginase I and II expression were measured by western blot. Arginase activity was measured with an arginase activity assay kit. NO concentrations were quantified by chemiluminescence.

Summary of results Arginase I expression was similar for PAECs cultured under hypoxic conditions in the absence and presence of all concentrations of L-citrulline (n=7). Arginase II expression (n=6) and levels of arginase activity (n=11) were greater (p<0.05) for piglet PAECs cultured in concentrations of L-citrulline exceeding 0.5 mM compared to PAECs cultured in the absence of L-citrulline. NO concentrations were greater (n=14, p<0.05) for all concentrations of L-citrulline supplemented hypoxic PAECs compared to those cultured without L-citrulline.

Conclusions Supplemental L-citrulline increases NO production in hypoxic PAEC. When a threshold concentration is exceeded, L-citrulline increases arginase II expression and arginase activity in hypoxic PAEC, which has the potential to enhance vascular remodelling. These findings suggest that despite the ability to increase NO production, there may be a dose that should not be exceeded when evaluating the efficacy of L-citrulline to treat hypoxia-induced PH.

Neonatology Pulmonary II

Concurrent Session

3:15 PM

Thursday, January 24, 2019

64 MASK RESUSCITATION AND CONTINUING NON-INVASIVE RESPIRATORY SUPPORT LEADS TO BETTER ALVEOLAR FORMATION COMPARED TO MECHANICAL VENTILATION (MV) RESUSCITATION AND CONTINUING MV OF PRETERM LAMBS

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Purpose of study Chronic lung disease of prematurity is histopathologically characterized by alveolar simplification. We

showed, using our preterm lamb model, that 3d of mechanical ventilation (MV) leads to thicker and less secondary septated distal airspace walls, both being indices of alveolar simplification, compared to preterm lambs supported by 3d of non-invasive respiratory support. An unknown is whether preterm lambs that are not endotracheally intubated, and therefore not supported by MV, will have improved architectural formation of alveoli. Therefore, the aim of this study was to develop a preterm lamb model in which lambs were resuscitated non-invasively by facial mask.

Methods used Preterm lambs (delivered by Cesarean-section at 128d gestation; term ~150 d; equivalent to ~28 w gestation in humans) were either (1) intubated at birth, resuscitated by MV, and continued on MV respiratory support ('MV'; n=4; control group) for 3d or (2) resuscitated by facial mask and continued with non-invasive respiratory support ('Mask'; n=5) for 3d. The mask group was supported non-invasively by nasal cannula. All lambs were given surfactant prior to delivery and caffeine citrate after delivery. Both groups received two sustained lung inflations (35 s). Quantitative histology was used to measure indices of alveolar formation.

Summary of results MV-managed preterm lambs had significantly thicker distal airspace walls ($2.5 \pm 0.2 \mu\text{m}$) compared to the mask-managed preterm lambs ($2.0 \pm 0.1 \mu\text{m}$; $p < 0.05$ by unpaired t-test). Volume density of secondary septa was not significantly different in the MV group ($4.8\% \pm 1.6\%$; $p = 0.6$) compared to the mask group ($8.3\% \pm 1.8\%$) of preterm lambs.

Conclusions Mask resuscitation and continuing non-invasive respiratory support leads to better alveolar formation compared to MV resuscitation and continuing MV of preterm lambs. Supported by R01 HL110002 and Div of Neonatology.

65 BALANCE BETWEEN PROLIFERATION AND APOPTOSIS OF INTERSTITIAL CELLS REMAINS CONSTANT IN THE LUNG OF FORMER PRETERM LAMBS, REGARDLESS OF THE MODE OF RESPIRATORY SUPPORT AFTER PRETERM BIRTH OF PRETERM LAMBS

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Purpose of study Alveolar simplification is the characteristic histopathology for bronchopulmonary dysplasia. We showed, using our chronically ventilated preterm lamb model, that days or weeks of mechanical ventilation (MV) leads to thicker distal airspace walls, an index of alveolar simplification, compared to non-invasive respiratory support. We also showed that the increased thickness is related to disproportionate proliferation of mesenchymal cells compared to their apoptosis. Our new former preterm lamb studies indicate that their lungs have alveolar walls that are persistently thicker at 5 months corrected postnatal age (cPNA) compared to unventilated term lambs matched for PNA. An unknown is whether the former preterm lambs have persistently disrupted proliferation versus apoptosis of alveolar wall interstitial (mesenchymal) cells.

Methods used Preterm lambs (delivered by Cesarean-section at 128d gestation; term ~150 d; equivalent to ~28 w gestation in humans) were either (1) intubated at birth, resuscitated by MV, and continued on MV respiratory support for 6d (MV; n=6) or (2) resuscitated non-invasively by facial mask and continued with nasal CPAP for 6d (Mask; n=4). Both groups were weaned from all respiratory support and lived for ~6 months (m; former preterm (FPT) lambs; ~5 m corrected postnatal age; ~6 y human). Term lambs were not ventilated and lived 5 m. Quantitative immunohistochemistry was used to quantify proliferation and apoptosis.

Summary of results FPT lambs managed by MV or mask during their first week of postnatal life had comparable proliferation index (0.87 ± 0.49 and 0.97 ± 0.18 , respectively; mean $\pm$ SD; not different) and apoptotic index (apoptotic interstitial cells/total epithelial cells; 0.85 ± 0.70 and 0.60 ± 0.25 , respectively; not different). These indices were comparable to those for term unventilated lambs (0.64 ± 0.41 for apoptotic index and 0.99 ± 0.51 for proliferation index).

Conclusions Our results suggest that the persistently thicker alveolar walls of FPT lambs that had been resuscitated and subsequently supported by MV may be related to sustained numbers of mesenchymal cells in airspace walls earlier in their life. Supported by R01 HL110002 and Division of Neonatology.

66 DURATION OF MECHANICAL VENTILATION EARLY IN LIFE ALTERS LUNG MECHANICS AND ALVEOLAR STRUCTURE LATER IN LIFE

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Purpose of study This study evaluates lung mechanics, airway reactivity, alveolar simplification, and airway smooth muscle (ASM) thickness in former preterm lambs that had one of 3 modes of respiratory support during the first days of postnatal life.

Methods used Preterm lambs (128 d; term ~150 d) were resuscitated and supported by 1) mask, 2) ~3 hour mechanical ventilation (MV) and subsequent non-invasive nasal support, or 3) ~6 d MV before weaning from all respiratory support. They lived for ~6 months (m; former preterm (FPT) lambs; ~5 m corrected postnatal age; ~6 y human). Term lambs were not ventilated and lived 5 m. Lung mechanics were measured by forced oscillation technique (FOT) and airway reactivity by changes in FOT parameters after methacholine (MCh) challenge.

Summary of results Increased duration of MV led to significantly altered indices of lung mechanics and airway reactivity (figure 1), and alveolar architecture and ASM thickness (figure 2).

Conclusions Longer duration of MV leads to persistent functional and structural changes in the lung of FPT lambs and may set-up the FPT lambs for adverse reactions to subsequent infection or inflammation. R01 HL110002 and Div of Neo.

Abstract 66 Figure 1

Abstract 66 Figure 2

Surgery I

Concurrent Session

12:45 PM

Thursday, January 24, 2019

67 USE OF THE NOVEL SURPAS TOOL TO ASSIST INFORMED CONSENT IMPROVES PATIENT SATISFACTION AND SURGEON EFFICIENCY

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10.1136/jim-2018-000939.67

Purpose of study The purpose of this study was to determine the efficacy of use of the Surgical Risk Preoperative Assessment System (SURPAS) tool in assisting in the surgical informed consent process when compared to different surgeons' routine consent process.

Methods used Patient's perception of the informed consent process was surveyed. We employed the survey in two cohorts of patients; the first was patients who were consented using the 'routine' process employed in each of 10 surgeon's clinics. The same 10 surgeons were then taught to use SURPAS and employed it for guiding the informed consent process on a subsequent cohort of consecutive patients. The SURPAS tool is an individualized risk prediction tool incorporated into the EHR with visual displays of common adverse surgical outcomes. Patients were surveyed after completion of the 'routine' or SURPAS-guided consent process to evaluate their perception of

the informed consent process. Patient responses were compared using Fisher's exact test and the Cochran-Mantel-Haenszel test which accounts for patients within surgeons.

Summary of results Patients' ages, gender, race-ethnicity, and complexity of surgery were similar in the two cohorts ($p \geq 0.10$). Of 169 patients, 100 underwent the 'routine' consent process (RTNE pts), and 69 underwent SURPAS-guided consent (SRPS pts). 100% of SRPS pts reported surgeons spent enough time discussing risks, vs. 72% of RTNE pts ($p < 0.0001$). Mean time spent on the consent process as estimated by patients was 28 mins for RTNE pts vs. 11 mins for SRPS pts ($p < 0.0001$). 100% of SRPS pts were satisfied or very satisfied with the risk discussion vs. 88% of RTNE pts ($p < 0.0001$). 81.2% of SRPS pts reported the risk discussion made them more comfortable to have surgery and 98.5% reported somewhat or greatly decreased anxiety vs. 19% and 20% of RTNE pts, respectively (both comparisons: $p < 0.0001$).

Conclusions The SURPAS tool improved the informed consent process for patients compared to the 'routine' process: SURPAS provides preoperative surgical patients a level of comfort and understanding that current practice is unable to do. In addition, it achieves this in a more efficient manner, and increases patient satisfaction despite their perception that it requires less time for consent.

68 COMPARISON OF DIFFERENT FOOT PEDAL ILLUMINATION STRATEGIES AND THEIR EFFECT UPON SPEED AND ACCURACY OF ACTIVATION AND DARK ADAPTATION

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10.1136/jim-2018-000939.68

Purpose of study Endourologic procedures frequently employ foot pedal activation in a low-light intensity operating room (OR) environment. However, operating foot pedals in low-light may result in unintentional instrument activation and patient harm, while bright light may hinder dark adaptation during surgery. The purpose of this study is to compare speed and accuracy, dark adaptation, and surgeon preference for foot pedal operation under two types of pedal illumination, as well as in a dark and brightly lit OR.

Methods used During a simulated Percutaneous Nephrolithotomy (PCNL) procedure, the foot pedals for a c-arm, holmium laser, and ultrasonic lithotripter (USL) were randomized to 3 positions. 20 participants activated the pedals in a randomized order under 4 settings: dark OR with blacklight illumination, dark OR with glow stick illumination, dark OR only, and brightly lit OR only. Endpoints included time to pedal activation, number of attempted, incomplete, and incorrect pedal presses, dark adaptation, and surgeon preference. Analysis was performed using a Mann-Whitney U Test with $p < 0.05$ considered significant.

Summary of results Compared to no illumination, the glow stick (6.77 s vs. 8.47 s, $p < 0.001$) and blacklight illumination (5.34 s vs. 8.47 s, $p < 0.001$) were both associated with

decreased combined and individual pedal activation times ($p < 0.05$ for c-arm, laser, and USL). The blacklight system resulted in a significant decrease in attempted, incomplete, and incorrect pedal presses compared to a dark OR (0.30 vs. 3.45, $p < 0.001$; 1.25 vs. 7.75, $p < 0.001$; 0.35 vs. 1.25, $p = 0.035$, respectively), while being comparable to a brightly lit OR. Dark adaptation was significantly improved with blacklight illumination compared to a brightly lit OR ($p < 0.001$). Subjectively, 100% of participants preferred illuminated pedals for endourologic procedures compared to the dark OR, with 90% preferring the blacklight system.

Conclusions During a simulated PCNL, color-coded blacklight foot pedal illumination significantly improved the accuracy and efficiency of instrument activation compared to the conventional dark OR setting, while also maintaining dark adaptation for the surgeon.

69 DAILY POSTOPERATIVE SILDENAFIL DECREASES INFECTION IN A MOUSE MODEL OF PERIPROSTHETIC JOINT INFECTION

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10.1136/jim-2018-000939.69

Purpose of study Prosthetic Joint infections (PJI) remain a devastating problem in orthopaedic surgery. Recent work demonstrated that myeloid derived suppressor cells (MDSC) may play a role in blunting host immune response during *S. aureus* PJI. Sildenafil was shown to down-regulate MDSC in an *in vitro* model. We hypothesize sildenafil will decrease bacterial burden *in vivo* in an established mouse model of PJI.

Methods used Surgery was performed on 8 to 12 week-old C57BL/6 mice to place a titanium implant into the distal femur and inoculate each knee with bioluminescent *S. aureus* (1×10^3 [CFUs]). The treatment group received daily i.p. injections of sildenafil (20 mg/kg in 100 μ L). The infected control group received daily injections of saline. Bacterial burden was monitored with *in vivo* bioluminescence imaging. Implant and tissue were harvested for CFU enumeration on post-operative day (POD) 28.

Summary of results The sildenafil group had significantly lower bioluminescent signal from POD7-POD28 (figure 1; $p < 0.05$, Mann-Whitney U). Mean CFUs from implants were lower for the sildenafil group vs infected control, with CFUs enumerated from 8% (1/12) of sildenafil treatment implants vs 50% (6/12) of infected controls (figure 2; $p < 0.05$). Tissue CFUs were lower in sildenafil treated mice compared to infected control mice but was not statistically significant (figure 3; $p > 0.05$).

Conclusions This study demonstrates in a previously established and clinically relevant animal model of PJI that sildenafil has a positive impact on bacterial burden and implant infection rates. However, this study does not directly identify the mechanism of action of sildenafil on infection. Work is ongoing to measure MDSC populations in this model of PJI.

Abstract 69 Figure 1 Mean total flux (photons/s/cm²/sr) measured over the knee joint of each mouse

Abstract 69 Figure 2 CFUs adherent to implants

Abstract 69 Figure 3 CFUs from tissue

Abstract 69 Figure 4 Images of representative mice with bioluminescent data overlay

70

THE EFFECT OF ANNUAL SURGEON VOLUME OF TOTAL KNEE ARTHROPLASTY ON PATIENT REPORTED OUTCOMES

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10.1136/jim-2018-000939.70

Purpose of study Patient Reported Outcomes (PRO's) have become increasingly utilized in the assessment of medical interventions. Their role in orthopaedics continues to evolve and commonly affects reimbursement and reporting. Surgeon volume and PRO's have not been extensively studied. The goal of this study is to provide information for orthopaedic surgeons to facilitate an understanding of how the number of Total Knee Arthroplasties (TKAs) they perform in a year may affect the outcomes and complications as reported by their patients.

Methods used A total of 2877 patients who underwent TKA and completed a series of preoperative and postoperative PRO surveys were studied. Available demographic information included gender, age, BMI, and payer status. Pre-surgery, 3 month post-surgery, and 1 year post-surgery Knee injury and Osteoarthritis Outcome Score (KOOS) survey responses were

collected using a novel web-based collection system. One-way ANOVA and independent sample t-tests were used to compare KOOS central tendency measures between volume categories to assess significant differences.

Summary of results Surgeons were categorized into the following groups based on their annual surgical volume between 2014 and 2016: 0–12, 13–59, 60–145, >145 TKA procedures. When comparing these groups at the 3 month and 1 year follow up, there were no significant differences in average KOOS scores. However, patient reported complications were significantly higher ($p < 0.0001$) for the lowest volume category at the 3 month and one-year post-operative timeframes. Surgeons who performed 0–12 TKA per year had a 7.7% patient reported complication rate, while surgeons who performed 13–59, 60–145, and >145 had patient reported complication rates of 2.6%, 2.4%, and 3.8%, respectively.

Conclusions Annual surgeon volume for TKA procedures is not significant in determining PROs as measured by average overall KOOS scores at the 3 month and 1 year post-operative time periods. However, patient reported complication rates were higher in lowest volume surgeon group at both of these post-operative time periods.

71 OUTCOMES USING THE SUPRACLAVICULAR ARTERY ISLAND FLAP IN MUCOSAL VERSUS CUTANEOUS HEAD AND NECK RECONSTRUCTION

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10.1136/jim-2018-000939.71

Purpose of study The supraclavicular artery island (SAI) flap is a fasciocutaneous rotational flap used for head and neck reconstruction. It may provide a better option than conventional flaps in select situations because it is thin and pliable, reliable, easy to harvest and provides superior color match. However, to better understand where to use SAI flaps, it is important to know whether complication rates vary depending on reconstruction site. Our goal was to address this question by determining whether SAI flap complication rates differ between mucosal and cutaneous reconstruction sites.

Methods used We reviewed 107 consecutive SAI flaps performed by the senior author from 2010–2018. We recorded the site of reconstruction (mucosal vs. cutaneous) and any post-operative complications. Complications were categorized as total (100%) or partial (<100%) flap necrosis, fistula, and flap dehiscence at recipient site. We further categorized each complication as major (defined as total flap necrosis or any complication requiring a second surgery) or minor (all other complications). We used Chi-square test for all analyses. We determined statistical significance at $p < 0.05$.

Summary of results SAI flaps were used to reconstruct cutaneous and mucosal defects at a similar rate (56% vs. 44%, $p = 0.09$). Compared with cutaneous reconstruction sites, SAI flaps for mucosal sites had higher rates of total complications (54% vs. 34%, $p = 0.04$), flap dehiscence at the recipient site (32% vs. 14%, $p = 0.03$), and major complications (21% vs. 5%, $p = 0.02$). Complication rates for total flap necrosis, partial flap necrosis and minor complications were similar for mucosal and cutaneous sites.

Conclusions The SAI flap is more appropriate for use in cutaneous reconstruction of the face, neck, and parotid/temporal bone regions than mucosal reconstruction.

72 NOVEL PAN FIBER FOR TREATMENT OF MACULAR DEGENERATION SHOWS EFFICACY AND BIOCOMPATIBILITY IN EYE

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10.1136/jim-2018-000939.72

Purpose of study Age related macular degeneration (AMD) is one of the leading causes of blindness in the United States. AMD has been linked to an aberrant complement system, with genetic studies finding an increased risk of developing AMD with a single nucleotide change in the complement factor H (CFH) gene. Currently, there is no effective treatment for dry AMD, and treatment for wet AMD involves monthly intraocular anti-VEGF injections. As such, considerable efforts have been directed toward developing a better therapy option. The *AmpVision Intravitreal Implant*, is composed of a protein adsorbing polyacrylonitrile (PAN) polymer that has been shown to bind complement factor (CF). It is hypothesized that the permanent implant will decrease the amount of CF

in the eye, thereby slowing disease progression of both wet and dry AMD. We tested the degree of CF affinity, biocompatibility, and efficacy of AmpVision.

Methods used *Ex Vivo* efficacy was tested by subjecting diabetic human vitreous fluid to PAN fibers for 30 min. Biocompatibility was tested in Brown Norway rats ($n = 5$) with endpoint ERG and histology, and New Zealand White cross rabbits ($n = 5$) with histology. *In vivo* efficacy was tested in an AMD mouse model homozygous CFH $-/-$ ($n = 19$) with serial ERG, OCT thickness, and cell counts to measure changes in the retina. Devices were implanted in the right eye, and the left eye was used as a control in all animals. Data presented as means and standard errors.

Summary of results *Ex vivo*, the vitreous exposed to PAN fiber showed a significant decrease in CF in comparison to the control group (19.7 ± 3.2 ng/ml vs. 596.0 ± 21.1 ng/mL, $p = 0.0003$, Student's *t*-test). The PAN fiber was well tolerated, showing no difference in the outer nuclear layer cell counts between eyes (Rabbit: RE = 172.8 ± 5.8 , LE = 176.5 ± 4.4 , $p = 0.5721$ Student's *t*-test, Rat: RE = 145.5 ± 4.3 , LE = 140.5 ± 4.1 , $p = 0.4190$ Student's *t*-test). Endpoint ERGs in the rats demonstrated no difference in step 3A between right and left eyes (RE = -79.3 ± 16.8 , LE = -103.4 ± 15.8 , $p = 0.0762$ Student's *t*-test).

Conclusions In summary, our preliminary studies have shown biocompatibility of the PAN device in two animal models and efficacy in removing CF from vitreous *ex vivo*. We will continue testing *in vivo* efficacy in the CFH $-/-$ model.

73 ASSESSING THE STERILITY OF HOLLOW BORE INSTRUMENTS USED IN PLASTIC SURGERY

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10.1136/jim-2018-000939.73

Purpose of study The sterility of surgical instruments is crucial in preventing infections during surgery. To fully clean these instruments, cleaning, disinfection and sterilization are all required. The sterilization process typically uses an autoclave which heats the instruments up to about 121°C – 134°C at 15–30 psi for 20–30 min. Autoclaving of hollow surgical instruments is more of a challenge because of the shape of these tubes. It is possible that the autoclave does not fully kill all microbial life and/or remove all biologic material throughout the length of the hollow instrument. Difficulties in sterilization of intestinal endoscopes have been studied extensively demonstrating residual DNA and protein after standard cleaning protocols. The sterility of other hollow instruments, such as liposuction cannulas and endoscope sheaths has not been well studied. The purpose of this study was to determine whether hollow surgical instruments contain significant amounts of microbial life, residual protein and DNA.

Abstract 73 Table 1

	1	2	3	4	5	6	7	8
Protein (μg)	15.1	12.7	6.1	2.9	26.4	12.6	18.4	11.2
DNA ($\text{ng}/\mu\text{L}$)	42.3	32.5	14.6	11.3	54.2	29.0	39.8	25.5

Methods used Eight different hollow instruments were studied after sterilization before use and after surgery. Under sterile conditions, fifteen mL of 0.9% saline solution was passed through the tubes using a syringe and the residual fluid was collected. The method for collecting the sample was based on studies that collected samples from gastroscopes to assess for microbial material and their DNA and protein levels. Portions of the samples were plated on Petri dishes and microbial growth was evaluated at day 3, 5 and 10. Portions were then tested to assess for residual DNA and protein levels in these instruments.

Summary of results There was no microbial growth on any of our culture plates on days 3, 5, and 10. Protein and DNA levels measured after sterilization are summarized in table 1.

Conclusions Although there was no microbial growth in these instruments, trace protein was detected across instrument types as was DNA. The authors postulate whether or not hollow bore instruments should all be disposable.

74

DOES REPETITIVE TORQUE RESULT IN MORPHOLOGICAL CHANGES OF THE LATERAL ELBOW OF THE SKELETALLY IMMATURE BASEBALL PLAYER? A PROSPECTIVE MRI STUDY

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10.1136/jim-2018-000939.74

Purpose of study Morphologic changes to the shoulder joint are documented to occur from stresses associated with overhead throwing in the youth baseball player. No previous work has been done to identify potential changes of the elbow in the growing child, although the valgus torque stresses can be greater than the forces seen at the shoulder joint. The purpose of this study was to identify potential changes in skeletally immature elbows of children playing baseball via repeated magnetic resonance imaging.

Methods used A prospective study was conducted on pre-adolescents who played Little League baseball. Before the Spring season started, they initially underwent bilateral elbow MRI and a thorough evaluation of history related to throwing, followed by physical examination. Three years later they were asked to return for repeat MRI and physical examination. Further evaluation of continued play or new onset of pain was performed. Measurements were then compared in all three planes of both the radial head and the capitellum, both osseous and cartilaginous.

Summary of results Twenty-six children agreed to participate obtaining their first MRI at a mean age of 11.5 years (range 10 to 13 years). Half of the kids were year round baseball players, and 58% were still playing at the 3 year MRI. 62% reported being either/both a pitcher/catcher, as their primary position. All measures changed significantly between baseline and 3 years, as expected in growing children ($p < 0.001$). When comparing the difference of growth (change in size of radial head relative to distal humerus in the dominant arm compared to same ratio in the non-dominant arm) in the coronal plane between those still playing and those no longer playing, there was no significant abnormal growth ($p = 0.15$). Furthermore, there were no

significant changes in ratio of growth for the axial ($p = 0.59$) or sagittal ($p = 0.13$) planes of the radius or for the capitellum.

Conclusions This prospective MRI evaluation of children that play baseball demonstrated that continued torque at the elbow joint does not result in morphologic changes. The historical belief that long-term play of overhead sport can result in larger radial heads and capitellum does not appear to be more than anecdotal.

75

OUTCOMES OF ROBOTIC RADICAL PROSTATECTOMY IN PATIENTS WITH RENAL FAILURE AND SUBSEQUENT RENAL TRANSPLANTATION

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10.1136/jim-2018-000939.75

Purpose of study Renal failure patients with prostate cancer do not routinely undergo radical prostatectomy due to shorter life expectancy and increased surgical morbidity. However, robotic-assisted laparoscopic radical prostatectomy (RALP) may reduce surgical morbidity and increase overall survival in stage 5 chronic kidney disease (CKD 5) patients by allowing subsequent renal transplantation. The purpose of this study is to review outcomes of RALP in patients with CKD 5 and those that subsequently receive renal transplants.

Methods used A retrospective review of 43 patients with CKD 5 who underwent RALP for prostate cancer between 2008 and 2017 was performed. Patients who underwent subsequent renal transplantation were further reviewed to determine oncologic and renal outcomes after transplant. Continence was defined as 0–1 security pads/day. Postoperative complications were graded with the Clavien-Dindo scale.

Summary of results Forty-three patients with CKD 5 underwent RALP for prostate cancer. The mean BMI was 28.6 (20.0–39.3 mg/kg²) and mean age was 59.9 (40–78 years). The mean preoperative PSA was 4.65 (1–19 units). Six patients (14.0%) had positive margins. There were 2 UTIs (Clavien-Dindo I) within 30 days of surgery. All patients had an undetectable ultrasensitive PSA at latest follow-up. Following RALP, 14 patients underwent renal transplantation. At transplant, 2 patient required intraoperative urologic consultation to localize the contracted bladder. Another anuric patient had a bladder neck contracture, required urethral dilation (Clavien-Dindo IIb), and remains continent with no recurrent stricture at 72 months. One patient (7.1%) was incontinent at 12 months following RALP and two additional patients, who were dry prior to renal transplant (1L urine per day), developed incontinence after transplant. The mean creatinine at one-month post-transplant was 2.0 mg/dL. Mean survival to date is 7.4 years post-RALP. Three patients are now deceased. No patients have developed metastatic disease.

Conclusions Patients with CKD 5 may have unique comorbidities following RALP that should be anticipated. When treated with RALP, CKD 5 patients have excellent oncologic outcomes, acceptable morbidity, and following transplant, a potential 10 year survival.

Cardiovascular II

Concurrent Session

3:15 PM

Thursday, January 24, 2019

76 HYPOTHYROIDISM, SEX AND AGE PREDICT FUTURE THROMBOEMBOLIC EVENTS AMONG YOUNG PEOPLEJA Martinez, F Qeadan, MR Burge. *University of New Mexico Health Sciences Center, Albuquerque, NM*

10.1136/jim-2018-000939.76

Purpose of study Thyroid hormone plays a central role in metabolic homeostasis. Occurrence of a hypercoagulable state during hypothyroidism suggests an increased risk for thromboembolic events (TEE). We hypothesize that individuals with hypothyroidism will experience more thromboembolic events than those with normal thyroid function.

Methods used Data from the Electronic Medical Record between 2005–2007 were used to classify adult patients according to Thyroid Stimulating Hormone (TSH) level as Hyperthyroid (n=624), Euthyroid (n=10,320), Subclinically Hypothyroid (n=843), or Overtly Hypothyroid (n=326). ICD-9/10 codes were used to identify subsequent TEEs during 10–12 years of follow-up through 2017. Known hypercoagulable conditions were excluded. The Chi-squared test was used to compare rates of TEE across study groups, and multiple logistic regression was used to determine the odds of TEE after adjusting for covariates.

Summary of results There were 232 TEEs among 12 113 individuals over 5.1 ± 4.3 years of follow up. Risk for TEE varied significantly across categories and was modified by age while controlling for sex. As shown in the Data table 1, Overt Hypothyroidism conferred a significantly higher risk for TEE than Euthyroidism for people below age 40. Also, men were at higher risk for subsequent TEE than women when controlling for age (OR=1.48, 95% CI=1.14–1.93). When analyzing the data on smoking status (n=5,068; 86 cases of TEE), similar results were found while adjusting for age and sex, with smokers having 2.19 higher odds of experiencing TEE relative to non-smokers (95% CI 1.40–3.40).

Conclusions In this study, Overt Hypothyroidism conferred an increased risk of a subsequent TEE over the next 10 years as compared to Euthyroidism for individuals below the age of 40, and men were at higher risk for a subsequent TEE as compared to women regardless of thyroid status or age.

Abstract 76 Table 1 Overt hypothyroidism vs euthyroidism

Age at Classification	OR for TEE	95% CI
30 years	5.42	1.69–17.38
35 years	3.60	1.55–8.35
40 years	2.39	1.28–4.48
45 years	1.59	0.83–3.03
50 years	1.07	0.44–2.54
55 years	0.70	0.21–2.34
60 years	0.47	0.10–2.24

77 VASCULAR HEALTH OF CHILDREN CONCEIVED VIA IN VITRO FERTILIZATIONWY Zhang, E Selamet Tierney, A Chen, R Fleischmann, V Baker. *Stanford University School of Medicine, Los Altos Hills, CA*

10.1136/jim-2018-000939.77

Purpose of study Although *in vitro* fertilization (IVF) has helped infertile couples for nearly four decades, there is a paucity of knowledge regarding the long-term health of offspring. The cardiovascular system is one of the first to develop and is thus particularly sensitive to perturbations during the periconceptual period. IVF conceptions begin in the laboratory and initial embryonic development occurs in a maternal endocrine milieu which is not physiologic. Therefore, we hypothesized that IVF may have an adverse effect on the cardiovascular health of offspring.

Methods used We recruited 17 children aged 10–14 years who were conceived via IVF with autologous oocytes at Stanford. Endothelial pulse amplitude testing (EndoPAT) was used to assess endothelial function, carotid ultrasound to determine intima-media thickness, and pulse wave velocity (PWV) to determine arterial stiffness. These are all reliable, non-invasive modalities agreed upon by the American Heart Association to be standard research assessment tools and sensitive markers to assess vascular health, which have been predictive of later development of cardiovascular disease. We compared the study cohort to published norms or to historical Stanford controls.

Summary of results The participants had a normal mean body mass index (18.45 ± 2.0) and mean systolic BP (104 ± 6 mmHg). Diastolic BP was slightly high for age (mean 65 ± 2.0 mmHg, 55th percentile). Compared to Stanford historical controls, IVF children had significantly thicker common carotid artery IMT (0.44 ± 0.027 mm vs. 0.38 ± 0.04 mm, $p=0.0001$), higher mean elastic modulus (395 ± 80 mmHg vs. 289 ± 97 mmHg, $p=0.015$), and higher $\beta_{\text{stiffness}}$ (2.65 ± 0.37 vs. 2.28 ± 0.26 , $p=0.0008$). Mean EndoPAT index for our cohort was 1.66 ± 0.52 with 71% of the cohort having abnormal values defined as <1.9 . The mean PWV was 4.69 ± 0.55 m/s compared to the normative 4.73 ± 0.50 m/s ($p=0.76$) with 47% of the cohort having abnormal values.

Conclusions Overall, this study suggests that children conceived via IVF have evidence of abnormal vascular health including thicker artery intima and increased arterial stiffness, indicating potential increased long-term cardiovascular risks. Future studies are needed to further investigate the pathophysiology leading to these changes and to assess the long-term vascular health of IVF offspring.

78 PROTECTION FROM HEART DISEASE IN PEOPLE WITH DOWN SYNDROME IS UNLIKELY THE RESULT OF CHANGES IN THE ATHEROSCLEROTIC PATHWAY^{1,2}AT Pham, ^{1,2}A Rachubinski, ^{1,2}K Sullivan, ^{1,2}J Espinosa. ¹University of Colorado School of Medicine, Aurora, CO; ²Linda Crnic Institute for Down Syndrome, Aurora, CO

10.1136/jim-2018-000939.78

Purpose of study People with Down syndrome (DS), a condition caused by trisomy 21 (T21), present with unique co-morbidities. While these individuals are more likely to develop risk factors for heart disease – including obesity and

hypothyroidism – few adults with DS develop this condition. Thus, T21 may confer a protective mechanism that mitigates traditional heart disease risk. This study therefore aims to investigate the effects of T21 on the atherosclerotic pathway, which is the underlying cause of heart disease.

Methods used We used published datasets comparing individuals with and without DS (Sullivan et al., 2016; Sullivan et al., 2017). This included RNAseq of fibroblasts and monocytes, SOMAscan proteomics, and Meso Scale Discovery assay. We also used flow cytometry data on monocytes. These datasets were then compared to previously reported factors that either confer protection from or predisposition to atherosclerosis.

Summary of results Apolipoproteins may be downregulated (Fold Change 0.721; padj=0.076). Proinflammatory cytokines, including TNF alpha (FC 1.434; padj=0.031) and MCP1 (FC 1.305; padj=0.015), have increased expression. Scavenger proteins, MSR1 (FC 1.302; padj=0.028) and OLR1 (FC 1.310; padj=0.048), are upregulated. Among monocyte subpopulations, there is a decreased percentage of CD14 ++CD16 monocytes (p=0.0005) and an increased percentage of CD14 ++CD16+ as well as CD14 +CD16+ monocytes (p=0.005; p=0.002). Moreover, there is an increase in absolute numbers of CD14 ++CD16+ and CD14 +CD16+ monocytes (p=0.016; p=0.019). Among bulk CD14 + monocytes, RNAseq reveals decreased expression of ALOX5AP (FC=0.540; padj=0.00002) and increased expression of COLEC10A (FC=1.541; padj=0.0007), which are specific to classical and intermediate monocytes respectively.

Conclusions People with DS are predisposed to potentially decreased lipid metabolism, chronic inflammation, and altered monocyte subpopulations. All these factors should increase heart disease risk. Thus, changes in the atherosclerotic pathway do not explain how T21 leads to protection from heart disease. Future studies are needed to examine lipids and their metabolism.

79 SURGICAL REPAIR OF EBSTEIN'S ANOMALY

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10.1136/jim-2018-000939.79

Purpose of study Ebstein's anomaly is a rare congenital malformation characterized by an abnormality of the tricuspid valve and right ventricle. It often requires surgical intervention due to progressive tricuspid valve regurgitation and development of clinical symptoms. However, there is currently a controversy regarding the optimal surgical approach to this complex congenital heart defect. In addition, the optimal timing of surgical intervention remains uncertain, largely due to the wide variability of this disease. The purpose of the current study was to review our surgical experience with Ebstein's anomaly at a single institution.

Methods used This was a retrospective review of 47 patients with Ebstein's anomaly who underwent surgical repair at Stanford from 2004 to 2017. Our surgical approach repairs the leaflets at the pre-existing level and does not attempt to create an anatomic annulus. The median age at surgery was 17 years (range 3 to 52 years). Pre-operatively, the median degree of

tricuspid regurgitation was graded as moderate-to-severe, and the median right ventricular function was graded as mildly decreased.

Summary of results Forty-seven patients underwent surgical repair without any mortality. Thirty-eight patients (81%) had a successful repair, as evidenced by a decrease in the amount of tricuspid regurgitation to a median grade of 'trace' regurgitation. Nine patients ultimately proved to have an unsuccessful long-lasting repair, as evidenced by recurrent tricuspid regurgitation. Six of these patients underwent re-repair, while two patients (4%) required tricuspid valve replacement. One patient has persistent severe tricuspid regurgitation and will require re-operation in the future.

Conclusions The data demonstrate that repair for Ebstein's anomaly can effectively reduce the amount of tricuspid regurgitation in the majority of patients. In our series, 13% of patients required a future re-repair and only 4% of patients required eventual tricuspid valve repair.

80

DOES ANTI-THYMOCYTE GLOBULIN INDUCTION TRULY LEAD TO INCREASED CYTOMEGALOVIRUS INFECTION AFTER HEART TRANSPLANTATION IN THE CURRENT ERA?

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10.1136/jim-2018-000939.80

Purpose of study Anti-thymocyte globulin (ATG) is commonly used as induction therapy immediately after heart transplantation (HTx). ATG has been associated with an increase in cytomegalovirus (CMV) infection when used with maintenance cyclosporine. In the current era, tacrolimus has replaced cyclosporine as the main maintenance immunosuppressive agent. It

Abstract 80 Table 1

Endpoints	ATG Induction n=342	No ATG n=312	P-Value
2 Year Freedom from CMV Infection	93.6%	96.5%	0.082

Endpoints	ATG Induction (n=342)				P-Value
	CMV Mismatch (D+R-), n=79	D+R +n=166	D-R +n=65	D-R- n=32	
2 Year Freedom from CMV Infection	89.9%	94.6%	92.3%	100.0%	0.231*
2 Year Freedom from Any-Treated Rejection	73.4%	80.1%	83.1%	90.6%	0.169**
2 Year Freedom from Acute Cellular Rejection	87.3%	95.2%	90.8%	93.8%	0.148
2 Year Freedom from Antibody-Mediated Rejection	87.3%	88.6%	92.3%	93.8%	0.603

*Pairwise Analysis: CMV Mismatch vs D-R-, p=0.060 **Pairwise analysis CMV Mismatch vs D-R-, p=0.050

is not clear whether ATG induction does indeed lead to more CMV infection in the tacrolimus era.

Methods used Between 2010 and 2016, we assessed 342 patients who received ATG induction therapy and compared them with HTx patients who did not receive ATG (n=312). ATG is usually administered to patients with renal insufficiency to delay tacrolimus initiation and to sensitized patients (PRA $\geq$ 10%). Patients treated with ATG were then divided into their CMV serologies and analyzed for the development of CMV infection. Incidence of rejection was also evaluated.

Summary of results There was a trend towards an increase in CMV infection in patients who received ATG induction therapy after HTx (see table 1). When the ATG population was analyzed by CMV serology, CMV mismatch (D+R-) had a numeric increase in CMV infection but this result was not statistically significant. When compared to the D-R- group on pairwise analysis, there was a trend towards increased CMV infection and any-treated rejection in the CMV mismatch group (see table 1). Of note, valcyte induction was similar between groups per the HTx protocol.

Conclusions ATG therapy trends towards increased CMV infection post-HTx. Patients who have been treated with ATG and have CMV mismatch may have increased CMV infection as well as rejection. Larger numbers are needed to confirm these findings.

81 MANY LOW RISK WOMEN AND MEN EVALUTED IN A CHEST PAIN UNIT CAN BE SAFELY AND RAPIDLY DISCHARGED WITHOUT PRE-DISCHARGE CARDIAC TESTING

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10.1136/jim-2018-000939.81

Purpose of study Management of patients at low risk for acute coronary syndrome (ACS) presenting to the emergency department with chest pain remains challenging. We examined a cohort of low risk women and men admitted to our chest pain unit (CPU) with negative cardiac injury markers, normal ECG, and clinical stability. We predicted that both low risk women and men could be safely and rapidly discharged without pre-discharge testing.

Methods used The study group comprised 719 consecutive low risk patients, including 371 (52%) women, evaluated over 2 years. Utilization of pre-discharge testing (PDT), test results, and follow-up MACE (cardiac death, myocardial infarction, and revascularization) at 30 days and 6 months were compared between women and men.

Summary of results Women were older (60 vs 55 years, p<0.0001), had similar number of cardiac risk factors (mean 1.9 vs 2.0), and were less likely to have a history of coronary artery disease (11% vs 18%, p=0.006). A large proportion of both sexes did not undergo PDT, although the frequency of no PDT was higher in women: 50% vs 42%, p=0.02. When referred for PDT, women more often underwent myocardial stress scintigraphy (MPS) (23% vs 16%, p=0.02) and less often received treadmill exercise testing (19% vs 33%, p<0.001). Positive results of PDT were significantly less in women than men (3/184, 2% vs 12/203, 12%, p=0.02). LOS was shorter for patients who did not undergo

PDT compared to patients who did receive PDT (5.3 hours vs. 10.2 hours, p<0.0001) without altering post-discharge MACE. Follow-up revealed low risk for MACE in women and men at 30 days (0 vs 0) and 6 mos (3/287, 1.0% vs n=3/235, 1.3%).

Conclusions Our findings suggest that both women and men admitted to the CPU have: 1) low clinical risk profiles for ACS, 2) large proportions not referred for PDT, 3) brief LOS in the CPU, and 4) modest rates of MACE at 6 mos post-discharge. Thus, many low risk women and men can be safely and rapidly discharged without PDT and with low risk for MACE early and at 6 mos of follow-up. Further, no PDT was associated with significantly reduced LOS, with the potential for cost savings in this large patient population.

82 THE EVOLVING LONG-TERM OUTCOME OF HEART TRANSPLANTATION IN AMYLOID PATIENTS

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10.1136/jim-2018-000939.82

Purpose of study Both amyloid light chain (AL) amyloidosis and transthyretin-related (TTR) amyloid are expanding indications for heart transplantation (HTx). In the past, AL amyloid, in particular, had been a contraindication to HTx given its systemic nature and the increased risk for mortality. Modern treatments including proteasome inhibitors have allowed amyloid patients to receive HTx at an increasing rate. We sought to assess long-term post-HTx outcome in amyloid patients in the current era.

Methods used Between 2010 and 2015, we assessed 27 patients (5 AL, 10 TTR-wildtype (wt), 12 TTR-mutant (m)) underwent HTx for cardiac amyloidosis at our single center. A non-amyloid restrictive cardiomyopathy control population was included (n=18). Endpoints included 3 year outcomes including survival, freedom from cardiac allograft vasculopathy (CAV, as defined by stenosis $\geq$ 30% by angiography), freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary

Abstract 82 Table 1

Endpoints	AL (n=5)	TTR wt senile (n=10)	TTR mutant (n=12)	Non-Amyloid Restrictive Control (n=18)	Log-Rank P-Value
3 Year Survival	100.0%	90.0%	83.3%	94.4%	0.790
3 Year Freedom from CAV	80.0%	80.0%	83.3%	88.9%	0.990
3-Freedom from NF-MACE	100.0%	90.0%	75.0%	100.0%	0.112
3-Freedom from Any-Treated Rejection	100.0%	100.0%	91.7%	94.4%	0.619
3 Year Freedom from Acute Cellular Rejection	100.0%	100.0%	91.7%	100.0%	0.518
3 Year Freedom from Antibody-Mediated Rejection	100.0%	100.0%	100.0%	94.4%	0.367

intervention, implantable cardioverter defibrillator/pacemaker implant, stroke), and freedom from any-treated rejection, acute cellular rejection, and antibody-mediated rejection.

Summary of results There was no significant difference between the AL amyloid, TTR-wt, TTR-m, and restrictive non-amyloid patients with respect to 3 year survival and 3 year freedom from CAV, NF-MACE, and rejection (see table 1). Endomyocardial biopsies post-HTx did not show amyloid. (see table 1)

Conclusions In the current era, both AL and TTR amyloid patients have acceptable mid-term outcome after HTx. Larger numbers and longer followup are needed to confirm these findings.

83 ELECTIVE LEFT PULMONARY ARTERY EMBOLIZATION FOR PULMONARY ARTERIOVENOUS MALFORMATIONS SECONDARY TO CAVOPULMONARY ANASTOMOSES NOT RESPONSIVE TO HEART TRANSPLANTATION

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Case report This is the first report to present a case of pulmonary arteriovenous malformations, PAVMs, which failed to resolve after isolated heart transplantation, HTx, in a child with history of cavopulmonary anastomoses, CVPAs. Additionally, this is the first reported case of therapeutic embolization of the left pulmonary artery, LPA, to correct severe cyanosis in this setting with excellent results. The patient was born with heterotaxy-asplenia syndrome and complex congenital heart disease. Several years after CVPAs procedures, she developed

PAVMs with associated cyanosis. The PAVMs persisted predominantly in the left lung, despite orthotopic HTx two years prior. She developed worsening cyanosis following an episode of acute rejection (O₂ saturation in the 60 s, and in the 70 s with supplemental oxygen). Elective transcatheter LPA embolization was performed and normalized her O₂ saturation, 94%, without a significant increase in pulmonary artery pressure (17 mmHg). The patient's quality of life improved significantly.

Panel 1: Patient's Anatomy Diagram A) At birth B) After a bilateral bidirectional Glenn and Kawashima connection C) After Fontan circulation D) After HTx

Panel 2: Chest CT Angiogram: Enlarged left pulmonary vessels in the anterior segment of the left upper lobe and basilar segments of the left lower lobe suggesting the presence of PAVMs

Panel 3: Heart Catheterization with LPA test occlusion A) Diffuse left lung PAVMs

B) Test occlusion of left pulmonary artery with sizing balloon

Panel 4: LPA Device Deployment: lateral projection of main pulmonary artery angiogram after LPA embolization with a 16 mm Vascular Plug

84 SURGICAL ABLATION OF REFRACTORY VENTRICULAR ARRHYTHMIAS GUIDED BY ELECTROPHYSIOLOGIC AND ELECTROANATOMIC MAPPING

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10.1136/jim-2018-000939.84

Introduction Percutaneous ventricular tachycardia (VT) ablation may be unsuccessful with limited epicardial

Abstract 83 Figure 1

Abstract 84 Table 1

Patient	Sex	Age (years)	LVEF (%)	Cardiomyopathy cause	Prior RFA (Endo/Epi) (Y=yes, n=no)	# Prior AADs	Etiology Pericardial Adhesion	Other Cardiac Surgery Planned	Surgical Approach	# VTs Targeted	Substrate Localization (LV=left ventricle)	Mapping Tool (1=pacer, 2=voltage, 3=activation/entrainment)	Acute outcome (1=noninducible for VT, 2=exit block, 3=neither achieved)
1	Male	65	66	Idiopathic	Y/Y	4	Prior surgical ablation	None	Lateral thoracotomy	1	Inferolateral LV base	1, 2, 3	1–2
2	Male	66	40	Non-ischemic	Y/Y	4	Prior ablation complicated by hemopericardium	None	Lateral thoracotomy	1	LV inferior and inferolateral base to mid-LV	1–2	2
3	Male	54	19	Non-ischemic	Y/N	5	N/A	LVAD	Median sternotomy	1	LV inferolateral wall: base to apex	1, 2, 3	1
4	Male	62	40	Ischemic	Y/Y	2	Prior ablation complicated by hemopericardium	None	Lateral thoracotomy	2	LV inferior and inferolateral base to mid-LV	1, 2, 3	1–2
5	Female	71	18	Non-ischemic	N/N	2	N/A	LVAD	Median sternotomy	1	LV lateral base to mid-LV	1–2	2
6	Male	65	17	Ischemic	Y/N	3	N/A	LVAD	Median sternotomy	1	Septum; anterior and posterior LV walls	1–2	2
7	Male	69	40	Ischemic	Y/Y	3	N/A	None	Lateral thoracotomy	1	Inferolateral LV: base to apex	1, 2, 3	1–2
8	Male	62	36	Non-ischemic	Y/N	2	Prior extensive epicardial ablation	None	Lateral thoracotomy	1	LV summit	1–3	3
9	Male	69	30	Non-ischemic	Y/N	2	N/A	LVAD	Median sternotomy	1	LV summit	1, 2, 3	2

access. Open surgical ablation (SA) is an option but precision is challenging without electrophysiological (EP) data. We describe our SA experience using EP and electroanatomic mapping (EAM) in patients with refractory VT storm.

Methods Nine patients with recurrent VT despite antiarrhythmic drugs (AADs) and prior catheter ablation who needed surgical epicardial access or cardiac surgery underwent open SA using intra-operative EAM and EP mapping.

Results Table 1 shows baseline and procedural data. Patients were 65 ± 5 years, 8 (89%) were male, had a mean left ventricular ejection fraction of $34 \pm 15\%$; 4 (44%) had left ventricular assist device (LVAD) implantation with SA. Contemporary EP and EAM modalities and cryoablation were used in all; radiofrequency energy was additionally used in 2 (29%). Goals of VT non-inducibility or exit block pacing within isolated regions at high output were achieved in 8 (89%). AADs continued in all on discharge. In a median follow-up of 557 days, 8 (89%) patients had ventricular arrhythmia suppression and did not require further treatment; one had severe heart failure, recurrent VT and subsequently underwent orthotopic heart transplantation within one month of SA.

Conclusion Open surgical mapping and ablation of refractory VT using contemporary EP tools can help manage patients with contraindication to percutaneous epicardial access or with indication for cardiac surgery.

85

EARLY DETECTION OF ATRIAL FIBRILLATION-ATRIAL FLUTTER USING REMOTE PATIENT MONITORING

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10.1136/jim-2018-000939.85

Purpose of study Remote patient monitoring (RPM), patient-reported outcomes (PROs), and biomarkers may be useful for early detection of major adverse cardiac events. We present a 64 year man enrolled in a precision medicine study in whom RPM detected the presence of atrial fibrillation-atrial flutter (AFib-Flutter), facilitating prompt treatment.

Methods used Patients with ischemic heart disease (IHD) were monitored over 12 weeks. RPM data included a wrist-worn sensor to track activity and heart rate (Fitbit) and weekly recordings of electrocardiogram rhythm stripes (AliveCor). PROs were collected using PROMIS, Seattle Angina Questionnaire, and Kansas City Cardiomyopathy Questionnaire. Biomarkers were obtained by monthly self-administered fingerpricks using a microsampling device (Mitra[®]).

Summary of results Fitbit data reported daily average of 18.9 hours of sedentary time. At week 9, the patient felt palpitations and chest pain. His AliveCor reported 'possible AFib', which led him to call paramedics and subsequently be

Abstract 85 Figure 1 PROs and RPM

admitted to the hospital. He received expedited treatment, converting to sinus rhythm within 12 hours and was discharged. Leading up to this event, PROs declined in self-reported quality of life (figure 1).

Conclusions Using RPM may be useful for detecting AFib-Flutter and improving IHD outcomes. By utilizing changes in real-time RPM, PROs, and biomarkers, there is potential to impact health-related outcomes, leverage cost effective strategies, and predict unplanned hospitalizations.

Community Health I

Concurrent Session

3:15 PM

Thursday, January 24, 2019

86

ENDO ECHO REDUCES HEALTH DISPARITIES BY BRIDGING GEOGRAPHICAL BARRIERS FOR PATIENTS WITH COMPLEX DIABETES AND OTHER ENDOCRINE CONDITIONS IN MEDICALLY UNDERSERVED AREAS

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10.1136/jim-2018-000939.86

Purpose of study Rural patients with complex diabetes are distinctly vulnerable to health disparities, a problem worsened by

the national shortage of endocrinologists. Project ECHO (Extension for Community Healthcare Outcomes) is an education model that leverages videoconferencing technology to connect specialists with primary care providers (PCPs) in medically underserved communities in order to build new capacity for specialty level care through case based learning and best practices dissemination. We previously reported that application of the ECHO model to complex diabetes care (Endo ECHO) improved PCP and community health worker (CHW) self-efficacy. We now report the impact of Endo ECHO on travel distance for patients in rural New Mexico seeking endocrine care. **Methods used** We partnered with PCPs and CHWs at 10 federally qualified health centers (FQHCs) across New Mexico who participated in weekly ECHO videoconferencing sessions. Participants presented de-identified patients over the ECHO network and received best practices guidance from a multidisciplinary team of specialists and other network peers. Presentations were tracked using iECHO software from November 2014 through June 2018 in order to estimate miles saved between the FQHC and the referral center in Albuquerque, NM. IRS medical rates and US Census median household income data were applied to estimate savings from travel cost and work productivity loss respectively.

Summary of results During the evaluation period, we received 538 patient presentations over the network. On average, 300 miles of travel distance were saved per patient presentation, for a total of 1 59 908 miles. We estimated a savings of \$28 784 from travel costs and \$93 231 from work productivity loss.

Conclusions Application of the ECHO model to complex diabetes and endocrine care in New Mexico bridged geographic barriers to care for patients in medically underserved

communities. Ongoing evaluation of patients enrolled in the Endo ECHO program will determine to what extent clinical outcomes are affected by improving access to care in these communities.

87 WILL MY FOOD RUN OUT? FACTORS THAT INFLUENCE LATINOS PARTICIPATION IN POSITIVE LIFESTYLE BEHAVIORS

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Purpose of study Despite the economic prosperity of the US and although California produces close to half of the nation's fruits and vegetables, 1 in 8 Californians struggle with food insecurity. Food insecurity (FI), defined as the limited or uncertain availability of nutritionally adequate and safe foods, has a significant impact on an individual's well-being. Persons experiencing FI have limited access to nutritious foods and besides associated depression and anxiety, can have physical health problems, lowered workplace productivity and increased risk of obesity.

Though seemingly counterintuitive, obesity and FI are directly correlated. People who experience FI often turn to inexpensive, unhealthy foods that can lead to obesity and its resultant negative health outcomes. This study sought to determine whether FI impacted an individual's intention to engage in positive lifestyle behaviors.

Methods used A survey was administered to monolingual Latinos (n=68) residing in Southern California. A two question, validated food security scale was used to determine the presence of FI; intention to make positive lifestyle changes (diet and exercise) was measured on a 4 point Likert scale.

Summary of results Our results showed that not worrying that food may run out was positively associated with increased intentions to eat healthy (p=0.011), the belief that one could improve exercise habits (p=0.017) and measures of self-efficacy to improve exercise habits (p=0.002) and eat healthy (p=0.001). Worrying whether foods would last was inversely correlated with intent to exercise (p=0.009) and intent to eat healthy (p=0.001).

Conclusions Hispanics in Southern California, have some of the highest rates of obesity; low income Hispanics especially also face significant challenges regarding food security. In order to appropriately address and combat the obesity epidemic in this population it is important to understand that their willingness to initiate healthy lifestyle habits may be influenced by food access. Collaborative efforts to facilitate programs to allow low cost access to healthy foods as a part of lifestyle interventions may help to increase community participation and engagement which tends to be among the lowest of all groups in Hispanics.

88 PRE-HEALTH MENTORSHIP: CULTIVATING RELATIONSHIPS BETWEEN YOUTH FROM THE SPOKANE TRIBE AND STUDENTS FROM THE UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE – SPOKANE (UWSOM)

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10.1136/jim-2018-000939.88

Purpose of study The Spokane Tribe reservation community has historically struggled with post-secondary educational attainment, specifically in health-related fields. In comparison to neighboring towns, tribal members are statistically more likely to drop out of high school and not pursue higher education. At present, demographic data notes that the Spokane tribal population is growing with 36% of the population under 20 years of age. As such, there is opportunity for early intervention programs to target educational achievement gaps.

Methods used A literature review was performed in PubMed, Embase and MEDLINE to identify programs helping students from traditionally underserved backgrounds overcome barriers to post-secondary education. Search terms were 'Native American youth empowerment' and 'pre-health pipeline programs for underserved communities.' A series of interviews were conducted with clinicians, U.S. Public Health Service workers and leaders of the Spokane Tribal Network (STN) – a non-profit organization engaged in tribal youth resiliency efforts – to identify community perceived need and establish goals for potential programming. Community interviews also revealed other areas of concern including: suicide risk, sexual abuse and prevalence of chronic diseases at young ages.

Summary of results Information from the literature review and interviews were used to propose a mentorship program that matches Spokane tribal youth to a 1st or 2nd year medical student at UWSOM. In collaboration with UWSOM's Underrepresented in Medicine student group and STN, the mentorship program will allow medical students to facilitate a big brother/sister relationship with tribal youth through one on one meetings and monthly meet-up events. The program planning is ongoing, but a pilot is scheduled within the 2018–2019 school year.

Conclusions With 120 current 1st and 2nd year UWSOM students in Spokane, there exists a large resource for positive mentorship with tribal youth. The proposed mentorship program aims to not only build capacity for youth, but also show that post-secondary education and professional degree programs are realistic goals. Some next steps include identifying interested medical students and tribal youth as well as identifying funding sources through STN and UWSOM.

89 KEEP OUR KIDS AT PLAY, LOCK YOUR GUNS AWAY: A COMMUNITY-BASED APPROACH TO INCREASE SAFE STORAGE OF FIREARMS WITHIN FAMILY HOMES OF RURAL WYOMING

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10.1136/jim-2018-000939.89

Purpose of study Household gun ownership is a strong independent determinant of gun-related injury, and while firearms represent major threats to child and adolescent safety, more than half of US households do not safely and securely store firearms within the family home. Alarming, among youth ages 15–24 in Wyoming, suicide is the second leading cause of death after unintentional injuries, and of all firearm deaths in Wyoming between 2010 and 2014, 86% were suicides. As such, interventions aimed at improving both access to safe firearm storage modalities and education surrounding safe gun

storage represent very relevant public health aims for rural Wyoming counties. The purpose of this project is to increase the prevalence of secure firearm storage within family homes of the rural community Douglas, Wyoming.

Methods used Through the completion of a comprehensive evidence-based literature review, formation of community partnerships with local Public Health and County Sheriff Departments, and the design of educational material, this project was able to utilize a widely attended community event to distribute gun safety education and firearm cable locking devices to community members. Cable locking devices were provided free-of-charge along with demonstration of proper use.

Summary of results This project was able to distribute gun safety education and free-of-charge gun locking devices to approximately 100–150 local families and community members. This method represents a promising way to raise awareness of safe gun storage in rural areas, while also providing the physical means to safely store and secure firearms within family homes, eliminating financial barriers.

Conclusions The initial phases of this project have demonstrated that utilizing community events is a promising way to distribute both firearm locking devices and educational material surrounding safe storage of firearms within family homes. Additionally, this project has demonstrated that partnering with respected community organizations such as county Sheriff Departments and Public Health agencies greatly increases the strength of this type of intervention. Next steps could include expansion to additional events and potentially state-wide events.

90 CHILDHOOD OBESITY: PARENTAL EDUCATION LEVEL AS A PREDICTOR OF SODA INTAKE

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10.1136/jim-2018-000939.90

Purpose To investigate parent education as a predictor of soda consumption in obese/overweight children.

Methods A day camp called ‘Operation Fit’ was conducted by medical and nutrition students from Loma Linda University Health. Children ages 9–15 years with unhealthy BMI (>85 percentile) were referred by their primary care physicians in San Bernardino County. The children learned through interactive games and activities about healthy eating and exercise, using the ‘7+3’ approach to health. An educational activity about the dangers of drinking soda leading to sugar overconsumption and one evening of family education occurred during the camp.

Summary of results

Data Demographic and health data was collected from participating households via surveys. Parents were asked about their highest education level obtained; grade school, high school, or some college and beyond. The parents reported how many sodas a day their children consumed, and the children were split into daily soda drinkers and no soda drinkers. A logistic regression was performed.

Results Of 713 children sampled, 431 did not drink any soda daily and 282 drank at least one can, or more. Results are

Abstract 90 Table 1

Parent Education Level	P value (Pr>ChiSq)	Likelihood of Drinking Soda Exp(Est)
Grade school or less	<0.001	4.844
High school	0.0015	3.064
Some college and beyond	0.0045	2.756

summarized below. Children whose parents only completed ‘grade school or less’ were 4.84 times more likely to drink at least one can of soda a day ($p<0.001$). Soda consumption and parental education level did not predict BMI.

Conclusions

Discussion Because all of the p-values are significant, there was a significant difference between soda drinkers and non-soda drinkers across all parental education levels. There was a clear correlation between education and soda intake; the more education a parent completed, the less likely a child was to drink at least one can of soda a day. The p-values decreased as parental education decreased; less education is a stronger predictor for soda consumption. Thus, educating parents and children about the dangers of soda consumption is important because children are at a higher risk of soda consumption with low parental education level.

91 DROWNING PREVENTION: A COMMUNITY APPROACH TO WATER SAFETY

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10.1136/jim-2018-000939.91

Purpose of study Brewster, Washington, is a rural community located at the confluence of the Columbia and Okanogan Rivers. These rivers offer a variety of recreational water activities. They also pose a risk to those without proper water safety knowledge and swim ability. Brewster has a population of roughly 70% Hispanics, with a large proportion having little or no swim ability. Limited swim ability, which is more common among minority populations, increases the risk for drowning. A community program to address drowning prevention was initiated in Brewster, with the goal of improving water safety knowledge and access to formal swim lessons.

Methods used Interviews were conducted with the director of the Brewster Boys and Girls Club (BGC), and the manager of the community pool. The community pool offers swim lessons in the summer, with limited availability due to a lack of qualified instructors. Additional barriers include: cost of lessons, no Spanish-speaking instructors, and no adult classes. At the Brewster BGC, many of the kids in their summer program have not completed formal swim lessons. Interviews with families at the Brewster Family Health Center (FHC) further supported that a high proportion of individuals have limited swim ability.

Summary of results Interventions encompassed water safety knowledge and access to swim lessons. The community pool was provided with information on funding from the USA

Swimming Foundation. At the Brewster BGC we piloted a water safety course for the kids using materials from Safe-Kids and the Red Cross. The Brewster FHC was provided a screening toolkit created by the Everyone Swims Initiative for assessing swimming ability, and referring patients for swim lessons. Both English and Spanish language water safety brochures, created using materials from the American Academy of Pediatrics, were provided to community partners.

Conclusions Drowning prevention strategies can be initiated using low-cost and simple interventions. Creating brochures and a water safety program were both simple options for improving water safety knowledge. A screening toolkit for swim ability, and creating a referral system between the clinic and pool, was another easy intervention that can improve access to swim lessons. The cost of swim lessons remains a barrier. Future steps include identifying other grants and community resources to offer affordable swim lessons for families.

92 EFFECT OF MARIJUANA LEGALIZATION ON THE NUMBER OF MARIJUANA-RELATED SUSPENSIONS IN A RURAL OREGON HIGH SCHOOL

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10.1136/jim-2018-000939.92

Purpose of study In 2015, recreational marijuana was legalized in Oregon for adult use. Little information exists on the impact of marijuana use among youth in states where it is legal.

Our study objective is to determine if there has been an increase in marijuana-related suspensions (MRS, suspension defined as 10 days off campus) in a rural Oregon high school since its legalization. A secondary goal of this research is to determine if students on an Individualized Education Plan (IEP) are more likely to be suspended for marijuana use than non-IEP students post-legalization. We hypothesize that there has been an increase in MRS among high school students since legalization and that IEP students will be at greater risk for suspension compared to non-IEP students.

Methods used MRS and demographic data were collected retrospectively from a rural Oregon high school for the years 2012–2018. Student information was de-identified and separated into IEP and non-IEP populations. We used a 2-proportion t-test to compare the number of overall suspensions for pre vs. post-legalization. We used the same test to compare the number of suspensions pre vs. post-legalization for IEP students vs. non-IEP students.

Summary of results For the years 2012–2018, 9214 student records were reviewed. There were 32 marijuana-related suspensions in the total student population between 2012–2015. After legalization in 2015, the number of MRS from 2015–2018 increased to 101 ($p \leq 0.0001$). Prior to legalization, there were 5 IEP MRS compared to 27 non-IEP MRS. Post-legalization there were 26 IEP MRS compared to 75 non-IEP MRS.

There was no significant difference in suspensions pre-legalization when comparing IEP to non-IEP students, but post-legalization the IEP student population saw an increase compared to their non-IEP peers ($p = 0.0031$).

Conclusions We found an increase in marijuana-related suspensions since marijuana legalization in this rural high school setting, especially for IEP students. Further study is needed to determine if these findings are generalizable.

93 DEVELOPING THE TOBACCO CESSATION CAPACITY FOR THE HOMELESS IN KODIAK, ALASKA

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10.1136/jim-2018-000939.93

Purpose of study Tobacco use remains a significant public health concern across Alaska. The problem is magnified in the homeless population where smoking rates are 70% or higher. This project addressed tobacco cessation in the homeless population in Kodiak, Alaska. The City of Kodiak is a small fishing community of 6100 persons on Kodiak Island. A handbook was developed to promote tobacco cessation in clients staying at the Kodiak Brother Francis Shelter (KBFS). The goal of this intervention was to promote tobacco cessation in homeless individuals.

Methods used The baseline health characteristics of Kodiak were initially investigated. Interviews were then conducted with representatives from the KBFS and the Kodiak Area Native Association's (KANA) Substance Abuse Services to determine how they were promoting tobacco cessation in the homeless population. A review of the literature regarding tobacco use and cessation in the homeless was then completed. A handbook was then developed and delivered to the KBFS to help develop their tobacco cessation resources.

Summary of results The interview with the operations manager at the KBFS revealed that a tobacco cessation group had once been held at the shelter in collaboration with KANA. In an interview with representatives from KANA, the details of this cessation group were discussed.

A review of the literature revealed two feasible pilot interventions that applied group counseling sessions, pharmacotherapy, and access to state quit lines in the shelter setting. Another article showed that training shelter staff in brief tobacco interventions increased the provision of quitting resources to shelter clients.

The handbook included recommendations for tobacco use policy changes on the shelter grounds, an outline for training staff in brief tobacco interventions, and a guide for restarting the tobacco cessation group. Resources from the Alaska Tobacco Quit Line were also provided along with the literature review.

Conclusions The handbook was submitted to the KBFS. The next steps for this project will be to facilitate a meeting between the KBFS and KANA to solidify plans for the tobacco cessation group. The shelter staff should be trained in brief tobacco interventions and their policies regarding tobacco use on the campus should also be adjusted to promote a smoke-free environment.

94 COMMITMENT TO UNDERSERVED PEOPLE CLINICS: AN INTEGRATED STUDENT-RUN FREE CLINIC SYSTEM SERVING SOUTHERN ARIZONA

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10.1136/jim-2018-000939.94

Purpose of study The UA College of Medicine – Commitment to Underserved People (C.U.P) provides student-run free clinics caring for uninsured patients in Southern Arizona. These clinics operate year-round, offering a reliable source of medical care in the community. Due to high patient demand and multitude of available services, we have implemented an electronic medical record (EMR) that creates an integrated health-care delivery model to ensure patients receive high quality care between all clinics.

Methods used System Organization: The C.U.P. Health System consists of MIND Clinic (Psychiatry), Women's Clinic (OB/GYN), Shubitz Clinic (Family Medicine), Sight Savers (Ophthalmology), and TotShots (Pediatrics). The EMR allows for real-time communication between clinics, seamless referrals, and comprehensive documentation of patients, helping providers efficiently step into patient care pathways. In the case of patient referrals, C.U.P. has partnered with specialists in the community, who provide pro-bono services for our patients. Furthermore, C.U.P. collaborates with the Pima County Health Department and the Centers for Disease Control to obtain free vaccines for adults and children.

Summary of results Services Provided: The patient population is diverse and upon entering the clinic, patients encounter an electronic sign-in and sign-out, and medical student translators. Medical students provide: comprehensive women's health services, well-child checks, vaccine administration, in-house laboratory testing, EKGs, psychiatric evaluations, nutrition and diabetic care counseling classes, and Medicaid enrollment assistance, under the supervision of attending physicians. Following their visit, patients are notified of test results and able to follow-up with providers. Other telemedicine initiatives are being implemented, including video and phone visits.

Conclusions With increased changes in national healthcare policy, C.U.P. acts as a safety net for those who lose insurance coverage. C.U.P. is a one-of-a-kind patient-centered medical home that allows medical students to care for vulnerable populations facing increased health disparities in Southern Arizona. We believe that this is a valuable and reproducible model that can aid other communities facing similar challenges.

95 BICYCLE ROUNDUP: INCREASING BICYCLE SAFETY AWARENESS IN GLASGOW, MONTANA

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10.1136/jim-2018-000939.95

Purpose of study The Bicycle Roundup seeks to address the issues of bicycle safety in Glasgow, MT. The pediatric population is increasing steadily in this rural community as more young adults are moving back to their community or staying, necessitating the need for the development of bicycle safety programs in the community.

Methods used Throughout community interviews, the focus turned many times onto the children of Glasgow and the

importance of their health and support in the community. From these conversations, connections with Mayor Erickson, Prevention Specialists and Officers at the Glasgow Police Department, as well as community corporations, such as Frances Mahon Deaconess Hospital, Burlington Northern Santa Fe Railway, Montana-Dakota Utilities, and Markle's Hardware, were formed in support of the Bicycle Roundup and its mission to provide free helmets and bicycle safety education to the children of the community.

Summary of results These partnerships were strategically developed with organizations that are willing to continue their support of this event into the future, whether that is through volunteer support by the Police Department, Valley County Sheriff's Office, and the Montana Highway Patrol, or financially through the corporations listed previously. The community welcomed the event and its purpose, and many parents brought their children to learn about safety and to receive a free fitted helmet as well as a bicycle license plate.

Conclusions The Bicycle Roundup is an event that allows the community to address known factors that affect helmet usage, such as cost, peer pressure, and comfort. Increasing access to helmets and knowledge on safety has the opportunity to increase their utilization in the community. The Glasgow Police Department has recently received a grant for use in sponsoring events such as this into the future, ensuring this positive message will continue to impact the community.

Global Health I

Concurrent Session

3:15 PM

Thursday, January 24, 2019

96 USING VIDEO TO IMPROVE DIABETES EDUCATION AND INSULIN SELF CARE IN NEPAL

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10.1136/jim-2018-000939.96

Purpose of study Transition toward urban living in Nepal has been accompanied by a radical increase in diabetes. Near Kathmandu in the town of Dhulikhel, a community hospital has been striving to educate its patients regarding diabetic risk factors, complications, screening and treatment recommendations, and prevention through lifestyle adjustment. This education has been conducted in biweekly sessions reaching about 20–30 patients. The aim of this project was to create a video capturing elements of these sessions so that education accessibility might be increased – the video could be shown on hospital monitors and in community outreach centers in the Dhulikhel area.

Methods used Three nurse educators, a pharmacist, nutritionist, and physical therapist worked together to create scripts for a six-part educational video. During filming, professionals lectured using slides and scripts the team devised. The video was edited using iMovie and underwent three revisions. The first included a reshoot after input from the team regarding errors in content and quality concerns. The second draft was then shown to patients from the various settings and feedback was used to create the third edition, which addressed any

remaining issues. After positive patient reception of this 40 min video detailing type 1 and 2 diabetes, the team made another video 35-minute video on insulin self-injection.

Summary of results Eight healthcare professionals including those who starred in the video evaluated the first version and edits were made. To obtain further qualitative feedback, 30 patients viewed the second draft of the diabetes video and were asked about video clarity as well as overall learning and satisfaction. Notably, patients were asked what they enjoyed about the video and what might be changed, and they were also questioned about what lifestyle changes could be made to manage the disease. Following the video, patients were able to either explain or inquire more deeply about prevention factors including diet, exercise, and smoking cessation. Data collection is ongoing for the insulin video, but staff has given positive feedback to the first edition.

Conclusions The diabetic team hopes to use these videos in the hospital and community due to their informative content and short timespan. The videos may allow countless more patients to receive education about the disease in the Dhulikhel area.

97 ANTENATAL CARE PRACTICES AND DELIVERY SUPPORT IN A RURAL DISTRICT OF NEPAL

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10.1136/jim-2018-000939.97

Purpose of study In the most remote regions of Nepal, it is estimated that up to 8% of women and 20% of newborns do not survive childbirth. Few studies have described current antenatal care practices and delivery support in rural Nepal. The purpose of this study was to gather baseline information regarding current antenatal care practices and access to delivery support in a rural district of Nepal prior to implementing a comprehensive maternal child health (MCH) program.

Methods used The study took place in Solukhumbhu district, Nepal and involved surveys of randomly selected women who had delivered a baby within the previous 24 months. Trained health workers conducted a standardized survey based on WHO recommendations of best MCH practice. The study was approved by the Nepal Ministry of Health and the University of Utah IRB. Data was collected in an app based survey tool and analyzed using STATA.

Summary of results A total of 391 women in 10 townships were surveyed between December 2015 and February 2018.

Maternal care 70% (291/391) had a birth preparedness plan, 52% (202/391) were screened for anemia, 93% (367/391) had blood pressure checks, and 29% (108/368) received oxytocin.

Intrapartum care 22% (84/380) of deliveries had resuscitation equipment available. 35% (136/391) of deliveries occurred in a hospital or birthing center. Complications occurred in 15% (57/391) of deliveries. 33% (126/383) were attended by a skilled birth attendant with training in neonatal resuscitation. Only 37% (142/387) of infants were weighed at birth.

Essential newborn care 76% (262/343) were immediately dried after birth, 23% (79/343) were placed skin-to-skin, and 73% (251/345) were breastfed within the first hour.

Conclusions The majority of women in rural Nepal do not receive high quality healthcare during pregnancy and childbirth. Most women living in the remote regions of Nepal have limited access to antenatal care and deliver at home assisted only by family members. An intervention that would make antenatal care and delivery support more accessible could improve maternal and infant outcomes in those regions. This data will be used to develop a pilot project through a collaboration between the local community, the Ministry of Health, a Nepali based NGO, and the University of Utah.

98 INTEGRATION OF PEDIATRIC RESIDENTS INTO AT-RISK URBAN YOUTH CLASSROOMS TO ADDRESS OBESITY, BULLYING, AND SEX EDUCATION IN IMPOVERISHED COMMUNITIES

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10.1136/jim-2018-000939.98

Purpose of study Adolescents are at risk for engaging in behaviors with lifelong negative health consequences, with those from a lower socioeconomic background at even greater risk. Fresno County, located in the heart of the San Joaquin Valley of California, has rates of obesity, sexually transmitted infections, and teen pregnancy that are higher than the national average, while threats of bullying are also greater in impoverished populations. Although a typical single-session school educational session is unlikely to change long-term behavior, effective and sustainable changes in behavior have been shown to correlate with longer and more intense educational efforts, especially when combined with peer-led educational efforts to improve adolescent health. The UCSF-Fresno Pediatric Residency Program thus partnered with Roosevelt High School students/faculty to develop an interactive peer-led longitudinal curriculum emphasizing the importance of teen decision making.

Methods used To develop the curriculum, residents initiated surveys to identify what the students themselves found interesting and relevant, and utilized a 'youth as partner' approach when developing the curriculum in order to maximize adolescent engagement and active learning.

Summary of results High school students decided that the topics most pertinent to them were nutrition, bullying, and sex. Pediatric residents then collaborated with Roosevelt High School teachers and students to create peer-led lesson plans to educate high school students in these areas.

Conclusions Several factors can affect the ability of pediatric residents to have a sustained presence in community outreach efforts. Peer-led collaborative educational efforts can empower adolescents to initiate positive changes on their own, allowing them to be involved in efforts to initiate and sustain lifestyle changes. This process is now being initiated at 5 new high school sites while expanding the pipeline to include medical students enrolled in the San Joaquin Valley Prime program at the UC Davis School of Medicine.

99

DRIVING SUSTAINABLE BEHAVIORAL CHANGE: A PARTICIPATORY DESIGN APPROACH IMPROVES ORAL HEALTH BEHAVIORS IN AN ISOLATED HIMALAYAN COMMUNITY

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10.1136/jim-2018-000939.99

Purpose of study Previous health screens in a boarding school within Northern India have identified a large proportion of children with dental caries, oral pain, and poor oral self-care. Last year, a participatory design approach was used to devise community generated, self-sustaining solutions to improve oral health. The objectives of the project were to decrease the number of children with cavities and oral pain, increase brushing frequency, and assess whether changes in dental hygiene behaviours are sustainable.

Methods used The main participants in this study were the 530 students age 3 to 19 attending Munsel-ling, a boarding school nestled in Spiti Valley, India. Perspectives of students and select community members were investigated through focused interviews and surveys. These quantitative and qualitative data regarding oral health behaviours and dental complications were analyzed using Microsoft Excel and NVivo. With a participatory design in mind, we used information from the questionnaires and interviews to both inform educational sessions and implement programs aimed at improving oral hygiene.

Summary of results Over one year, there was a 22.8% decrease in dental pain and a 43.5% rise in the number of children brushing at least once per day. Surveys reveal that students and school personnel believed the changes were sustainable. By working with the school, the following community ideas were brought to life: giving donated brushes to children who needed them, installing additional toothbrush storage systems in the student hostels, starting a twice-daily brushing routine, and filming a student-driven collaborative video emphasizing the importance of oral hygiene and nutrition.

Conclusions The improvement in brushing frequency coupled with a decrease in self-reported oral pain suggests that the participatory approach can cause significant behavioural changes in a pediatric population over a short period of time. Such changes, if sustained, can produce a long-term reduction in the burden of oral disease within the community.

100

SUN EXPOSURE, SUN PROTECTIVE BEHAVIOR, AND SKIN CANCER PREVENTION EDUCATION IN THE VIETNAMESE COMMUNITY

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10.1136/jim-2018-000939.100

Purpose of study The purpose of this study was to characterize sun exposure, sun protective behaviors, and sun safety knowledge and perceptions in rural Vietnam.

Methods used We conducted a cross-sectional survey of 245 patients at a free primary care clinic in Long An Province, Vietnam from June 23, 2016 to June 29, 2016. This study was conducted by the Project Vietnam Foundation with support from Tan Tao University.

Summary of results Among the 245 participants, 158 (64.5%) were female, and the mean age was 40.1 years (SD 14.9). A

high percentage of patients reported getting sunburned in the past year (40.4%, 97) and spending at least half of their workday under the sun (35.6%, 86). Male gender and lower education were significant risk factors for increased sun exposure and multiple sunburns ($p < 0.05$). The predominant form of sun protection was protective clothing (long-sleeved shirt, 78.0%; hat, 75.1%; pants 64.9%); however, sunscreen usage was low at 8.6% (21). Some of the reasons for not applying sunscreen include wearing long clothing instead (23.3%), not having sunscreen (16.7%), high expense (14.7%), and inconvenience (18.0%). As high as 65.7% (161) were unaware that suntans are unhealthy, 75.9% (186) did not realize they can get sunburned on a cloudy day, and 59.6% (146) did not know that darker skin can be damaged by the sun.

Conclusions Although much progress has been made in understanding skin cancer and sun safety in skin of color, these topics remain understudied in the native Vietnamese population. Our study findings suggest that the Vietnamese population has high sun exposure and incidence of sunburns, but low awareness of their skin cancer risk. Although incidence of skin cancer is lower in people with skin of color, morbidity and mortality rates have been reported to be higher. This may be due, at least in part, to a more advanced stage at presentation. The native Vietnamese population may therefore benefit from public health efforts in skin cancer prevention education and sun safety.

101

EVALUATION OF A SICKLE CELL DISEASE EDUCATION WORKSHOP FOR MOTHERS IN THE INDIGENOUS THARU POPULATION OF NEPAL

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10.1136/jim-2018-000939.101

Purpose of study Sickle cell disease (SCD) is a non-communicable blood disorder that leads to the production of atypical hemoglobin causing red blood cells to be sickled, increasing occlusion and decreasing oxygen delivery. Previous research estimated a 9.3% prevalence of SCD in the indigenous Tharu people in Nepal, potentially due to the protective nature of SCD against malaria and high intermarriage rates. Early intervention and treatment of SCD can improve quality of life through pain management, and reduction of infections and organ infarct complications. Our team has been working with a local Nepali NGO to improve access to SCD screening and diagnosis since 2015.

Our goal is to develop an effective and sustainable educational workshop that emphasizes the importance of early childhood screening and diagnosis of SCD in rural Nepal.

Methods used We developed a workshop to educate mothers in the communities in the Dang District of Nepal about the importance of early childhood SCD screening and diagnosis. With interpreters, we taught this workshop to local female community health workers (CHW). Three of our trained CHW then travelled to neighbouring villages to deliver this workshop to groups of mothers.

We asked 200 mothers to complete the same nine yes-no question survey before and after attending the session. Seven questions assessed knowledge about SCD while the last two questions probed whether the mothers and their children had been screened for SCD, or if they would get screened after attending the session.

Summary of results The results showed an increase in SCD understanding by a factor of 1.55 ($p < 0.001$) following the session. 88.8% (95/107) of mothers who had not been screened for SCD, and 92.7% (102/110) of the mothers whose children had not been screened said they would get themselves or their children screened now, respectively.

Conclusions In addition to difficult access to screening and diagnostic facilities, the limited knowledge of SCD in the Tharu population of Nepal has been a barrier to early diagnosis and care. By delivering our education program to the community through the local CHW, we begin to address these barriers in a sustainable way. Increasing awareness of SCD contributes to our long-term goal of implementing SCD neonatal screening in Nepal.

102 IDENTIFYING BARRIERS TO HEALTH CARE FOR THE INDIGENOUS THARU POPULATION IN DANG, NEPAL

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10.1136/jim-2018-000939.102

Purpose of study Members of the indigenous Tharu ethnic group inhabiting the Terai (lowlands) of Dang, Nepal face unique health issues including having a high prevalence of hemoglobinopathies such as sickle cell disease (SCD). A recent effort to make SCD detection and management more accessible revealed that health care resources are often inaccessible for individuals suffering from SCD. The purpose of this follow-up qualitative study was to identify themes relating to the local Tharu population's perception of barriers to health-care access. Long term goals include using these findings to improve health-care access and developing a comprehensive SCD-care plan for the region.

Methods used A total of 167 participants were enrolled in 28 focus groups on community health care needs in May 2017. Inclusion criteria included Tharu ethnicity and >7 years of age. Community members were recruited through randomized phone invitations and word-of-mouth, and recruitment was conducted by a local non-profit Nepalese organization that works closely with the Tharu population in Dang. The interviews were conducted in Nepali and Tharu (the local dialect) with the assistance of members of the non-profit organization, recorded, and later translated into English. All interviews were semi-structured with open-ended questions, allowing participants to guide conversation.

Summary of results Analysis from the focus groups revealed three major themes related to barriers in healthcare access: 1) inadequate local resources; 2) the financial burdens of care; and 3) the need for greater health education in the region. Numerous sub-themes within each major theme were identified, such as the limited spectrum of care available at local health posts, the inability to afford the cost of travel to health services, and the general lack of knowledge about health.

Conclusions The specific themes identified can help guide future projects in the region and support advocacy efforts to inform national health policies on sickle cell detection and management. Focusing on addressing the identified barriers to accessing healthcare is fundamental in developing a sustainable, accessible, and comprehensive SCD-care plan as

well as improving the overall health of community members.

103 RAPID BASELINE ASSESSMENT SURVEY OF ANTENATAL CARE IN RURAL INDIA

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10.1136/jim-2018-000939.103

Purpose of study In India, the maternal and neonatal mortality rates are among the highest in the world, Antenatal care aims to prevent and provide early detection and treatment for pregnancy related conditions and is a crucial component for safe childbirth both the mother and the fetus. Delivery of an effective antenatal care program can be challenging, particularly in rural areas where access to care is limited and documentation is difficult. Ther purpose of this survey is to perform a rapid baseline assessment of antenatal care delivery and documentation in rural Gujarat, India.

Methods used This study took place in the villages surrounding the Shree Chhotubhai A.Patel Hospital (SCAPH) and Community Health Center, Gujarat, India. We reviewed existing antenatal care records and interviewed a total of 26 mothers admitted to the hospital after delivery between June and August 2018. The data collection sheet was designed based on current government recommendations for antenatal and was collected by a local field team manager and medical students trained in data collection. Reporting of the current status of antenatal care in rural Gujarat is descriptive.

Summary of results All 26 women interviewed delivered at SCAPH; 8/26 (31%) women were primigravida. Mean birth weight was 2668 grams (range 1870 grams to 3420 grams). 15/24 (62.5%) were born low birthweight. 7/26 (27%) were delivered by caesarean section. All women received at least one ANC visit; 9/26 (35%) had 4 or more ANC visits and 24/26 (92%) used the government ANC report card. 25/26 women had a prenatal US. 20/26 (77%) had hemoglobin checked; 17/20 (85%) women met dx for anemia; mean Hgb value 9.9. All women received routine urine, weight assessments, TT vaccination, PNV and Blood group testing. 4/26 (15%) received counseling of pregnancy danger signs. No women had Hepatitis B testing, HIV testing sickle screening documented.

Conclusions Basic antenatal care services are offered in rural India, but effective delivery of the recommended care has not yet been successful. Continued investigation and gap analyses are needed to determine how to best provide ANC services to this vulnerable population.

104 COMPARING THE LONG TERM FEASIBILITY OF REUSABLE MENSTRUAL HYGIENE MANAGEMENT STRATEGIES IN A POPULATION OF ADOLESCENT FEMALES IN A REMOTE HIMALAYAN COMMUNITY

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10.1136/jim-2018-000939.104

Purpose of study In rural India, women face barriers managing menstruation: limited menstrual hygiene products available, cost and limited disposal options. The Menstrual Hygiene

Management (MHM) project delivered reproductive health workshops and piloted qualitative research to understand MHM product preferences based on personal, cultural and geographic factors in remote, low-resource Himalayan communities. The study explored strategies like reusable cups and pads.

Methods used Munsel-ling Boarding School, located in Spiti Valley, India has a longstanding partnership with UBC, aiming to improve students' long term health outcomes through community-driven projects and education programs. Female students aged 14 years and older who had their first menses were recruited. Each participant was invited to a women's health workshop where they were provided: 1 menstrual cup, 4 reusable pads, cleaning supplies and 1 menstrual diary with training on proper usage and cleaning.

Participants were asked to document monthly for 1 year, their choice of product(s), along with their experience with each product. At the end of the study, diaries were collected and participants were invited for semi-structured individual interviews to assess qualitative and quantitative variables.

Summary of results Of the 42 eligible recruits, 100% chose to enroll in the study, 36% submitted completed diaries and 24% attended focus groups. Attrition was due to graduation/withdrawal from Munsel'Ling, lost diaries and absences/schedule conflicts with focus groups.

Of the participants analyzed, 100% tried reusable pads, 52% reusable cups. After 1 year, 80% were using the reusable pad, 30% the reusable cup and 6.7% other means of MHM.

Conclusions Reusable cups and pads are feasible, culturally appropriate and sustainable alternatives to current MHM practices used by women in remote, low-resource settings. Reproductive health education efforts and increased access to more sustainable and practical MHM methods can improve well-being, reduce environmental impact and empower young women to be leaders and advocates in their communities. Emerging themes from the project are the power of choice of MHM products with factors such as community, reusability, comfort, aesthetic and ease of cleaning playing a role in decision making.

105

IMPROVING KNOWLEDGE OF HYPERTENSION THROUGH A BROCHURE AND POSTER CAMPAIGN IN NAIVASHA, KENYA

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10.1136/jim-2018-000939.105

Purpose of study Heart disease is the fastest growing cause of mortality in Kenya. Over half of adults over age 50 in Nakuru County, where Naivasha is located, have hypertension: over 70% of whom are uncontrolled, with only 15% regularly taking medication and 2% with diet modification. The aim of this project was to promote hypertension awareness through sustainable, community-based education about proper diet, exercise, regular blood pressure checks, and adherence to medication.

Methods used Information regarding hypertension as a cause of cardiovascular disease and how to manage hypertension through balanced diet, exercise, and regular clinic follow-up was synthesized. These messages were then adapted for local culture and with the assistance of health workers associated with Naivasha District Hospital (NDH) and the Kenyan Red

Cross, translated into English and Swahili and placed on posters and brochures. Effectiveness of the materials was measured by comparing scores on a pre-intervention and post-intervention test of hypertension knowledge.

Summary of results A pre-test was provided to 30 community members from Naivasha affiliated with the YMCA to test their baseline knowledge of hypertension. Half of the 30 volunteers received a review of the information in English and in Swahili, as well as given a brochure to take home. A week later, the same test was provided again. The average score of the control group remained approximately the same, 48.6% to 49.6%, whereas the group who received the educational materials had an increase in average score from 51.6% to 68.9%. Posters were placed at the YMCA, Red Cross and the NDH outpatient clinic. Brochures were also available at these locations for interested persons to take home, as well as provided to patients at discharge from NDH. Digital copies of all educational materials were also provided to leaders in these locations to continue to share and print as necessary.

Conclusions This educational project increased knowledge of hypertension as a cardiovascular risk factor, and provided tips on how to manage it comprehensively with balanced diet, exercise and regular follow-up with a physician. The brochures and posters were positively endorsed by community members and the education will be sustainable with the continued provision of the materials by providers at NDH and NDH outpatient clinic.

Hematology and Oncology I

Concurrent Session

3:15 PM

Thursday, January 24, 2019

106

ABSTRACT WITHDRAWN

107

PREDICTORS OF ADHERENCE TO LUNG CANCER SCREENING IN A MULTI-CENTER REFERRAL PROGRAM

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10.1136/jim-2018-000939.106

Purpose of study The National Lung Screening Trial demonstrated a 20% relative reduction in lung cancer-specific mortality with CT-based lung cancer screening (LCS), and LCS is now recommended for high-risk current and former smokers. Mortality benefits may be diminished if adherence to LCS recommendations is low, but there are few studies of adherence in real-world settings. The objectives of this study were to examine LCS adherence and determine key factors associated with adherence.

Methods used This is a retrospective study of participants in a multi-center LCS program who had a baseline screen from

2012 to April 30, 2017 (n=645). The LCS tracking database, electronic health record and radiology reports were reviewed for demographics, CT findings and follow-up information. Recommended follow-up was standardized by the Lung Imaging Reporting and Data System (Lung-RADS). Adherence was defined as completing recommended follow-up within 90 days. Those who died, did not qualify or relocated were excluded from adherence analyses (n=72). We examined factors associated with adherence using chi-squared testing. We used logistic regression to identify independent predictors of adherence.

Summary of results The median age of participants was 63 years and 65% were men. Current (53%) and former (46%) smokers had a median smoking history of 53 pack-years. 90% of screens were negative or probably benign (Lung-RADS 1–3) and 10% had suspicious findings (Lung-RADS 4). There were 18 lung cancers diagnosed (2.8%). Adherence was 46%, and ranged from 39% for normal screens to 87% for participants with Lung-RADS 4 ($p < 0.001$). In a multivariable model, adherence was more likely those older than the median age (OR: 1.52, 95% CI: 1.02–2.27), and former smokers (OR: 1.92, 95% CI: 1.28–2.88). Those with Lung-RADS 3 (OR: 4.03, 95% CI: 1.90–8.58) or 4 (OR: 12.7, 95% CI: 5.35–30.3) were more likely to be adherent.

Conclusions Overall adherence to LCS follow-up was low and adherence was less likely in younger participants and current smokers. The strongest predictor of adherence was a suspicious finding. Interventions are needed to improve adherence, particularly for subgroups who are most likely to benefit from ongoing LCS, such as current smokers and younger high-risk participants.

108

TARGETING PPM1D IN ER⁺ BREAST CANCER WITH NOVEL ANTICANCER COMPOUND LCW20

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10.1136/jim-2018-000939.107

Purpose of study The serine-threonine protein phosphatase PPM1D, also known as PP2C δ or WIP1, is a nuclear type of 2C protein phosphatase (PP2C) that is observed to have high expression in many types of cancers, such as breast cancer, ovarian cancer, gastric carcinomas, and pancreatic adenocarcinoma. Activation of PPM1D has been identified to negatively regulate the stress response pathways (SRP) by inhibiting the p53 dependent response to environmental stress. When PPM1D is activated, it reduces the phosphorylation of p53, which in turns suppress critical proteins for cellular stress response, including p38 MAPK, Chk1, Chk2, and ATM. This phosphatase has been demonstrated to have oncogenic properties and play an essential role in regulating several vital processes for tumor development and progression, such as cell cycle arrest and apoptosis. Therefore, PPM1D is an attractive target for developing therapeutic treatment for cancer. There are a few PPM1D inhibitors in the field, including CCT007093, small molecules SPI-001 and GSK2830371; however, these compounds lack favorable pharmacodynamic and pharmacokinetic characteristics.

Methods used Here, through virtual screening with high-throughout, we have identified a novel PPM1D inhibitor,

LCW20, which has demonstrated to effectively inhibit cell proliferation in ER +breast cancer cell line, MCF-7; while having minimal effect on normal breast cell line, MCF-10A.

Summary of results Treatment with LCW20 was able to elicit inhibition of PPM1D (as assessed by phospho-p38 measurement) and anti-migration characteristic in MCF-7 cell line, suggesting that LCW20 has anti-cancer activities against ER +breast cancer cells through inactivating PPM1D.

Conclusions Therefore, LCW20 has proven to be a promising novel anticancer compound in developing targeted therapy for breast cancer patients with high PPM1D expression.

109

QUALITY INITIATIVE IN CLINICAL PRACTICE: A SINGLE INSTITUTION APPRAISAL OF QUALITY METRICS IN THE MANAGEMENT OF NEWLY DIAGNOSED DIFFUSE LARGE B-CELL LYMPHOMA BASED ON THE AMERICAN SOCIETY OF HEMATOLOGY PRACTICE IMPROVEMENT MODULE

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10.1136/jim-2018-000939.108

Purpose of study In 2014, the American Society of Hematology (ASH) established a practice improvement module (PIM) incorporating quality metrics for management of diffuse large B cell lymphoma (DLBCL). Such PIMs have allowed physicians to monitor quality of care in their practice. We implemented a DLBCL quality improvement initiative (QII) at our institution in January 2015. In appraisal of this initiative, we reviewed the ASH PIM metrics and included several others to assess adherence to guidelines for treatment of DLBCL and to examine the need for institutional improvement.

Methods used Patients who were newly diagnosed with DLBCL and received treatment at our institution from January 2006 through December 2017 were identified. Electronic medical records were reviewed for documentation of ASH PIM quality measures. We also reviewed patients who had assessment of prognosis by revised International Prognostic Index (r-IPI) score, testing for hepatitis C (HCV), HBV, and HIV, chemotherapy education, and the addition of rituximab in the treatment regimen of CD20 +DLBCL.

Summary of results Following implementation of the QII, our institution saw improvements in most quality metrics including reporting of key molecular features (45.45% to 91.6%, $p < 0.0001$), screening for HBV (41.82% to 91.67%, $p < 0.001$) and HIV infections (33.94% to 87.5%, $p < 0.0001$), providing chemotherapy education to patients (92.73% to 100%, $p = 0.053$) and use of rituximab for CD20 +DLBCL (83.64% to 100%, $p = 0.05$). There was no change in the pattern of G-CSF administration (22.42% to 20.83%, $p = 0.828$). All patients had a PET-CT scan for staging and there was a significantly lower use of bone marrow biopsy (61.2% to 33.33%, $p = 0.011$) since the QII.

Conclusions Implementation of a quality initiative and employing standardized metrics can aid in improving institutional quality of care for patients with newly diagnosed DLBCL and allow opportunity to build and ensure better adherence to evolving national and professional patient care guidelines.

110

CYTOKINE PROFILING FOR THE DIFFERENTIATION OF MULTIPLE MYELOMA FROM PATIENTS WITH MONOCLONAL GAMMOPATHY WITH UNKNOWN SIGNIFICANCE

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10.1136/jim-2018-000939.109

Purpose of study To determine if comparing serum cytokine concentrations in samples of normal individuals against those with monoclonal gammopathy of unknown significance (MGUS) and Multiple myeloma (MM) would allow differentiation of MGUS and MM patients based on levels of IL-16 and/or other cytokines. MM is a disease of dysplastic plasma cells that localize to bone marrow, producing high levels of immunoglobulin heavy and light chains, which can lead to hypercalcemia, renal disease, anemia, and bone lesions. MM is often preceded by increased immunoglobulin production but no clinical symptoms referred to as MGUS. Investigation of cytokine profiles of patients with MM has shown that IL-16 expression in bone marrow is increased and is an important growth-promoting factor in the development of myeloma. In tissue culture studies, GM-CSF, B cell activating factor (BAFF), and IL-17 are related to the increase in IL-16.

Methods used A multiplexed cytokine assay was utilized to test patient sera for IL-16, GM-CSF, BAFF, and IL-17 with the goal of creating a monoclonal protein cytokine panel. This study included 13 MM, 14 MGUS and 30 normal patient specimens determined by IFE/SPEP testing and medical review.

Summary of results IL-16 was more strongly expressed in sera from MM compared to MGUS patients (97.3 vs 71.0 pg/mL, $p < 0.05$). BAFF expression was significantly elevated in MGUS patients (986 pg/mL) compared to both MM (262 pg/mL, $p < 0.05$) and normal patients (460 pg/mL, $p < 0.05$). IL-17 and GM-CSF was not expressed in measurable concentrations in any of the patient groups.

Conclusions Using our monoclonal protein panel, we are able to detect significant differences in IL-16 and BAFF concentrations when comparing MM, MGUS and normal patient samples. Detecting these changes in serum cytokines may serve a role in therapeutic monitoring of patients with MGUS and MM as well as following cytokine levels in patients with known MGUS in order to predict when they advance to MM necessitating treatment.

111

THE ASSESSMENT OF THERAPEUTIC AUTOPHAGY INHIBITION IN NF1 MUTATED TUMORS

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10.1136/jim-2018-000939.110

Purpose of study Upregulation of Ras-Raf-MEK-ERK pathway through various mutations is critical across many different tumor types including CNS tumors. Neurofibromin 1 (NF1) protein functions as a tumor suppressor by negatively regulating Ras proteins through GTPase activity. A loss of function mutation in the NF1 gene results in

upregulation/ERK pathway. Neurofibromatosis type 1 (NF1) is one of the most prevalent brain tumor predisposition disorders. NF1 is associated with peripheral nerve sheath tumors (MPNST) as well as optic gliomas and is often resistant to surgical resection. MEK inhibition (MEKi) remains a standard therapy for tumors associated with NF1 although studies have shown development of resistance towards these therapies.

We have previously shown that CNS tumors harboring BRAF^{V600E} mutation exhibit an increase in autophagy. Additionally, we have shown autophagy inhibition improves the response of tumor cells to BRAF inhibition. There has been little investigation on the role of autophagy in NF1 cells. We hypothesize that these cells are autophagy dependent and therefore sensitive to autophagy inhibition. Targeting autophagy could provide a new therapeutic option for a difficult to treat patient population.

Methods used NF1 wild-type and knockout HSC1 λ (immortalized human Schwann) cells were evaluated for response to autophagy inhibition. Pediatric SF188 cells were used as controls. MAPK/ERK pathway upregulation due to NF1 knockout was evaluated via Western Blot analysis. Autophagic activity was assessed via Western Blot analysis of autophagic flux. The efficacy of autophagy inhibition on decreasing cell growth and survival was analyzed via Incucyte growth and CellTiter Glo assays, respectively.

Summary of results NF1 mutated cells demonstrated upregulation of the MAPK/ERK pathway as expected. Preliminary studies show increased autophagic flux in NF1 mutated cells compared to wild-type.

Conclusions Evidence supports increased autophagic dependency in NF1 mutated tumors. Future studies will further characterize how autophagy regulate NF1 driven tumor cells and the specific role of autophagy inhibition.

112

ASSESSING THE QUALITY OF ONLINE INFORMATION FOR CERVICAL CANCER PATIENTS

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10.1136/jim-2018-000939.111

Purpose of study The Internet acts as an important source of information for many cervical cancer patients, but the quality of the resources that patients access can vary widely. Organizations that publish information for cancer patients are also moving beyond traditional websites, and are increasingly engaging with patients on social media platforms such as Twitter, Instagram and YouTube. We sought to systematically evaluate the quality of cervical cancer information resources available against a range of metrics, including content breadth and accuracy, readability, and accountability. We also began to explore whether there may be need to expand our evaluation methodology beyond webpages to include social media.

Methods used We performed an internet search using the term 'cervical cancer' using Google and two meta-search engines, Dogpile and Yippy. We evaluated the 100 websites returned across all three engines using a validated structured rating tool. We recorded the number of websites maintaining a presence on a social media platform and the number hosting YouTube videos targeted to cancer patients.

Summary of results Websites provide the most coverage for etiology, risk factors, and prevention (>90% of websites). Most content categories were well covered (>74%), except for prognosis (49%), staging (52%), side effects (47%), and follow up (25%). The content provided was completely or mostly accurate for most topics; few websites had inaccurate information. There was no listed author on 68% of websites and no references on 62%. Only 64% had been updated in the last two years. Readability was at least university-level for 19% of websites, and at least high-school level for 78%. For social media, 79% of the websites linked to at least one platform, averaging 4.1 different platforms; 32% hosted information videos for cancer patients on YouTube.

Conclusions While some topics such as screening are well covered, many important topics like prognosis are underrepresented. Most websites are accurate, but many lack accountability or recent updates. Advanced reading levels may impact accessibility for patients. Many websites that provide information to patients also maintain a social media presence; updating our methodology to evaluate the quality and types of information shared on these platforms may represent an important avenue for future work.

113 ADENOVIRUS HEPATITIS AS THE INITIAL PRESENTATION OF ACUTE LYMPHOBLASTIC LEUKEMIA

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10.1136/jim-2018-000939.112

Case report A 13-year-old female presented to the ED with 10 days of pruritus, 2 days of scleral icterus, headache, generalized malaise and decreased appetite. Upon presentation, patient was afebrile and non-toxic appearing. Labs showed hemoglobin of 13 g/dl, white blood cell count (WBC) of 4,200/mm³, platelets of 154 K/mm³, total bilirubin of 4.0 mg/dl, and transaminitis with aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of 548 and 741 U/L, respectively. Hepatitis panel and mono screen were negative. Abdominal ultrasound showed no gallstones or hepatic lesions. She was diagnosed with a likely viral illness.

One week after that initial visit, she returned to the ED due to diffuse abdominal pain, RUQ fullness and an urticarial rash. Her icterus and pruritus had resolved at this time. She was febrile to 101.1 F. A weight loss of 3 lbs was also noted in the past week. A repeat abdominal ultrasound was unremarkable. CMP showed total bilirubin was improved, now 1.4 mg/dl with direct bilirubin of 0.8 mg/dl. Her transaminitis also improved with AST and ALT of 108 and 312 U/L, respectively. However, she was now bicytopenic with WBC of 1,000/mm³ and hemoglobin of 10.2 g/dl. Her CRP and ESR were elevated at 12.9 mg/L and 47 mm/hr, respectively. Her absolute neutrophil count (ANC) was abnormally low at 350/mm³ and reticulocyte count was also found to be low at 0.3%. Over the course of her hospitalization, she became hemodynamically unstable and was persistently febrile. Ultimately, she stabilized with fluid resuscitation and empiric triple antibiotic therapy. Flow cytometry showed a small population of circulating

lymphoid blasts and a bone marrow aspiration confirmed the diagnosis of B-cell ALL. Eventually EBV, CMV, ANA and autoimmune hepatitis panel were all negative. Adenoviral IgM was elevated at 1:128.

Immunocompromised persons are at high risk for fulminant hepatitis and disseminated infections caused by HAdV. Although viruses can present as severe illnesses causing pancytopenia, this case highlights the need to pursue further investigation in patients presenting with severe adenovirus infections for B-ALL. Further research would be needed to identify other viral associations that immediately precede diagnoses of cancer.

114 LEPTOMENINGEAL CARCINOMATOSIS FROM CARCINOMA OF UNKNOWN PRIMARY

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10.1136/jim-2018-000939.113

Case report

Purpose of study Leptomeningeal metastases are a rare but frequently devastating complication of advanced cancer. The most common solid tumors giving rise to leptomeningeal metastases are breast, lung, melanoma and cancers of unknown primary. We are presenting a rare case of leptomeningeal metastases from carcinoma of unknown primary with increased intracranial pressure.

Methods Retrospective chart review.

Summary of results A 32-year-old Hispanic woman who initially presented with shortness of breath and was found to have mediastinal and retroperitoneal lymphadenopathy. Biopsy of the mediastinal node revealed poorly differentiated carcinoma positive for cytokeratin and placental alkaline phosphatase (PLAP) suggestive of germ cell tumor vs carcinoma of unknown primary. She received 3 cycles of Carboplatin and Docetaxel with significant improvement. However, she started to have headaches. MRI brain revealed leptomeningeal enhancements suggestive of leptomeningeal carcinomatosis. She was started on intrathecal methotrexate. After the injection, she developed worsening of headaches with photophobia and meningismus. Lumbar puncture (LP) was repeated and showed significant elevation of cell count to above 400 which turned out to be malignant cell with opening pressures of 600 mmH₂O. Serial LPs performed to reduce pressure. She developed fever but her infectious workup came back negative. Given worsening of symptoms, patient was switched to Cytarabine IT twice a week. Serial brain imaging did not show hydrocephalus but due to need for frequent LPs lumbar drain was suggested. Repeated cytology of CSF showed persistent presence of malignant cells plus placental alkaline phosphatase. In the attempt to find the primary source a repeat biopsy of cervical lymph node performed which showed the cytokeratin profile and expression of cdx2 are most consistent with intestinal differentiation. She developed a hematoma at the serial LP site and in light of severe leptomeningeal disease which confers a poor prognosis, the patient and her family proceeded with comfort care measures at hospice prior to any diagnostic investigation.

Conclusion Leptomeningeal carcinomatosis has a poor prognosis and clinicians should have high level of suspicion in the right clinical settings for prompt diagnosis.

Neonatology General II

Concurrent Session

3:15 PM

Thursday, January 24, 2019

115 ERYTHROCYTE-COATED NANOPARTICLES REDUCE CYTOTOXIC EFFECTS OF GROUP B *STREPTOCOCCUS* (GBS) BETA-HEMOLYSIN/CYTOLYSIN (β -H/C)

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10.1136/jim-2018-000939.114

Purpose of study GBS β -H/C toxin induces necrosis of host cells, thereby enabling microbial dissemination by way of immune defense subversion. Human red blood cell (hRBC)

membrane-coated nanoparticles, or 'nanosponges' (NS), are non-specific biomimetic 'decoys' with the ability to neutralize toxins including β -H/C. We demonstrate that hRBC-NS can successfully inhibit GBS β -H/C toxin, preserve epithelial viability, and decrease mortality in murine GBS sepsis models.

Methods used Hemolysis assays employing: (1) stabilized β -H/C toxin, (2) different strains of GBS known to produce varied amounts of β -H/C, and (3) β -H/C knockout mutants (Δ cylE) as negative controls were completed following exposure to hRBC-NS. Cell viability assays on A549 lung epithelial cultures exposed to either live bacteria or stabilized β -H/C were also completed using ATP-based cytotoxicity assays.

Summary of results The use of hRBC-NS reduced the hemolytic activity of each live GBS strain and stabilized β -H/C in a dose-dependent manner. Δ cylE mutant strains demonstrated no hemolytic activity. Cytotoxicity assays on A549 cultures exposed to live GBS bacteria or stabilized β -H/C have reduced cell death when the cells are treated with hRBC-NS.

Conclusions hRBC-NS is a detoxification strategy that may provide a novel treatment option for neonatal sepsis by inhibiting toxin activity.

Abstract 115 Figure 1 Hemolysis by different strains of GBS (A), by NCTC GBS (B). Hemolysis by NCTC GBS is reduced in a dose-dependent manner by hRBC-NS treatment (C). Hemolysis by β -H/C extract in different quantities (D), and subsequent dose-dependent reduction in hemolysis by hRBC-NS (E). A549 lung epithelial cells have improved viability when treated with hRBC-NS while infected with (F) 2 ul β -H/C extract, (G) 5 ul β -H/C extract, and (H) live NCTC GBS at MOI 20

116

IN VITRO INHIBITORY POTENCY OF ZINC PROTOPORPHYRIN MICROSPHERES ON HEME OXYGENASE ISOZYME ACTIVITY

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10.1136/jim-2018-000939.115

Purpose of study Heme oxygenase (HO) is the rate-limiting enzyme in the bilirubin production pathway and exists as 2 well-described isozymes: HO-1 and HO-2. Synthetic heme analogs (metalloporphyrins) are competitive inhibitors of HO, and thus have potential as chemopreventive drugs for treating neonatal hyperbilirubinemia. Identification of metalloporphyrins that can selectively inhibit the inducible HO-1 without affecting the constitutive HO-2 isozyme is the most desirable. We have shown that zinc protoporphyrin (ZnPP) shows the most promise but is not orally absorbable. Thus, to enhance its oral absorptivity, we have designed a formulation of ZnPP incorporated in lipid microspheres. In this study, we evaluated the *in vitro* potency and selectivity for the inducible HO-1 isozyme of this formulation.

Methods used Adult male FVB (29–33 g) were sacrificed to harvest spleen (primarily HO-1) and brain (primarily HO-2) tissues. Various concentrations of ZnPP microspheres were added to reaction mixtures containing tissue sonicates, heme, and NADPH. HO activity was determined using gas chromatography and expressed as pmol carbon monoxide/h/mg fresh weight. Percent inhibition of HO activity was calculated and the concentration of ZnPP microspheres to inhibit HO activity by 50% or I_{50} was interpolated and compared with the native ZnPP. A selectivity index (SI) for HO-1, defined as the I_{50} for HO-2 (brain) over the I_{50} for HO-1 (spleen), was calculated.

Summary of results ZnPP microspheres at concentrations of 0.26–2.0 μ M decreased *in vitro* HO activity 30%–76%, and 27%–68% in the spleen and brain, respectively. I_{50} 's were 0.625 μ M for both spleen (HO-1) and brain (HO-2), respectively, with a HO-1 SI of 1.00. These I_{50} values were lower and hence resulted in a higher HO-1 SI compared with those we found for the native ZnPP (7.75 and 6.75 μ M for spleen and brain, respectively, with a HO-1 SI of 0.87), suggesting that the presence of the lipid microspheres increases the inhibitory potency and HO-1 selectivity of ZnPP.

Conclusions The incorporation of ZnPP in lipid microspheres not only allows increased oral absorptivity, but also appears to increase the potency and HO-1 selectivity of ZnPP. We therefore conclude that ZnPP microspheres has potential for use in the treatment of neonatal hyperbilirubinemia.

117

A NOVEL POINT-OF-CARE DEVICE FOR MEASURING GLUCOSE-6-PHOSPHATE DEHYDROGENASE ENZYME DEFICIENCY

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10.1136/jim-2018-000939.116

Purpose of study Neonatal jaundice occurs in up to 80% of otherwise healthy, term and late-preterm newborns during the first week of life and is usually benign and transitional. However, in newborns who are undergoing hemolysis, extreme hyperbilirubinemia can occur and lead to bilirubin neurotoxicity if not treated in a timely manner. Infants at a particularly

high risk are those with glucose-6-phosphate dehydrogenase (G6PD) deficiency (affects 3.5% of all births), who need to be identified early so that exposures to known triggers of hemolysis can be avoided. Here, we evaluated a novel prototype device that quantitatively measures G6PD enzyme activity using a digital microfluidics platform.

Methods used G6PD enzyme activity was quantified using FINDER (Baebies, Inc, Durham, NC), which measures fluorescence kinetically on ~50 μ L of whole blood. We first evaluated intra- and inter-instrument and intra- and inter-day imprecision (CVs) using 2 instruments on blood donated by a normal adult male. The assay was performed by 2 separate operators. We then measured G6PD activity in a convenience sample of 19 discarded blood samples using FINDER, which were compared with those measured by a reference laboratory by linear correlation and Bland-Altman analyses.

Summary of results Overall reproducibility for the assay across 5 days performed by 2 operators on 2 instruments was 4.8%. Mean intra- and inter-instrument variabilities were 3.3% and 3.4%, respectively (n=28), with a user variability of 5.3%. Mean (range) G6PD activity was 5.81 ± 4.33 (0.21–15.01) and 5.92 ± 4.65 (0.10–15.00) U/g Hb for FINDER and reference method, respectively, (patient age range: 1-mos–69 years). FINDER strongly correlated with the reference laboratory (r^2 of 0.93; slope=0.90; y-intercept=0.50) with a mean bias of -0.11 ± 1.28 U/g Hb.

Conclusions The prototype instrument can measure G6PD enzyme activity reproducibly in bench studies. In the clinical setting, FINDER was found to highly correlate with the standard biochemical test with minimal bias and imprecision. We conclude that the instrument could be used as an accurate point-of-care screening tool for early newborn G6PD screening. Its clinical performance and diagnostic utility need to be further validated in a multicenter observational study.

118

BILIRUBIN PRODUCTION IS INCREASED IN NEWBORN MICE TREATED WITH LIPOPOLYSACCHARIDE

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10.1136/jim-2018-000939.117

Purpose of study Heme oxygenase (HO) is the rate-limiting enzyme in the bilirubin production pathway. Increased bilirubin production due to hemolysis can lead to severe neonatal hyperbilirubinemia and if left untreated, to bilirubin neurotoxicity. Neonatal sepsis is a known risk factor for severe hyperbilirubinemia, however, the underlying mechanisms have not been well studied. Lipopolysaccharide (LPS), an endotoxin derived from the outer membrane of Gram-negative bacteria, is commonly used to induce systemic inflammation in animal models. Here, we evaluated whether an exposure to LPS induces HO-1 in newborn mice and further increases bilirubin production after heme loading.

Methods used 3d-old newborn FVB mouse pups were injected with LPS (1,250 μ g/kg, s.c.) or saline (controls). At 24, 48, 72 and 96 hour post-LPS treatment, pups were sacrificed and total liver HO enzyme activity was measured by gas chromatography (GC). Next, to evaluate whether the LPS-mediated HO-1 induction increases *in vivo* bilirubin production rates, pups were given a heme load (18 mg/kg, s.c.) 24 hour after LPS treatment. Pups were then placed in 5 mL chambers supplied with air (~13 mL/min) for measurements of bilirubin

production as indexed by total body carbon monoxide (CO) excretion rates (VeCO) and monitored up to 4 hour. All data were expressed as percent of age-matched control (HO activity) and fold change over baseline (VeCO) levels.

Summary of results LPS significantly increased liver HO activity $137\% \pm 13\%$ ($n=6$, $p<0.0001$), $137\% \pm 11\%$ ($n=6$, $p<0.001$), and $107\% \pm 6\%$ ($n=7$, $p=0.05$) at 24, 48 and 72 hour, respectively, post-exposure. HO activity returned to control levels by 96 hour ($105\% \pm 7\%$, $n=6$). Compared with heme-only treated pups ($n=5$, 2.90 ± 0.42 fold, 192 ± 15 min), bilirubin production in heme-treated LPS-exposed pups ($n=6$) was higher (3.91 ± 0.77 fold) and peaked earlier (167 ± 21 min), translating to a 1.35-fold ($3.91/2.90$, $p=0.03$) higher peak VeCO.

Conclusions We conclude that LPS exposure can induce HO-1 expression in the liver and may explain the development of severe hyperbilirubinemia in septic infants, especially in those undergoing hemolysis.

119 INCREASED RATE OF CHORIOAMNIONITIS AMONG PREGNANT IMMIGRANT WOMEN LIVING IN UTAH

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10.1136/jim-2018-000939.118

Purpose of study Immigrants represent a unique population living in the United States. Over 43 million immigrants currently live in the United States, approximately 13% of the total population. Many immigrants experience barriers to accessing healthcare. The outcomes of pregnant immigrant women and their infants are not well described in the current literature. The purpose of this study is to describe the outcomes of pregnant immigrant women and their infants living in Utah.

Methods used Birth certificate data from the Utah State Department of Health was reviewed. Logistic regression models were created using STATA. Immigrant status was defined as women born outside the United States. Immigrants were also compared using World Bank categories to look for trends in outcomes by world region.

Summary of results Immigrant women living in Utah gave birth to 59 244 infants between 2009 and 2016, 14.1% of all births in Utah. As a combined group, immigrant women had a lower odds of preterm birth, a higher odds of having a low birth weight infant, and no difference in the rate of admission to the Neonatal Intensive Care Unit (NICU). Immigrant women were found to have an increased odds of clinically diagnosed chorioamnionitis [OR 1.4 $p<0.001$]. Immigrants from South Asia had the highest odds of chorioamnionitis [OR 3.3 $p<0.001$]. Odds of chorioamnionitis varied by country of birth with the highest odds among women born in Bhutan [OR 5.0 $p<0.001$], Iran [OR 4.8 $p<0.001$], and Nepal [OR 3.6 $p<0.001$]. Infants of immigrant women from South Asia were found to have a higher odds of admission to the NICU [OR 1.4 $p<0.001$].

Conclusions Immigrant women appear to have higher rates of chorioamnionitis that vary by maternal country of birth. This may be due to barriers to accessing healthcare, differences in pregnancy practices, or differences in native bacterial flora. It is possible that the higher prevalence of chorioamnionitis is leading to an increased risk of infection among their infants and the higher rate of NICU admission. Future studies will focus on NICU based data to determine reason for NICU admission, length of hospital stay and long-term outcomes.

120

RETICULOCYTE HEMOGLOBIN AND FERRITIN AS MARKERS OF IRON DEFICIENCY IN THE NEONATE

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10.1136/jim-2018-000939.119

Purpose of study Preterm infants are at great risk for iron deficiency due to substrate demands for growth, erythropoiesis and brain development. Exogenous erythropoietin (EPO) further increases this demand for iron. Specific monitoring guidelines are currently lacking. This study will evaluate the potential utility of reticulocyte hemoglobin levels in ongoing monitoring of iron sufficiency in stable preterm infants who are receiving EPO to stimulate red cell production.

Methods used We performed a retrospective chart review of 117 preterm infants treated at the University of New Mexico newborn ICU in 2017–2018.

Summary of results Average gestational age of EPO-treated infants was 29w6d compared to 32w6d in non-treated infants ($p<0.01$). Mean initial ferritin concentrations prior to EPO administration did not differ significantly between EPO-treated and non-treated infants at 250 ng/mL and 202 ng/mL respectively. Treated infants showed a rapid response to EPO, and mean ferritin concentrations decreased to 61 ng/mL. An inverse relationship between ferritin concentration and absolute reticulocyte count indicated active erythropoiesis in EPO-treated infants ($R=0.57$, $p<0.01$). Ferritin concentrations positively correlated with reticulocyte hemoglobin in EPO treated infants ($R=0.58$, $p<0.01$).

Conclusions The addition of reticulocyte hemoglobin to routine monitoring for iron status in EPO-treated preterm infants is feasible, and correlates with ferritin concentrations in stable preterm infants.

Neonatology Pulmonary II

Concurrent Session

3:15 PM

Thursday, January 24, 2019

121

COMPARISON OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE WITH LOW FLOW OXYGEN VERSUS HEATED, HUMIDIFIED HIGH FLOW NASAL CANNULA FOR ORAL FEEDING OF THE PREMATURE INFANT (CHOMP TRIAL): A PILOT STUDY

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10.1136/jim-2018-000939.120

Purpose of study Preterm infants born before 28 weeks gestation are at risk for chronic lung disease and are usually dependent on non-invasive positive pressure ventilation (NIV) during their NICU course. This dependence on NIV may prevent them from starting oral feeds at a time during their development optimal for learning how to simultaneously breathe, suck and swallow. In extreme cases, this can lead to oral

aversion and a need for gastrostomy tubes. What is not known is which NIV device will continue to support their lungs and allow them to orally feed safely. The primary objective of our study was to assess whether a baby born at less than 28 weeks gestation who is 34^{0/7} weeks corrected gestational age and requiring non-invasive ventilation, will reach full oral feeds sooner on nCPAP or HHHFNC plus low flow oxygen (LF).

Methods used In this single center randomized control trial from 2014–2016, we assigned 40 preterm infants (born at <28 weeks EGA) dependent on nCPAP at 34+0 weeks CGA to either nCPAP +LF group or HHHFNC+LF group. All infants enrolled in the study were placed on an oral feeding protocol with breast and/or bottle feeds. Secondary outcomes included time on non-invasive ventilation, BPD, apnea accompanied by desaturation and/or bradycardia, feeding intolerance and weight gain. Statistical analysis of the primary outcome was performed with the Wilcoxon Rank Sum test.

Summary of results 40 infants were randomized to two intervention groups. Of these, 15 (38%) were transferred or broke protocol. 25 infants (12 in nCPAP group and 13 in HHHFNC group) in total concluded the trial. The days to full oral feeds between the nCPAP and HHHFNC groups were 36.5 days (Interquartile range 25.5, 43 days) and 29 days (IQ range 20, 44 days) respectively. P value=0.35. There were no significant differences in the secondary outcomes between the two groups.

Conclusions Despite the small sample size and lack of statistical significance, there was a trend towards a faster time to full oral feeds in the HHHFNC+LF group compared to the nCPAP +LF group.

122 PERINATAL NICOTINE EXPOSURE-INDUCED OFFSPRING ASTHMA PHENOTYPE TRANSMITTED VIA MALE VS. FEMALE GERM LINE

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10.1136/jim-2018-000939.121

Purpose of study In a well-established rat model, we have recently demonstrated that perinatal nicotine (Nic) exposure-induced hyperresponsive lung phenotype, which is transmitted transgenerationally (TG), and this transmission is sex-specific, with a more pronounced phenotype in males in both F1 and F3 generations. Evidence suggests that finely-tuned developmental programs like that of the lung may be affected by specific environmental challenges in a sex-specific manner, however, whether this is true for the TG transmission of the Nic-induced lung phenotype and whether it is transmitted via the male vs. female germ line are not known.

Methods used Pair-fed pregnant Sprague Dawley rat dams received diluent or Nic 1 mg/kg daily from e6 until postnatal day (PND) 21. Following delivery at term, F1 pups were breast fed ad libitum.

Some F1 rats were weaned at PND21 to serve as F2 breeders. At PND60, NIC-exposed males (NM) in F0 pregnancy were mated with naïve (non-nic exposed females, CF) in F0 pregnancy (NM ×CF), or vice versa (NF ×CM), to generate F2 offspring, without any subsequent exposure to Nic. At PND21, F2 pups were studied to determine pulmonary function (total airway resistance and compliance) and tracheal tension response in a sex-specific manner.

Summary of results Since, we have previously noted a more robust perinatal Nic-induced asthma in males, only male data are presented. Compared to controls (CF ×CM), there was a significant increase in total airway resistance and decrease in total airway compliance after methacholine (Mch) challenge in both NM ×CF and NF ×CM male offspring, indicating a clear asthma phenotype. Similarly, compared with CF ×CM group, there was a significant increase in the tracheal constriction response to acetylcholine in both NM ×CF and NF ×CM male offspring.

Conclusions Based on pulmonary function data, the Nic-induced TG transmission of asthma appears to be mediated in a non-selective manner, i.e., via both male and female germ-lines. It suggest that Nic's effect on germline epigenetics are either exerted on primordial germ cells before their differentiation into male and female germline or these effects are non-specific, i.e., affecting male and female germline similarly. Grant support: HL127137, HD071731 (NIH); 23RT-0018 and 27IP-0050 (TRDRP).

123 TLR4 MEDIATED NEONATAL LUNG INJURY IS NOT SEX SPECIFIC

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10.1136/jim-2018-000939.122

Purpose of study Perinatal exposure to inflammatory stress (chorioamnionitis, sepsis) is an independent risk factor for developing bronchopulmonary dysplasia. Previous studies have demonstrated that there is a sex-specific response to various stimuli injurious to the lung, with injury being more significant in males vs. females. Whether there is a sex-specific response to TLR4 mediated lung injury in the neonatal period is unknown.

Methods used Neonatal(P0) male and female mice were exposed to LPS(IP; 5 mg/kg; 0/1/5 hours and 7 days). Lung surface area (SA), medial linear intercept(MLI) and airspace area(ASA) were determined(Metamorph). Baseline expression of TLR4 innate immune signaling was examined by Western blot and qPCR. The expression of pro-inflammatory target genes and signaling pathways previously demonstrated to show sex-specific differences in hyperoxia-induced neonatal lung injury was assessed. n=4–6 animals per group, all performed in triplicate.

Summary of results Early postnatal LPS exposure caused significant lung injury in both male and female mice, as measured by decreased SA, increased MLI and ASA (p<0.05). The degree of injury was not significantly different between sexes. The baseline expression of TLR4, MyD88, p50, p65, and cRel was similar in male and female neonatal mice. Interestingly, LPS exposure significantly increased the expression of pro-inflammatory target genes previously demonstrated to be associated with neonatal lung injury (IL-6, IL-1b, Cxcl1, Cxcl2, and TNF-a), and this did not differ between male and female mice. Previous studies have implicated NFkB signaling in sex-specific response to neonatal hyperoxic lung injury. Here, NFkB activity, as measured by inhibitory protein degradation and p65/p50 nuclear translocation, was similar in LPS-exposed neonatal male and female mice.

Conclusions Pulmonary expression of key regulators of TLR4 innate immune signaling is similar in male and female neonatal mice. In contrast to hyperoxia-induced neonatal lung injury, TLR4 mediated injury is not sex specific. These results

suggest that there may be unique mechanisms of injury following exposure to LPS-induced systemic inflammatory stress, and targeting these pathways may attenuate lung injury in both male and female high-risk infants.

124 STRAIN DIFFERENCES IN THE TRANSCRIPTOME OF MONONUCLEAR PHAGOCYTES HIGHLIGHT THE GENETIC BASIS FOR INTERINDIVIDUAL DIFFERENCES IN PULMONARY IMMUNITY

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10.1136/jim-2018-000939.123

Purpose of study Mice differ in their response to respiratory disease. However, the genetic basis of susceptibility to lung inflammation is not known. Determination of the genes conferring susceptibility or resistance would be an important advance in the understanding of pulmonary immunity.

Methods used C57BL/6J and DBA/2J mice sensitive and resistant, respectively, to inflammation were examined for transcriptomic differences in lung mononuclear phagocytes (MP). Alveolar macrophages (AM), interstitial macrophages (IM), and monocytes (Mo) were isolated from the lung by fluorescence-activated cell sorting. Gene expression was determined by RNA-seq. Open regions of chromatin were determined using ATAC-seq. Data were analyzed with HOMER and MMARGE. **Summary of results** Lung MP from C57BL/6J and DBA/2J mice showed distinct gene expression profiles. Clustering of RNA-seq data from both strains segregated samples by cell type with strain as a secondary determinant. We identified several strain-specific genes for each MP. For example, AM from C57BL/6J mice were enriched in mitosis genes whereas AM from DBA/2J mice were enriched in tissue remodeling. The transcripts that most distinguish AM in both strains are enriched in fat cell differentiation and cholesterol metabolic process. Transcripts that most distinguish IM are enriched in genes associated with the inflammatory response and leukocyte migration. To further explore the molecular determinants of MP diversification, we analyzed the effects of genetic background on chromatin accessibility. We found >11 000 regions that showed at least 2-fold difference in each lung MP subset and identified putative transcription factors underlying the phenotype of lung MP.

Conclusions The core set of genes present in both strains in each lung MP subset highlights essential functions underlying

the phenotype of these cells. A significant fraction of each cell type's most distinguishing transcripts are not shared within both strains. The magnitude of interstrain variability in gene expression in lung MP under baseline conditions could form the basis for understanding human interindividual variability in susceptibility to respiratory disease.

125 RATES FOR BRONCHOPULMONARY DYSPLASIA VARY BASED ON DEFINITION AND CORRECTION FOR ALTITUDE

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10.1136/jim-2018-000939.124

Purpose of study Various definitions for bronchopulmonary dysplasia (BPD) exist. Current respiratory support strategies can hinder use of these definitions. We have shown increased rates of BPD at high altitude which decrease with FiO₂ correction for altitude. Our objective was to assess the effect of altitude correction on BPD rates using 3 different BPD definitions.

Methods used This is a retrospective review of prospective data on neonates <30 weeks GA at the University of Utah NICU from 1/2010 – 12/2017. BPD was defined using the following definitions: 2001 NICHD Consensus (Jobe, Am J Respir Crit Care Med, 2001), 2018 NICHD Consensus (Higgins, J Pediatr, 2018), and Jensen (PAS 2018). Effective FiO₂ was determined at 36 weeks PMA based on weight, cannula flow rate and FiO₂ using Benaron and Benitz's equation (Arch Pediatr Adolesc Med, 1994). Altitude correction performed via ratio of average barometric pressure (BP) in our unit of 640 mmHg (BP at 5000 feet) to 760 mmHg (BP at sea level).

Summary of results 697 infants were identified (EGA 27.0±1.9 wks, BW 959±303 g). BPD rate was inversely proportional to EGA. BPD rate significantly decreased following altitude correction for all gestational ages (p<0.001) using 2001 NICHD definition and for the 27–29 week subgroup and overall (p<0.001) by the 2018 NICHD definition. There was no need for altitude correction with the Jensen definition (p=1). Post-altitude correction, 2001 NICHD BPD rates were significantly higher for all gestational ages (p<0.001) compared to Jensen and 2018 NICHD BPD definitions.

Conclusions Moderate to severe BPD rates differ based on the definition used. Altitude has less of an effect with the

Abstract 125 Figure 1

proposed 2018 NICHD BPD definition and no effect by the Jensen model, and may not need correction at our altitude. Further studies assessing the optimal BPD definition seem warranted.

126 DOES THE NRN BPD PREDICTION ALGORITHM CORRECTLY IDENTIFY BPD RISK USING DIFFERENT BPD DEFINITIONS AT ALTITUDE?

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10.1136/jim-2018-000939.125

Purpose of study To assess the validity of the Neonatal Research Network (NRN) BPD prediction tool after altitude correction using 3 different BPD definitions.

Methods used This is a retrospective review of prospective data on neonates <30 weeks GA at the University of Utah NICU from 1/2010–12/2017. BPD was defined based on the following definitions: 2001 NICHD Consensus (Jobe, Am J Respir Crit Care Med, 2001), 2018 NICHD Consensus (Higgins, J Pediatr, 2018) and Jensen (PAS 2018). Probability of death and/or moderate-severe BPD was calculated at 14 days of age using NRN BPD outcome estimator (<https://neonatal.rti.org>). Effective FiO₂ was determined by Benaron's equation (Arch Pediatr Adolesc Med, 2014) and corrected for altitude via ratio of average barometric pressure (BP) in our unit of 640 (BP at 5000 feet) to 760 (BP at sea level). Area under the curve (AUC) analysis and positive predictive values (PPV) were determined.

Summary of results 697 infants were identified (EGA 27.0±1.9 wks, BW 959±303 g). After altitude correction, moderate-severe BPD rates were significantly different by definition (2001 NICHD 41% vs 2018 NICHD 30% vs Jensen 23%; p<0.001). Probability risk of BPD or death by AUC was similar at 14 days for the 3 BPD definitions (figure 1). PPV for BPD or death varied based on BPD definition used (table 1) and increased as percentage risk of BPD or death increased.

Conclusions With correction for altitude, the NRN BPD outcome predictor at day of life 14 remains a useful tool in

Abstract 126 Figure 1

Abstract 126 Table 1

Predictive Risk	2001 NICHD	2018 NICHD	Jensen
≤60%	80%	65%	55%
≤70%	84%	70%	59%
≤80%	85%	76%	61%
≤90%	90%	86%	71%

determining risk of moderate-severe BPD or death in our NICU population when using recently proposed BPD definitions.

127 THE URINARY METABOLOME AND BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS TREATED WITH INHALED NITRIC OXIDE

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10.1136/jim-2018-000939.126

Purpose of study Recent findings suggest that inhaled nitric oxide (iNO) decreases bronchopulmonary dysplasia (BPD) in preterm infants of maternal Black/African American race/ethnicity (AA) but not in infants of maternal non-Hispanic White race (White). We assessed whether inhaled NO therapy and the development of BPD is characterized by changes in the urinary metabolome.

Methods used Using 171 preterm infants of three racial/ethnic groups from the Trial of Late Surfactant Study (TOLSURF), global metabolic profiles were measured on urine collected at study entry prior to iNO initiation (6–14 days postnatal age, off iNO) and again after receiving iNO at 20, 10 and 5 ppm (23–30 days postnatal age). Changes in individual metabolites (Metabolon, Inc.) were assessed using ANOVA, and shifts in the global metabolome were evaluated using a principal component analysis and random forests.

Summary of results We detected 1033 different biochemicals, of which 262 varied by postnatal age, 208 by race/ethnicity, and 52 by BPD at 36 weeks PMA (p<0.05). In AA but not White infants, BPD cases had significantly decreased levels of 3 neurotransmitters (histamine, N-acetylhistamine, serotonin with BPD Yes/No ratios of 0.20, 0.81, 0.63) and increased cystine and cysteine sulfinic acid (1.29, 1.29). Comparing time point 2 vs 1, levels of kynurenate, an inflammatory metabolite of typtophan, were significantly reduced in BPD infants of all racial/ethnic groups (0.63–0.81); in AA but not White infants, cysteine and metabolites were reduced in BPD infants (0.51–0.70), and polyamines (putrecine, spermidine, 4.43, 1.46) were increased in No BPD infants.

Conclusions In a cohort of high-risk premature infants, we identified individual urinary metabolites and pathways that were associated with development of BPD, with several occurring in AA but not White infants. The findings implicate racial differences in metabolism, likely including metabolism of both endogenous and inhaled nitric oxide, that may contribute to respiratory outcome and are consistent with observed epidemiological data on rates of BPD following iNO treatment.

128

DOCOSAHEXAENOIC ACID CAUSES A DOSE-DEPENDENT DECREASE IN LUNG FATTY ACID BINDING PROTEIN 4 IN POSTNATAL GROWTH RESTRICTED RAT PUPS

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10.1136/jim-2018-000939.127

Purpose of study Despite advances in medical management of preterm infants, bronchopulmonary dysplasia (BPD) remains a major concern. A hallmark of BPD is impaired alveolar formation, and poor postnatal growth and inadequate nutrition contribute. One molecular mediator important in alveolar formation is peroxisome proliferator activated receptor gamma (PPAR γ). We demonstrated that postnatal growth restriction (PGR) reduces lung PPAR γ protein abundance in male rat pups only. We also showed the simultaneous decrease in circulating levels of the PPAR γ activator docosa-hexaenoic acid (DHA) only in male rat pups. Fatty acid binding protein 4 (FABP4) facilitates the transport of DHA to the nucleus to enhance PPAR γ transcriptional activity. However, the effect of PGR and DHA supplementation on FABP4 protein levels in the rat lung is unknown. We hypothesize that PGR and supplemental DHA will alter lung FABP4 protein abundance in a sex and DHA dose-dependent manner in rat pups.

Methods used We induced postnatal growth restriction by randomizing newborn rat pups into litters of 8 (control) or litters of 16 (PGR). Each litter was randomized to receive diets supplemented with DHA at 0.0%, 0.01% (Low), and 0.1% (High). Pup weights were measured every other day. Western blotting was used to measure FABP4 protein abundance in the lung at postnatal day 21.

Summary of results Results are PGR as% sex-matched control $\pm$ SD (* p <0.05). Rat pups in the PGR group weighed significantly less than control by postnatal d5 and continued to weigh less through d21 on all DHA diets. In male rat lungs, PGR did not affect FABP4 protein abundance (89% $\pm$ 9%). However, DHA resulted in a dose-dependent decrease in FABP4 protein abundance (Low 47% $\pm$ 21%*; High 54% $\pm$ 36%*). In female rat lungs, PGR increased FABP4 protein abundance (148% $\pm$ 19%*), while DHA again resulted in a dose dependent decrease in FABP4 (Low 47% $\pm$ 21%*; High 54% $\pm$ 36%*).

Conclusions We conclude that PGR and supplemental DHA alter lung FABP4 protein abundance in a sex and DHA dose-dependent manner in rat pups. We speculate that DHA supplementation downregulates total FABP4 protein abundance in association with increased nuclear localization. Ongoing studies are evaluating the effects of DHA on FABP4 nuclear localization and transcription of PPAR γ target genes.

129

MATERNAL VITAMIN D DEFICIENCY DECREASES DISTAL LUNG VASCULAR DEVELOPMENT AND PULMONARY ENDOTHELIAL CELL GROWTH AND FUNCTION

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10.1136/jim-2018-000939.128

Purpose of study Vitamin D deficiency (VDD) during pregnancy is associated with several maternal and perinatal

morbidities, including asthma and acute and chronic lung diseases after preterm birth. Past studies suggest that vitamin D (VD) plays a role in normal lung development and we have previously shown that VD preserves lung structure and prevents pulmonary hypertension (PH) in an experimental model of bronchopulmonary dysplasia (BPD). We have also shown that VD treatment increase pulmonary artery endothelial cell growth and function. However, the direct effects of maternal VDD on perinatal distal lung vasculature development is unknown. We hypothesize offspring from a maternal VDD rat model exhibit decreased distal vascular development and pulmonary endothelial cells (PEC) isolated from these pups have decreased growth and function.

Methods used Eight-week-old female rats were fed VDD chow and housed in a UV-B light shielded room to achieve 25-OHD levels less than 10 mg/ml at the time of mating and through lactation. Newborn rat lungs were assessed at 2 weeks of age for pulmonary vessel density (PVD) and radial alveolar counts (RAC). Pulmonary endothelial cells were isolated from the lungs of VDD offspring or CTL pups (Day 0–3). CTL and VDD PECs were expanded and used for proliferation and tube formation assays.

Summary of results Distal lungs from VDD offspring demonstrated decreased PVD by 32% (p <0.01) and decreased RAC by 15% as compared to CTLs (p <0.05). PECs from VDD offspring demonstrate decreased cell growth by 60% as compared to CTL (p <0.001) and decreased tube formation by 15% as compared to controls (p <0.05).

Conclusions Maternal VDD leads to abnormal fetal lung development with decreased distal lung vascular growth. In addition, PECs from VDD pups have decreased growth and function. We speculate that fetal disruption of VD signaling impairs distal lung structure and vascular growth, which increases the risk for late respiratory disease.

130

PROTECTIVE EFFECT OF ELECTRO-ACUPUNCTURE AT DIFFERENT MATERNAL ACUPOINTS ON PERINATAL NICOTINE EXPOSURE-INDUCED RAT LUNG PHENOTYPE

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10.1136/jim-2018-000939.129

Purpose of study To determine whether by regulating maternal hypothalamic pituitary adrenal (HPA) axis, electro-acupuncture applied to maternal ST 36 acupoint can modulate PTHrP/PPAR γ and Wnt/ β -catenin signaling pathways, which are critically involved in perinatal nicotine-induced lung phenotype in the exposed offspring.

Methods used 24 adult first time pregnant rat dams were randomly divided into four groups; (1) saline (S), (2) nicotine (N), (3) nicotine +electro acupuncture (EA) applied to ST 36 (n+ST 36), and (4) nicotine +EA applied to ST 40 (n+ST 40) acupoints. Nicotine was administered subcutaneously (1 mg/kg), once a day, and EA was applied to bilateral ST 36 or ST 40 points. Both interventions were administered from embryonic day 6 to postnatal day 21 (PND 21). Pulmonary function, lung morphometry, PPAR γ , β -catenin, and glucocorticoid (GR) levels in the lung tissue and corticosterone (CORT)

in the serum of the offspring were detected; HPA axis in the mother were also examined (pituitary ACTH and serum CORT levels).

Summary of results Compared with the S Group, forced expiratory volume, peak expiratory flow and total airway compliance in the N Group decreased significantly, while total airway resistance increased significantly ($p < 0.05$). The alveolar count decreased significantly, and mean linear intercept and septal thickness increased significantly ($p < 0.01$). The PPAR γ level decreased significantly, and β -catenin, GR and CORT levels increased significantly ($p < 0.05$). Interestingly, all of these changes were blocked in the n+ST36, while there was not protection in the n+ST40. Similarly, in the n+ST36 group, nicotine-induced increases ($p < 0.01$) in maternal pituitary ACTH and serum CORT levels were blocked, while there was no effect in the n+ST40 ($p > 0.05$).

Conclusions EA applied to ST36 alleviated perinatal nicotine-induced pulmonary phenotype, likely by modulating maternal HPA axis, providing a strong mechanistic basis for testing this exciting non-conventional approach in humans.

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Neuroscience I

Concurrent Session

3:15 PM

Thursday, January 24, 2019

131 CHARACTERIZATION OF EPIPEGNANOLONE AS A NOVEL HYPNOTIC

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10.1136/jim-2018-000939.130

Purpose of study It is generally accepted that common general anesthetics (GAs) induce hypnosis by either blocking neuronal N-methyl-D-aspartate (NMDA) receptor and/or potentiating gamma-aminobutyric acid (GABA) currents. However, these effects may be the basis for their developmental neurotoxicity. Hence, it is important to investigate new hypnotic agents with different mechanisms of action. It has been previously demonstrated that the endogenous neuroactive steroid epipregnanolone blocks T-type calcium channels (T-channels) but lacks any GABA-mimetic and NMDA receptor-blocking properties. This work seeks to investigate the potential sedative/hypnotic properties of epipregnanolone and to characterize its use as an adjuvant agent to GAs.

Methods used Epipregnanolone was administered via intraperitoneal injection to adult wild-type (WT) mice and T-channel (Cav 3.1, 3.2, 3.3) knockout mice of both sexes.

Onset time and duration of Loss of Righting Reflex (LORR) and Loss of Withdrawal Reflex (LOWR) were assessed as endpoint measurements of hypnotic/anesthetic state. **Summary of results** We found that epipregnanolone is an efficacious hypnotic agent with an ED₅₀ for LORR of 55.5 mg/kg

in WT male mice, and 41.2 mg/kg in WT female mice. We noted a prominent sex-dependent difference in LORR response to epipregnanolone. Across all genotypes and drug doses, females were sedated for significantly longer than males. We also found that epipregnanolone administration lowered the concentration of isoflurane necessary to induce LOWR in WT mice. Finally, we report a significant difference in the hypnotic responses between WT mice and Cav 3.1 KO mice. In general, Cav 3.1 KO mice demonstrated LORR for approximately only half of the duration of the WT mice.

Conclusions Endogenous neuroactive steroids devoid of GABA-mimetic properties that target neuronal T-channels may have an important role as adjuvants to anesthetic agents. To our knowledge, this work is the first to report on the hypnotic properties of epipregnanolone in rodents. These results indicate that epipregnanolone may be useful in lowering required amounts of GAs used to induce surgical anesthesia. This is important because there is mounting research that GAs administered in early life can induce neurotoxicity causing detrimental health effects.

132 RESTORING CNS HOMEOSTASIS: EFFECTS OF IMMUNOMODULATION ON NEUROPATHOLOGY IN OLD LATE-STAGE MURINE MODELS OF ALZHEIMER'S DISEASE

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10.1136/jim-2018-000939.131

Purpose of study Previously, we have shown that immunomodulation with glatiramer acetate (GA) in adult (10–13 month-old) mouse models of Alzheimer's disease (AD) alleviates neuropathology and preserves synapses and cognitive function. However, given the argument that adult AD mouse models merely correspond to pre-clinical human disease, we explored the impact of GA immunization on old, late-stage double-transgenic APP^{swE}/PS1^{deltaE9} mice (ADtg; 21–24 months old), an age more analogous to clinical stages of the human disease.

Methods used Treatment included weekly subcutaneous injections of GA or PBS for 8 weeks, compared to age-matched naïve wild-type littermates (WT) (n=7 mice/group).

Summary of results Compared to PBS-treated controls, GA-immunized mice displayed markedly decreased cerebral GFAP⁺ reactive astrogliosis. Despite late disease stage, A β plaque burden was notably reduced in the entorhinal cortices of immunized mice. Additional assessment of plaque phenotype revealed a targeted response to large- and medium-sized plaques. In-depth analysis of astrocyte morphology and functional biomarkers showed highly reactive astrocytes and decreased overall expression of glutamine synthetase (GS), an astrocyte-associated enzyme involved in degradation of extracellular synaptic glutamate, in untreated ADtg mice. GA immunization restored astrocyte homeostatic GS levels comparable to WT levels. Given that synaptic loss is tightly associated with cognitive decline, we analyzed synaptic density and found enhanced pre- (Synapsin-II) and post-synaptic (PSD95) biomarker expression following GA immunization in areas of reduced A β pathology.

Conclusions This study demonstrates the neuroprotective effects of GA immunomodulation even in old, late-stage ADtg mice and provides the foundation to translate GA treatment to humans via observed benefits in AD-specific pathology, inflammatory response, glial cell phenotypes, and synaptic preservation.

133

ANGIOTENSIN 1–7 IMPROVES COGNITIVE FUNCTION IN MICE FOLLOWING MILD TRAUMATIC BRAIN INJURY

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Purpose of study Traumatic brain injury (TBI) is a leading cause of disability in the U.S., with approximately 2.8 million TBI-related emergency department encounters each year. Angiotensin 1–7, an endogenous peptide, acts at a MAS receptor to inhibit inflammatory mediators and decrease reactive oxygen species within the CNS. We sought to determine if Ang1–7 confers a neuroprotective role in mice following mild TBI by assessing cognitive function and markers of neuroinflammation and damage.

Methods used A rodent traumatic brain injury model was devised using a pneumatic impactor with retractable piston. A closed skull approach was used to target the left posteromedial parietal lobe of 24 C57/bl6 male mice under general anesthesia. Pre- and post-TBI cognitive function was tested using a novel object recognition (NOR) assay. Mice received either Ang1–7 (0.1 mg/kg, i.p.) (n=12) or normal saline (0.9%, i.p.) vehicle (n=12) at 2 hours post-TBI, 30 min prior to NOR testing on days 1–5 and day 18, and 30 min prior to sacrifice on day 25. Cortical and hippocampal tissues were used for immunohistochemistry and western blot analyses using Tau, p-Tau and GFAP antibodies.

Summary of results The administration of Ang1–7 daily for five days post-mTBI significantly increased cognitive function in the acute phase as compared to control saline treated animals (NOR ratio, $p < 0.05$). A long-term protective effect on cognition was also seen in the Ang1–7 treated group, represented by improved isolated and cumulative NOR performance on post-mTBI days 16 and beyond ($p < 0.05$). In addition, cortical and hippocampal structures of mice showed less neuronal cell death and reactive gliosis in the presence of Ang1–7. Moreover, biochemical studies showed that the mTBI-induced increase in the ratio of p-Tau to Tau in the hippocampus was significantly reduced by Ang1–7 treatment. Cortical GFAP expression indicative of reactive gliosis was also diminished in the Ang1–7 group.

Conclusions These are the first studies to demonstrate that sustained administration of Ang1–7 significantly improves outcomes and may offer a novel therapy that may prevent long-term CNS impairment after mild TBI.

134

MICROGLIAL DEPLETION ABOLISHES ISCHEMIC PRECONDITIONING-MEDIATED PROTECTION IN WHITE MATTER

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Purpose of study Transient ischemia confers robust protection against subsequent prolonged ischemic exposure. This phenomenon, ischemic preconditioning (IPC), has been described principally in gray matter-predominant models of injury. We previously demonstrated that IPC also induces axonal protection in a white matter (WM) model. This protection involves innate immune signaling and cells of myeloid origin. However, the role of microglia in WM IPC is unknown. Here we characterize the effects of pharmacologic depletion of microglia on IPC-mediated protection in WM.

Methods used PLX5622 is a CSF1R inhibitor that depletes microglia in the CNS. Mice were treated with either PLX5622-infused or control chow for 21 d. We used immunofluorescent microscopy to quantify the effect of PLX5622 on Iba1⁺ cells in mouse optic nerve (MON). We next applied our model for IPC in WM to PLX5622-treated or control mice. We induced IPC of the MON *in vivo* by surgically occluding the right common carotid artery (CCAO) for 15 min, then allowing reperfusion for 72 hour. Mice were euthanized and MONs both ipsi- and contra-lateral to CCAO were exposed to oxygen glucose deprivation (OGD) *ex vivo* for 45 min. A stimulator applied electrical pulses to each MON before, during and after OGD. Compound action potentials (CAPs), surrogate measures of axonal function, were then quantified. As an additional control, parallel experiments were carried out in PLX5622-treated and control mice that had not undergone prior CCAO preconditioning.

Summary of results Mice that received PLX5622 had a 99% reduction in the number of Iba1⁺ cells in MON indicating near-complete microglial depletion in WM. As expected, in mice that received control chow, CAP recovery following OGD was significantly greater (39 ± 3 vs $24 \pm 3\%$, $p < 0.01$, t-test) in preconditioned MONs. However, IPC-mediated axonal protection was abolished in mice treated with PLX5622. In mice that had not undergone prior CCAO, we found no statistical difference in CAP recovery between PLX5622-treated and control MONs.

Conclusions These results support the notion that microglia play a critical role in IPC-mediated axonal protection. Further characterization of innate immune responses following IPC in WM may lead to novel therapeutic strategies for stroke.

135

COMPRESSED SENSING IMAGE ACQUISITION AND PROCESSING FOR SINGLE PHOTON EMISSION TOMOGRAPHY STUDIES OF PARKINSON'S DISEASE

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Purpose of study SPECT imaging with 123-Ioflupane is a 3D Nuclear Medicine technique that is used detect dopamine deficiency in the evaluation of Parkinson's and related diseases. Long image acquisition times that lead to reduced quality due to unintended motion, patient discomfort, exposure to radiation, and high costs limit usage of SPECT. Our study uses a computational algorithm, compressive sensing (CS) with total variation (TV) to shorten SPECT imaging times in studies of patients with Parkinson's Disease (PD).

Methods used Reconstruction algorithms were developed in MATLAB using a virtual 123-Ioflupane 'phantom' image created from real patient data. Axial image reconstructions of

Abstract 135 Figure 1 SPECT reconstruction of 123-ioflupane studies in normal and parkinson's patients with and without TV

virtual data were compared using both Ordered Subset Expected Maximization (OSEM), the current standard of SPECT reconstruction, and OSEM with TV at various numbers of projections and times per projection (t/P). This same comparison was then performed on 123-Ioflupane studies from Parkinson's and normal patients.

Summary of results At both a lower number of projections and lower t/P, reconstruction of virtual sinograms yielded lower Normalized Mean Squared Error and higher Signal to Noise ratios for reconstructions using OSEM+TV as opposed to OSEM alone. Similarly, OSEM+TV reconstruction in both Parkinson's and healthy patients visually resembled ground truth images at half time imaging (figure 1).

Conclusions Compressive sensing algorithms with TV regularization may be used to shorten SPECT imaging times in diagnostic studies for Parkinson's and related diseases without compromising the clinical integrity of images.

136 USE OF T-TYPE CALCIUM CHANNEL BLOCKERS AS ADJUVANTS FOR GENERAL ANESTHESIA

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10.1136/jim-2018-000939.135

Purpose of study It is generally accepted that general anesthetics (GAs) induces hypnosis by targeting neuronal GABAA and NMDA receptors, which in turn may cause learning deficits in both rodents and children (Jevtovic-Todorovic et al., 2003; Ing et al, 2014). Previous *in vitro* study documented that CaV3.3 isoform of T-type calcium channels (T-channels) in the reticular thalamic nucleus (nRT) are inhibited by clinically-relevant concentrations of volatile GAs, including isoflurane (Joksovic et al, 2005, Br J Pharmacol). However, little is understood of the role CaV3.3 channels in anesthetic induced unconsciousness. The goal of this study is to first determine the effects of TTA-P2, a selective T-type calcium channel blocker, on the quality of isoflurane-induced anesthesia in C57BL/6J WT mice; and second, to better characterize the role of CaV3.3 channels in anesthetic induced unconsciousness.

Methods used The hypnotic effects and surgical depth of an anesthesia was measured by the% of Isoflurane at Loss of Righting Reflex (LORR) and Loss of Withdrawal Reflex (LOWR) respectively (n=10–12 mice per group). Additionally,

the quality of anesthesia was measured by the% isoflurane at which characteristic neuronal oscillations of 70% burst suppression Ratio (BSR) was elicited during electroencephalogram (EEG), which indicates disruption of thalamo-cortical information transfer.

Summary of results We found that intraperitoneal injection of TTA-P2 showed a dose-dependent (10, 30, 60 mg/kg) decrease in the requirement of isoflurane to reach LORR and LOWR in WT mice. Surprisingly, we found that there was an even greater decreased requirement of isoflurane to reach LORR and LOWR in Cav3.3 KO mice. Consistent with these findings, EEG recordings following injections of 60 mg/kg of TTA-P2 showed that mutant mice required significantly less isoflurane to reach 70% BSR when compared to WT mice.

Conclusions We propose that T-Type calcium channel blockers should be further explored as a valuable adjunct to reduce the usage of potent volatile anesthetics, and potentially decrease GA-induced neurotoxic effects of the developing brain. Furthermore, our findings point to the value of Cav3.3 channels in anesthetic induced unconsciousness.

137 ORPHANIN FQ/NOCICEPTIN REGULATES ENERGY HOMEOSTASIS IN A DIET-DEPENDENT MANNER

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Purpose of study Due to the increased prevalence of obesity, it is important to determine the underlying mechanisms as a means to prevent it. The appetite-stimulating peptide, orphanin FQ (OFQ), binds to the opioid receptor-like (ORL)-1 receptor and activates G protein-gated, inwardly rectifying K⁺ channels in anorexigenic proopiomelanocortin neurons in the hypothalamic arcuate nucleus (ARC), to cause hyperphagia and lower metabolism. We hypothesized that dysregulated energy homeostasis seen with obesity/insulin resistance is due to enhanced responsiveness to OFQ.

Methods used Wild type, gonadally intact male mice were given either regular chow diet or a 'Westernized' high-fat diet (HFD) for five weeks prior to a stereotaxic implantation of a cannula above the ARC. The animals were allowed one week of recovery prior to experimentation. Energy balance was monitored via a Comprehensive Lab Animal Monitoring System, which measured energy intake, energy expenditure and meal pattern continuously around the clock. After three days of acclimation, animals were given either 0.3 nmole/mouse of OFQ or its 0.9% saline vehicle every day for five days at 16:00. Data was analyzed using repeated-measures multifactorial analysis of variance (ANOVA) followed by a Least Significant Difference test.

Summary of results Overall, we found that OFQ caused a diet- and time-dependent increase in energy intake and reduction in energy expenditure. Cumulative energy intake and meal size were significantly increased in chow-fed mice; effects that were significantly augmented for HFD-fed mice, which also exhibited an increase in meal frequency. OFQ significantly decreased O₂ consumption in chow-fed mice at 1 hour post-injection; an effect that was extended to at least 4 hours post-injection in HFD-fed mice. The results for CO₂ production were nearly identical to those seen with O₂ consumption.

Conclusions OFQ significantly increased cumulative energy intake through alterations in meal pattern, and significantly decreased the O₂ consumed and CO₂ produced. These effects

were further exaggerated by diet-induced obesity. Therefore, our data support the hypothesis that dysregulated energy homeostasis is due, at least in part, to enhanced responsiveness to OFQ.

138

PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE DECREASES ENERGY INTAKE AND INCREASES ENERGY EXPENDITURE IN A DIET-SENSITIVE FASHION

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Purpose of study The arcuate nucleus (ARC) of the hypothalamus is regarded as a critical platform that integrates signals of hunger and satiety reflecting energy stores and nutrient availability. Among ARC neurons, the appetite-suppressing pro-opiomelanocortin (POMC) neurons have been shown to decrease feeding and increase energy expenditure through the excitation-induced release of the melanocortin receptor ligand α -melanocyte-stimulating hormone (α MSH). Neurons contacting POMC neurons from the Ventromedial Nucleus (VMN) express a neuropeptide called pituitary adenyl cyclase-activating polypeptide (PACAP) that is thought to play an important role in suppressing appetite and increasing energy expenditure. We hypothesize that PACAP administered directly into the ARC will produce anorexigenic effects manifest by robust hypophagia as well as increased energy expenditure in gonadally intact male mice.

Methods used We administered PACAP (30 pmole/mouse) or its 0.9% saline vehicle through a 26-gauge guide cannula stereotactically implanted into the ARC of gonadally intact males on either a high fat diet (HFD) or standard chow.

Summary of results We found a significant difference in energy intake, meal pattern and energy expenditure between males treated with PACAP and control groups. Overall, we found that mice administered with exogenous PACAP consumed a lesser amount of food, less frequently, than their saline vehicle counterparts. Furthermore, we found that PACAP-treated mice as well as the HFD mice displayed higher levels of O₂ consumption and CO₂ production. In terms of cumulative energy intake, meal size and O₂ consumption, the PACAP-induced changes were at least partially negated by the HFD, suggesting that these effects of PACAP may be compromised under conditions of obesity/insulin resistance.

Conclusions Our results support the notion that PACAP signals in the ARC to exert anorexigenic and metabolic accelerating effects that manifest in a diet-sensitive fashion. They are in line with our hypothesis that VMN PACAP neurons excite ARC POMC neurons to decrease energy intake and increase energy expenditure. These data have important implications when considering new therapeutic strategies for obesity and type II diabetes.

139

CASPASE-3 EXPRESSION IN THE RAT HIPPOCAMPUS AFTER PILOCARPINE INDUCED STATUS EPILEPTICUS

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Purpose of study Epilepsy is a chronic neurological condition in which spontaneous seizures develop. Status epilepticus (SE) is a related medical emergency that may preclude epilepsy and leads to the development of spontaneous seizures in animal models, a model for human epilepsy study.

Apoptosis has been investigated as a mechanism for neuronal death post-SE. The presence of apoptotic cell death post-SE is not clearly defined, specifically the expression of caspase-3, a key executioner protease in the apoptotic pathway.

In this study we investigated the expression of caspase-3 in hippocampal tissue obtained from rats after pilocarpine-induced SE to evaluate the relevance of apoptosis in the development of spontaneous seizures.

Methods used SE was induced in male rats using pilocarpine. Rats were sacrificed at various time points post-SE, and regions of the hippocampus were collected. Protein samples were then assayed using western blot analysis with an antibody which detects active and inactive caspase-3.

For immunostaining, coronal sections were stained with an antibody that detects active caspase-3. To detect degenerating neurons, sections were stained with Fluoro-Jade B.

Summary of results Western blot analysis demonstrated an increase in the expression of the inactive zymogen of caspase-3 in the induced-SE group compared to the control, however, no increase in active caspase-3 was detected during the first week post-SE.

An additional western blot assay demonstrated an increase in the inactive zymogen of caspase-3 compared to the control at 15 days post-SE, but no increase in the expression of active caspase 3 was found.

Immunohistochemical staining demonstrated increasing cell death as seizure level increased compared to the control, however, all treatment groups had lower stained active caspase-3 cell counts than control group.

Conclusions Since active caspase-3 was not expressed in western blot assays and minimally expressed compared to control groups in immunohistochemical staining, in this model caspase-3 is not entirely necessary for cell death following induced-SE, suggesting a limited role for apoptosis-related cell death post-SE.

140

CALPAIN-2 CONDITIONAL KNOCKOUT MICE EXHIBIT IMPROVED BEHAVIORAL PERFORMANCE, AS COMPARED TO WILD-TYPE MICE, AFTER REPETITIVE MILD TRAUMATIC BRAIN INJURY

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10.1136/jim-2018-000939.139

Purpose of study To assess the roles of calpain-2 in neuronal damage and cognitive and motor impairment in a repetitive mild traumatic brain injury (rmTBI) mouse model.

Methods used WT mice were C57 Bl/6 mice. Calpain-2 KO mice were generated by crossing male $Cre^{-/-}$ CAPN2^{loxP/loxP} with female $Cre^{+/+}$ CAPN2^{loxP/loxP}. Calpain-2 KO mice are $Cre^{+/+}$ CAPN2^{loxP/loxP} and their controls are $Cre^{-/-}$ CAPN2^{loxP/loxP}.

Mice were placed into a restraint bag. The impactor tip was lowered until it touched the helmet placed on their head. During impact, the tip was driven pneumatically to a depth of 3.75 mm. After impact, animals were removed from the

restraint bag and returned to their cage. Mice in the rmTBI group received 4 head impacts per day (separated by 2 hour) for 10 consecutive days (40 total). Sham/control mice underwent an identical procedure as the rmTBI group (placed into the restraint and had the helmet placed on, but with no impact).

Behavioral tests were carried out to assess motor function, risk taking behavior, depression, and learning and memory.

Summary of results WT exhibited impaired motor function 1 day after rmTBI as compared to sham WT mice; mice recovered by 1 week after rmTBI. At both 2 weeks and 1 month after rmTBI, WT mice showed an increase in risk taking behavior and an increase in immobility time in the tail suspension test, as compared to sham WT mice. Additionally, impaired learning and memory was also observed 1 month after rmTBI in WT. In contrast, calpain-2 KO mice exhibited significantly less impairment in motor and cognitive function following rmTBI as compared to WT and their control. Interestingly, calpain-2 KO mice exhibited better motor function, decreased immobility time in the tail suspension test and improved learning as compared to WT and control mice.

Conclusions The results indicate that calpain-2 significantly contributes to the negative consequences of rmTBI in motor and cognitive functions. They further validate our previous results indicating that a selective calpain-2 inhibitor significantly reduced neuronal damage and motor and cognitive function in a mouse model of TBI. Finally, they suggest that selective calpain-2 inhibition could provide a novel approach to limit the negative consequences of rmTBI in humans.

Abstract 141 Figure 1 Plain film demonstrating diffuse alveolar filling process with relative sparing of the bases

contrast demonstrated mild cerebral edema. A chest x-ray was also obtained (figure 1). The patient was diagnosed with exercise-associated hyponatremia with a rare complication of cerebral and pulmonary edema. The etiology of this disorder is primarily due to overzealous hypotonic fluid consumption and non-osmotic ADH secretion. The mechanism of the pulmonary edema is thought to be analogous to neurogenic pulmonary edema, which is seen in a multitude of cerebral insults.

Pulmonary and Critical Care I

Concurrent Session

3:15 PM

Thursday, January 24, 2019

141 HYPONATREMIA WITH SEIZURES AND PULMONARY INFILTRATES IN A YOUNG ADULT

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Case report A 31 year old male without previous significant past medical history presented to the emergency department after a witnessed acute seizure. The patient was playing rugby and had completed 3 outdoor matches immediately before his seizure. He had consumed 4 L liters of water and 3 large bottles of Gatorade during the matches, and endorsed not eating all day. Vital signs were unremarkable except for oxygen saturation of 97% on high flow nasal cannula supplemental oxygen with a FiO₂ of 40% at a flow rate of 40 L/min. His physical exam revealed orientation to self only, diffuse pulmonary crackles, normal cranial nerve function, and normal tendon reflexes with symmetric and intact muscle strength bilaterally. Laboratory studies showed a sodium of 122 mmol/L, serum osmolality 255 mOsm/kg, urine osmolality 270 mOsm/kg, and creatine kinase 1,750 U/L. A CT head without

142

ALWAYS IN HIND SIGHT: RAPIDLY FATAL RIGHT VENTRICULAR FAILURE FROM PULMONARY TUMOR THROMBOTIC MICROANGIOPATHY

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Case report A 35 year old Hispanic male, with no prior medical history, presented with subacute back pain and acute constant chest pain, associated with shortness of breath, dry cough, nausea, and syncope. Echocardiography was remarkable for severely dilated and hypokinetic right ventricle, with severe increase in pulmonary arterial systolic pressure and right atrial pressure. CT angiogram showed centrilobular groundglass opacities, enlarged pulmonary artery, but no pulmonary embolism. Right heart catheterization was scheduled, but he developed increased oxygen requirements with syncopal episodes resulting in cardiac arrest. Autopsy showed poorly differentiated gastric adenocarcinoma metastasized to the lumbar spine and pulmonary tumor thrombotic microangiopathy.

Pulmonary tumor thrombotic microangiopathy was first termed in 1990 by von Herbay et al. It occurs when tumor emboli in pulmonary arterioles cause activation of the coagulation cascade and fibrocellular intimal thickening, leading to acute and rapidly progressive pulmonary hypertension and cor pulmonale. It is highly associated with gastric adenocarcinoma, however, cases with lung, breast, and other GI tumors have also been described.

Of the few published reports, most cases are diagnosed post mortem due to lack of recognition and rapid decline. Patients may present with acute cough, thrombocytopenia, right heart failure on echocardiography, and nonspecific centrilobular micronodules on CT. These findings, together with a high level of suspicion, have prompted early lung biopsy for confirmatory diagnosis in deteriorating patients. Although PET and cytology samples from right heart catheter have been suggested, these have not been studied or fully validated. Unfortunately, while very few are diagnosed early, even fewer survive past diagnosis. Treatment with anticoagulation, chemotherapy, and imatinib has been reported.

Pulmonary tumor thrombotic microangiopathy remains significantly difficult to diagnose ante-mortem and is usually recognized in hind sight. It has an ambiguous presentation and is rapidly fatal. Increasing awareness could allow for early recognition.

143 THE CONTRIBUTION OF NURSING POINT-OF-CARE ULTRASOUND ON SEPTIC EMERGENCY DEPARTMENT PATIENTS

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Purpose of study Nursing led point-of-care ultrasound (POCUS) studies have been limited to guiding intravenous (IV) line access, urinary catheterization, and diagnosing heart failure. Research is needed on the use of POCUS in septic patient management. We studied how nurse-led POCUS could impact treatment decisions affecting septic patients in the emergency department.

Methods used Nurses trained in POCUS performed examinations three times (Hour Zero, Three, Six) on septic patients in the emergency department and made recommendations for fluid management. Emergency physicians (EP) were surveyed to compare their recommendations for fluid management and treatment to the nurse data.

Summary of results A total of 104 patients were scanned with a mean age of 60.4. EPs agreed with nursing US in 99% of cases. Nursing US changed management and increased confidence in treatment plan 83% and 96% of the time, respectively. EPs underestimated fluids 37.5%, overestimated 26%, and correctly estimated (within 500 ml) 36.5% of the time. Over the course of resuscitation, IVC became collapsible, the number of cases with B-lines was essentially unchanged, and less fluid was recommended.

Conclusions This study showed that nurse led POCUS is feasible and may have a meaningful impact on physician

diagnosis and septic patient management in the emergency department.

144 REVISED RISK ESTIMATES DO NOT ALTER THE RELATIONSHIP BETWEEN ASTHMA AND CARDIOVASCULAR DISEASE RISK IN TYPE 2 DIABETES

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Purpose of study Type 2 Diabetes (T2D) and asthma are independent risk factors for cardiovascular disease (CVD). We previously reported that CVD risk is reduced in people with T2D+Asthma compared to those with T2D alone when using the 2013 ACC/AHA Cardiovascular Risk Score, a tool based on validated biomarkers and clinical characteristics. But because the 2013 instrument may overestimate CVD risk, the model has been recently revised using newer data and modified statistical methods to correct these estimations (Yadlowsky et al., 2018). We hypothesize that using these revised risk score equations will not alter the relationship between asthma, T2D, and CVD Risk Score.

Methods used Data were extracted from the Electronic Medical Record using ICD-9/10 codes. Patients with both T2D and Asthma (n=603) were compared to a group of patients with T2D Alone who were matched for age and sex (n=603). Other respiratory diseases were excluded from analysis. Least squares mean estimates of the 10 year risk of a major CVD event using the 2013 CVD Risk Score and the newly revised equations were calculated using generalized linear models.

Summary of results As shown in the Data table 1, 10 year CVD risk was significantly increased in the T2D Alone group as compared to the T2D+Asthma group using both Risk Score estimates. Using the updated 2018 estimates, the 10 year risk for a CVD event was 0.4% higher in patients with T2D Alone compared to those with T2D+Asthma, and CVD risk is ~2% higher than with the 2013 instrument in both groups.

Conclusions In this study, Asthma conferred a statistically significant protective effect against CVD risk over the next 10 years for individuals with co-morbid T2D. This result was initially demonstrated based on the 2013 ACC/AHA Risk Score estimates and confirmed with the 2018 revised risk score estimates. These newer estimates yielded a higher overall risk and demonstrated an even greater protective effect of asthma.

Abstract 143 Table 1 Physician survey of nursing ultrasound

	Hour 0	Hour 3	Hour 6
Physician agrees with ultrasound	95/95 (100%)	73/75 (97.3%)	61/61 (100%)
Ultrasound changes management	74/93 (79.6%)	64/74 (86.5%)	51/60 (85%)
Ultrasound increases confidence in treatment plan	59/60 (98.3%)	45/48 (93.8%)	40/41 (97.6%)

Note: Nine subjects were not evaluated by EM physicians at Hour 0 and are excluded from this table.

Abstract 144 Table 1

	ACC/AHA 2013 CVD Risk Score [Mean (95% CI)]	Revised 2018 CVD Risk Score [Mean (95% CI)]
T2D Alone	4.7% (4.5%–5.0%) (n=536)	6.6% (6.3%–6.9%) (n=527)
T2D+Asthma	4.5% (4.3%–4.7%) (n=562)	6.2% (6.0%–6.5%) (n=563)
p-value	0.025	0.033

Mean=Least squares mean estimates from weighted generalized least squares (2013) and ordinary least squares regression (2018).

145

PREVENTION OF PNEUMOCYSTIS PNEUMONIA IN NON HIV PATIENTS ON STEROIDS IN THE USA (PREPOSTERUS)

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10.1136/jim-2018-000939.144

Purpose of study *Pneumocystis jirovecii* (PJP) is an opportunistic fungal infection that is increasingly seen in non-HIV hosts due to iatrogenic immunosuppressive regimens. PJP in non-HIV hosts causes significant morbidity, and a mortality higher than in HIV. Sulfa antibiotics remain the cornerstone of prophylaxis of PJP, but are often omitted in the non-HIV host. We sought to assess the scope of PJP in non-HIV, non-BMT hosts within our hospital system and to determine barriers to the use of prophylaxis (particularly in those treated with steroids).

Methods used Search of de-identified data within the University of Colorado Health System electronic medical record (EMR) between the years of 2009–2018. Inclusion criteria were a diagnosis of PJP as defined by ICD-9 or –10 codes. Exclusion criteria included a diagnosis of HIV or bone-marrow transplant (BMT) as defined by ICD codes. We assessed use and type of steroid, use of preventative antibiotics, and diagnosis of solid organ transplant or cancer.

Summary of results Of PJP cases 25.3% were solid organ transplant recipients, 29.3% had cancer, and 52.3% female. Based on 10 years of data, we estimated an incidence of 18 cases of non-HIV, non-BMT PJP/year in our health care system. Steroids were prescribed to 40% of PJP patients in the month before diagnosis, yet only 21% (half) had any evidence for PJP prophylaxis in the month before diagnosis. Steroids received before PJP were dexamethasone in 32%, methylprednisolone in 25%, prednisone in 39%, and prednisolone in 4%. Sulfa allergy may have been a barrier to prophylaxis as it was more 5-fold more common than expected in the general population (17.7% vs 3%).

Conclusions PJP related to steroids in non-HIV, non-transplant hosts is a significant iatrogenic illness. Highly effective prophylactic regimens appear to be underutilized in our health care system, consistent with published experience elsewhere. Sulfa allergy may be one barrier to prophylaxis. An expanded survey of national medical electronic databases is warranted to better understand the scope of iatrogenic PJP. Our data suggest that development of an electronic medical record sifting algorithm to capture PJP risk based on steroid use and other risk factors, with development of regional intervention protocols to increase prophylaxis is one strategy that may improve the burden of this illness.

146

CHRONIC PASTEURELLA MULTOCIDA INFECTION RESULTING IN FOCAL BRONCHIECTASIS IN A PEDIATRIC PATIENT

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Case report *Pasteurella multocida* is a gram-negative coccobacillus found in the respiratory secretions of domestic and wild animals. It is a known cause of wound infections after animal bites and scratches but can also cause respiratory illness, often in immunosuppressed patients or patients with existing pulmonary disease.

In this report, a 14-year-old girl presented to pediatric pulmonology with a 12 year history of chronic productive cough and recurrent high fevers. Her mother recalled the onset of her symptoms around 18–20 months of age with no precipitating illness. A chest X-ray ordered in February 2018 by her primary care provider was consistent with a left lower lobe pneumonia and her chest CT showed focal bronchiectasis. She was prescribed courses of amoxicillin/clavulanate, azithromycin and doxycycline with symptom recurrence after each cycle. In addition to her cough, she reported fatigue, headaches and back pain. Her past medical, surgical and family history were noncontributory to her disease. At the onset of her symptoms, the patient lived on a farm with several animals and currently lives with an indoor dog and cat. She denied international travel or recreational drug use. A bronchoscopy was performed and was notable for thick mucus diffusely, though more prominent on the left side. The respiratory culture was positive for *Pasteurella multocida* and the fungal culture was positive for *Penicillium* species. Her sweat chloride test and bronchial brush biopsy were negative, but the primary ciliary dyskinesia genetic panel was notable for two variants of uncertain significance. Her tuberculosis PCR, acid fast bacilli culture and coccidioidomycosis serology were negative and the lipid laden macrophage index was normal. She was prescribed an 8 week course of amoxicillin/clavulanate and itraconazole with good response, but her symptoms returned upon discontinuation of the medication.

This case is significant due to the very young age at probable initial infection and the rare progression of untreated respiratory *Pasteurella multocida* infection to bronchiectasis in a teenager. The initial response to antibiotic therapy is encouraging, and the plan is to restart the amoxicillin/clavulanate for a minimum of 8 weeks with repeat chest CT, bronchoscopy and ciliary function studies.

147

ARGININE AND ADMA RATIO IS ASSOCIATED WITH EXHALE NITRIC OXIDE-A LONGITUDINAL METABOLOMIC STUDY

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Purpose of study Arginine metabolism by competing enzymes, nitric oxide synthase and arginase lead to pathways that are important in asthma. A lower ratio of arginine and asymmetric dimethylarginine (ADMA) in the plasma was found to be associated with reduced lung functions and increased respiratory symptoms in previous cross-sectional studies of asthmatics. However, fractional exhaled nitric oxide (FeNO), plasma arginine/ADMA, lung functions, and asthma control test (ACT) scores are dynamic measurements and cross-sectional studies might not capture those dynamic changes. Our longitudinal study aims to measure those dynamic changes in severe asthmatics.

Methods used The study subjects were from the cohort of the longitudinal L-arginine randomized clinical trial which were recruited from the University of California-Davis Asthma Network clinics. Each subject had 6 visits (6 weeks interval) and plasma samples, FeNO measurements, and ACT scores were obtained at each study visit. Spirometry was obtained at visit 1, 3, 4 and 6 (12 weeks interval). Longitudinal plasma

arginine and ADMA levels were identified through hydrophilic interaction liquid chromatography (HILIC) positive mode method. A linear mixed effect model with individual subject intercepts were used for testing the association between arginine/ADMA ratio and outcomes. Body Mass Index (BMI) was included as a covariate for testing the association between the arginine/ADMA and FeNO.

Summary of results 46 subjects with 226 measurements were included in the analysis. A lower ratio of arginine/ADMA was associated with higher FeNO (p -value=0.03) and remained statistically significant after controlling for BMI (p -value=0.02). No significant association between arginine/ADMA ratio and lung functions or ACT scores were observed. **Conclusions** Our studies showed that a lower ratio of arginine/ADMA in a longitudinal setting was associated with higher FeNO suggesting a possible shift in arginine metabolism. It is unclear if the ratio is associated with worsening symptoms or poor lung function in the dynamic setting. A future study will focus on phenotyping those asthmatic patients and re-examining the relationship in different subgroups of asthmatics.

148

INTRAPERITONEAL LPS IMPAIRS HEPATIC SELENOCYSTEINE AND SELENOENZYME SYNTHESIS

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Purpose of study Selenium (Se) is a trace mineral incorporated into selenocysteine (Sec), which is critical for selenoenzyme function to defend against oxidative stress. Over 65% of plasma selenium content is the selenium transporter, selenoprotein P (Sepp), which is predominantly produced in the liver. In septic adults, low serum Se and Sepp levels correlate with multiorgan dysfunction, pneumonia, and death. Mechanisms determining how inflammatory insults compromise selenoenzymatic defense are not fully understood. Lipopolysaccharide (LPS) induces hepatic inflammation and dysfunction, and we hypothesized intraperitoneal (IP) LPS would dysregulate selenium metabolism and selenoenzyme production.

Methods used Wild type (WT) male 8–12 week C57/B6 mice were exposed to IP LPS (5 mg/kg) and sacrificed at 0, 8 and 24 hour. Serum and organs were collected. Hepatic inflammatory response was determined by gene expression for TNF α , IL1 β , and IL6. Hepatic mRNA and protein expression for factors essential in selenocysteine synthesis (PSTK, SepsecS/SLA, SBP2, EEFSec/SELB) and selenoenzymes (Sepp1, Gpx1, Gpx4, TrxR1, TrxR2) were measured by qPCR and Western blot.

Summary of results LPS increases TNF α , IL1 β , and IL6 mRNA at 8 hours (p <0.05, n =4–6). LPS decreases hepatic gene expression for factors that mediate selenocysteine synthesis, including PSTK, SepsecS, SBP2 and EEFSec at 8 hour (p <0.05, n =4–6) SELB and SLA protein expressions trend down at 24 hours (p =0.07, n =5). LPS decreases hepatic gene expression for the selenoenzymes Sepp, Gpx1, Gpx4, TrxR1 and TrxR2 at 8 hours (p <0.05, n =4–6). Gpx1 and TrxR1 mRNA expression remain low at 24 hours. Hepatic Sepp protein expression decreases at 8 and 24 hours (p <0.05, n =5). Gpx1, Gpx4, TrxR1, TrxR2 protein expressions did not change; activity levels pending.

Conclusions IP LPS downregulates numerous genes important in selenocysteine synthesis and hepatic selenoenzymes. We speculate that dysregulation in hepatic selenocysteine and selenoenzyme production contributes to LPS induced oxidative stress and organ injury by decreasing selenium delivery to other organs.

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149

A CASE REPORT AND DISCUSSION OF KAPOSI'S SARCOMA-ASSOCIATED HERPES VIRUS INFLAMMATORY CYTOKINE SYNDROME

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Case report Kaposi's Sarcoma-associated Herpesvirus (KSHV) Inflammatory Cytokine Syndrome, or KICS, is a rare, recently described entity with estimated 50% mortality. A case of KICS is described along with diagnostic and management dilemmas.

A 27 year-old woman with AIDS presented with sore throat, hemoptysis, weight loss, fever, and tender inguinal masses. Pulmonary Kaposi's sarcoma (KS) was diagnosed by bronchoscopy. Core lymph node biopsies were non-diagnostic for multicentric Castleman's disease (MCD). She developed bulky, friable lesions of the soft palate leading to upper airway obstruction, as well as vasodilatory shock and respiratory failure. Sepsis was ruled out with negative cultures. She was started on rituximab and liposomal doxorubicin for treatment of KICS. However, she developed multi-organ failure died.

KICS should be suspected in patients with HIV and KS who present with severe inflammatory symptoms. KSHV encodes a viral homolog of IL-6 by taking over host cellular gene expression. Viral IL-6 can stimulate human IL-6 pathways, leading to wasting, effusions, anemia, thrombocytopenia, elevated CRP, coagulopathy, and adenopathy, as well as vasodilatory shock, respiratory failure, and death. Our patient met criteria for KICS based on these clinical findings, as well as marked KSHV viral load and inability to make a histopathologic diagnosis of MCD. Ruling out MCD is a challenge due to the need for excisional lymph node biopsy. In addition, excessive time can be spent ruling out sepsis as a cause of vasodilatory shock; instead, therapy directed toward KICS with rituximab and liposomal doxorubicin should be initiated as soon as infection is reasonably excluded. Treatment should not be delayed due to inability to distinguish KICS from MCD.

Of note, surgical manipulation of KS lesions in the airways should be avoided due to risk of bleeding and aspiration. Advanced modalities for airway protection may be needed in patients with KICS.

150

MICE WITH DECREASED MATRIX BOUND SOD3 DEMONSTRATE EARLY ROBUST INFLAMMATORY RESPONSE AND EXAGGERATED NF κ B SIGNALING AFTER INTRATRACHEAL BLEOMYCIN

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Purpose of study The naturally occurring R₂₁₃G single nucleotide polymorphism (SNP) in the antioxidant enzyme extracellular superoxide dismutase (SOD3) lowers matrix binding affinity, redistributing SOD3 from the lung into the extracellular fluids. Humans harboring this SNP exhibit less severe COPD, suggesting elevated alveolar SOD3 levels protect against lung injury. We showed mice expressing R₂₁₃G SOD3 are protected from bleomycin-induced fibrosis. Intriguingly, R₂₁₃G mice have a robust early inflammatory response at 3 days followed by enhanced resolution of inflammation at 7 days. NFκB is a critical redox regulated transcription factor that regulates inflammation. Based on published work and analysis of RNA sequencing data, we hypothesized the R₂₁₃G early inflammatory response after intratracheal (IT) bleomycin is mediated by NFκB signaling.

Methods used Wild type (WT) mice and homozygous R₂₁₃G mice received IT bleomycin (100 ul) or phosphate buffered saline (PBS) and were sacrificed at 1 and 3 days. BALF cells were tested for TNFα and IL-1β mRNA expression. Nuclear and cytoplasmic extracts from whole lung homogenates were analyzed for p65, GAPDH and Laminin A/C protein by Western blot. Lung mRNA was evaluated for IκBκβ and IRF7.

Summary of results At 1 and 3 days, bleomycin increased lung nuclear p65 in both strains ($p < 0.05$ for exposure, $n = 2-3$). Post hoc analysis demonstrated higher nuclear p65 after bleomycin in R₂₁₃G compared to WT. At 3 days, bleomycin increased BALF cell TNFα and IL-1β mRNA ($p < 0.01$ for exposure, $n = 6$), with a greater increase in TNFα and IL-1β in R₂₁₃G compared to WT. At 3 days, bleomycin increased IκBκβ only in R₂₁₃G mice ($p = 0.03$, $n = 3$). Bleomycin also increased pulmonary IRF7 mRNA ($p < 0.05$ for exposure), with R₂₁₃G mice greater than WT ($p < 0.05$, $n = 3-5$).

Conclusions R₂₁₃G mice have an early robust inflammatory response after IT bleomycin, with higher cytokine expression in the alveolar fluid compared to WT mice. Intratracheal bleomycin induces NFκB signaling in the lungs of both WT and R₂₁₃G mice, with exaggerated activation in R₂₁₃G mice at early time points. Future work will need to interrogate how increased alveolar fluid SOD3 leads to enhanced resolution at later time points.

and inadvertent intravascular injection. In recent years, the pectoralis plane blocks (PECS), targeting the pectoral, third to sixth intercostal, and the long thoracic nerves have shown to be a less invasive technique to perform in patients undergoing mastectomies. Bashandy et al demonstrated improved analgesia with PECS blocks in Egypt, however, this study compares the efficacy of PECS blocks with general anesthesia (GA) compared to GA alone in a diverse academic institution in Northern California.

Methods used A retrospective chart review was performed using the electronic medical records available at the UC Davis Medical Center (Sacramento, California) to search for patients having undergone mastectomies between 2012 and 2018. Patients over the age of 18 years with unilateral or bilateral mastectomies were included in the study. The patients were subdivided based on whether PEC blocks were performed or not. The group who received PEC blocks received 10cc of 0.25% ropivacaine between pectoralis major and pectoralis minor muscles (PEC 1) and between pectoralis minor and serratus anterior muscles (PEC 2). Opioid consumption data at multiple time points (Intraop, PACU, POD1 and total) was collected and converted to IV morphine equivalents.

Summary of results Results of 152 patients (98 in PECS group vs 54 in GA only group) revealed statistically significant reduction of opioid consumption intraop, Post-PACU to POD1, and sum total in patients who received PEC blocks compared to those without blocks. PACU opioid consumption was not significantly different between groups.

Conclusions Pain after mastectomy is often severe and PECS blocks play an important role in multi-modal analgesia for patients. It is a novel yet easy to teach technique that may decrease opioid consumption and decrease prolonged hospital admission.

152

EPIDEMIOLOGY, OUTCOMES FROM TREATMENT, AND THE SPECTRUM OF SOFT TISSUE INFECTIONS OVER TIME IN HOSPITALIZED PATIENTS: A POPULATION-BASED DESCRIPTION OF INPATIENTS IN THE STATE OF CALIFORNIA

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Purpose of study Soft tissue infections (STIs) encompass a spectrum of disease, ranging from cellulitis to necrotizing soft tissue infections (NSTIs). The cellulitis spectrum is usually benign, while NSTIs are frequently deadly, with a mortality rate as high as 20%–40% in single site series. Despite high mortality and definitive morbidity, timely diagnosis is hampered by lack of characterization of the disease: for example, prior studies have reported its incidence with mandatory reportable disease data only (e.g., incidence of Group A Strep necrotizing fasciitis given as 0.4/100,000, actually the incidence of invasive GAS). More research is needed to determine the epidemiology of NSTIs, the spectrum of disease over time, and risks for more severe disease. This will facilitate earlier identification and treatment to reduce negative outcomes.

Methods used Retrospective analysis of the California Office of Statewide Health Planning and Development (OSHPD) Patient Discharge Database for the years 2012–2016 was used. Patients were selected using ICD-9 codes representative of

Surgery II

Concurrent Session

3:15 PM

Thursday, January 24, 2019

151

PREOPERATIVE PECTORALIS PLANE NERVE BLOCKS AND POSTOPERATIVE OPIOID CONSUMPTION IN A UNIVERSITY ACADEMIC INSTITUTION: A RETROSPECTIVE REVIEW

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Purpose of study Mastectomy patients often have severe pain after surgery with high risk of chronic postsurgical pain. Prior studies have shown that thoracic paravertebral nerve blocks decrease postoperative pain; however they are associated with complications such as pneumothorax, total spinal anesthesia

STIs as the principal diagnosis code with confirmation given by identifying relevant procedures using CPT codes. Those with >1 hospitalization were counted just once. Population based incidence for each year was calculated given number of cases and census obtained population for the given time periods. Comparisons were made between those with NSTI to other diagnoses.

Summary of results Using this database, we report the incidence of NSTIs within this population to be 23/100,000 or 0.23 per 1000. Of 1 30 000 patients hospitalized with a soft tissue infection, 8500 were NSTI, thus 7% of all hospitalized soft tissue infections.

Conclusions In conclusion, the prevalence of NSTIs is much higher than has been reported in previous literature. The availability of epidemiologic data for this disease process can allow for appropriate point of reference for surveillance, and also in the development of diagnostic tests or risk calculators as predictive values can be accurately assessed, thus leading to earlier diagnosis and time to interventions.

153 PROPHYLACTIC FIXATION VERSUS OBSERVATION OF THE ASYMPTOMATIC CONTRALATERAL HIP IN SLIPPED CAPITAL FEMORAL EPIPHYSIS

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Purpose of study Prophylactic fixation of the contralateral hip after SCFE is controversial. Children with unilateral SCFE whose contralateral hip is observed are at risk for contralateral slip and complications such as avascular necrosis. A comparison of adverse outcomes between observation and prophylactic pinning has not yet been performed.

Methods used We retrospectively reviewed 197 patients with unilateral SCFE over a 20 year period. Variables of interest included age, sex, BMI, Modified Oxford Bone Age Score, length of operation and estimated blood loss. Postoperative complications of the unaffected hip included pain, AVN, chondrolysis, abnormal gait and development of a limb length discrepancy.

Summary of results Of 197 patients, 100 (51%) received prophylactic fixation of their contralateral hip and 97 (49%) were observed. Average follow-up was 24.5 months. Those observed were older ($p<0.001$) and had a greater MOBA

score ($p=0.006$). No difference was found between groups for BMI or length of hospitalization. Patients in the prophylactic group had greater EBL during surgery ($p=0.004$) and longer operative time ($p<0.001$).

In patients with unilateral fixation, 19/97 (19%) developed a contralateral SCFE. Among these, 2/19 developed AVN or chondrolysis of the contralateral hip (2% overall). Additionally, 17/97 developed contralateral hip pain, 10/97 developed a leg length discrepancy, and 24/97 developed a limp. In patients with prophylactic fixation, 2/100 developed AVN, 10/100 developed contralateral hip pain, 4/100 developed a LLD and 26/100 developed a limp.

Conclusions For patients with unilateral SCFE, risk of AVN of the contralateral hip was similar whether the hip was prophylactically pinned or observed (2%). Additionally, there were similar outcomes for length of hospitalization, EBL and development of a limp. There was however a higher rate of LLD and pain in patients whose contralateral hip was observed.

154 EFFECTIVENESS OF RADIATION PROTECTIVE MEASURES IN SHIELDING RADIOSENSITIVE ORGANS DURING PERCUTANEOUS NEPHROLITHOTOMY PROCEDURE

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10.1136/jim-2018-000939.153

Purpose of study Despite steps taken to shield medical personnel from radiation during fluoroscopy, protective equipment does not completely prevent exposure. Radiation to upper body including in the thyroid, eyes, or hands is often considered in radiation studies, however, some of the organs most susceptible to adverse effects of radiation, such as the intestines and gonads, are in the lower body. We sought to quantify the risk of radiation exposure to upper and lower body organs using a cadaver model for a urological procedure routinely performed at our institution.

Methods used Following institutional review board approval, two male cadavers were obtained. The 'patient' (BMI 24.6) was positioned supine and underwent fluoroscopy consistent with a percutaneous nephrolithotomy (PCNL) procedure at our institution. The 'surgeon' (BMI 20.7) was placed upright 11 inches from the center of the radiation source to simulate the position of the surgeon during PCNL. Ten total trials were run, 5 trials

Abstract 153 Table 1 Unilateral and prophylactic descriptive statistics

		Unilateral (n=97)	Prophylactic (n=100)	P
Sex	Male	61	65	-
	Female	36	35	-
Age (years)		12.4	11.3	<0.001*
BMI		27.9	28.4	0.57
BMI Percentile		92.6%	93.5%	0.08
Modified Oxford Bone Age Score		20.6	19.6	0.006*
Operative Time (minutes)		48.6	86.5	<0.001*
Estimated Blood Loss (mL)		8.6	13.2	0.004*
Length of Hospitalization (days)		1.0	1.1	0.28
Length of Follow-up (months)		27.7	21.3	-
*Statistically significant difference between unilateral and prophylactic groups ($p<0.05$)				

with the surgeon wearing a 0.35 mm lead gown and 5 trials without lead. Twenty minutes of fluoroscopy were used per trial. Dosimeters were placed in the 'surgeon' in various radiation sensitive organs divided into two groups, those above the operating table (thyroid, lung, sternum, and liver) and those below (male gonads, kidney, bladder, colon). Mann-Whitney U tests were used to evaluate significance.

Summary of results A 96% reduction ($p < 0.001$) in radiation was recorded between unshielded (12.8 mrem) and shielded (323.1 mrem) organs. For shielded trials, the organs with highest radiation exposure were colon (19.6 mrem), bladder (15.6 mrem), and sternum (13.6 mrem). Organs showing lowest exposure were thyroid (9 mrem), lungs (10.2 mrem), and liver (10.4 mrem). Combined, the upper body and chest had significantly lower (32%, $p = 0.013$) radiation than those below.

Conclusions Although standard radiation protection measures dramatically reduce exposure to medical personal, when considered long-term, they may not be adequate in protecting organs most susceptible to radiation like the colon. In addition to wearing lead shielding surgeons, should take measures to reduce the fluoroscopy time and dose.

155 ABDOMINAL TRAUMA OUTCOMES AT A TERTIARY HOSPITAL IN SOROTI, UGANDA: A RETROSPECTIVE ANALYSIS

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Purpose of study To determine the rate of negative laparotomy in trauma at Soroti Regional Referral Hospital (SRRH), and to determine the severity of injuries associated with abdominal trauma.

Methods used Retrospective review of the SRRH trauma registry, OR registry, and patient charts for the period of April 1, 2017- June 1, 2018 for all patients admitted for treatment of abdominal trauma. Information collected included demographic, physiologic, and course of care data.

Summary of results There were 42 patients admitted to SRRH for treatment of abdominal trauma during the study period, with 39 having complete data. There were 14 poly-traumas and 25 uni-traumas. 18 were treated non-operatively and 21 were treated operatively. The most common mechanisms of injury included falls (39%), MVA (38%), blunt force (10%), stabbing (8%), assault (5%), and GSW (2%). Falls were the most prevalent cause of injury in the surgical group (52%), with 90% of these being falls from mango trees. There were significantly more male patients treated operatively (81%) than non-operatively (39%) ($p = 0.0100$). There were 17 positive laparotomies and 4 negative laparotomies (19%). Patients treated operatively had significantly lower rates of imaging upon presentation compared to the non-operative group ($p = 0.0489$); there was no difference in imaging between the positive and negative laparotomy groups. Injury Severity Score (ISS) in the operative group (10.71) was significantly higher than the non-operative group (4.94) ($p = 0.0052$). Overall rate of

unnecessary operations was 38.10% (8/21), determined using the Shock Index to identify hemodynamically stable patients in the operative group, which in retrospect could have been managed conservatively.

Conclusions This centre has a high negative laparotomy rate, at 19%. Patients treated operatively for abdominal trauma had significantly lower rates of imaging upon presentation, and significantly higher ISS values than those managed conservatively. The overall rate of unnecessary operations in abdominal trauma is 38.10%.

156 ESTABLISHING A BASELINE OF OPERATIVE TIME AND LENGTH OF STAY FOR DEGLOVING INJURIES

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Purpose of study Degloving soft tissue injuries are the result of skin and tissue avulsing from the underlying muscle, bone or connective tissue. This trauma is usually the result of a tangential force with an irregular surface catching a part of the body at a low velocity, such as when the tires of a car run over an arm in a motor vehicle accident. Important structures become exposed with considerable damage to the avulsed skin. Currently, there is no established expected operative time for degloving injury surgeries, nor has any study looked at the length of hospital stay and the number of required for reconstruction. The present study seeks to establish these baseline characteristics for extremity degloving injury management for ultimate comparison to newer techniques.

Methods used A detailed review of the electronic medical record from a level I trauma center for dates ranging from 06/2012 to 07/2018 revealed 186 trauma cases with potential degloving. Because there is no specific diagnosis code for a degloving injury, each patient's chart was reviewed for signs that the traumatic injury was specifically a degloving injury. The investigators reviewed the encounter history to find surgical, emergency, admission, and/or office visit events to find the desired information. Some of the main keywords that were looked for were in these events were 'degloving', 'avulsion' and 'skin flap' to identify a degloving case. The patients' ages, sex, location of the injury, cause of injury, and procedure done were all collected when possible, as well as the patient's length of stay from the date on the specific case in the list, the operative time (in minutes), and the number of procedures done to reconstruct the patient.

Summary of results Of the 186 trauma cases, 26 degloving patients were identified. The age range for patients identified was 2 to 58 with a mean of 32.9 years. The sex distribution was 69.3% male and 30.7% female. 100% were upper extremity injuries. The average length of stay for these patients was 8.54 days. The mean number of surgical procedures was 2.9. The total operative time was and average of 360.8 min.

Conclusions This study has produced a baseline measure of common economic parameters associated with degloving injuries. This data shall serve as comparative data for novel management protocols.

157

ENDOSCOPIC INSTRUMENTS INCREASES THE RADIATION EXPOSURE DURING URETEROSCOPY: A CADAVER STUDY

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Purpose of study Fluoroscopy units are most frequently operated in the Automatic Brightness Control (ABC) mode which automatically adjusts the settings (mA, KVP) to optimize image quality. In this setting, increased patient attenuation (obesity), increases the radiation exposure to patient and surgeon. During ureteroscopy, objects may be placed within the fluoroscopy beam path and the effect of this equipment within the beam is not known. The purpose of this study is to investigate the effects of surgical equipment within the fluoroscopy beam path.

Methods used Following institutional review board approval, a male cadaver (BMI 24.6) was draped in lithotomy position simulating a right ureteroscopy. Fluoroscopy was performed using ABC with no equipment over the beam path (control) and during 7 experimental settings where equipment was placed within the fluoroscopy path. Equipment placed in the fluoroscopy beam included: a flexible ureteroscope, a rigid cystoscope, a Kelly clamp, a beam splitting camera and light cords in straight and coiled positions, 3 EKG leads, and the table support beam. Ten 145 s fluoroscopy trials for each arm were performed. Mann-Whitney U tests were performed to compare radiation exposure between control and experimental arms.

Summary of results Compared to control ABC fluoroscopy with no equipment in the beam path (18.53 mGy), the presence of equipment in the fluoroscopy beam significantly raised radiation exposure for flexible ureteroscope (21.05 mGy; $p=0.0002$), rigid cystoscope (21.20 mGy; $p=0.0002$), Kelly clamp (19.38 mGy; $p=0.0022$), straight camera and light cords (19.30 mGy; $p=0.0051$), coiled camera and light cords (20.25, $p=0.0010$), and when the table support beam was included in the X-ray field (25.01; $p=0.0018$).

Conclusions Adjusting table position to exclude the support beam from the radiation field and avoiding placement of equipment within the fluoroscopy beam when the machine is operated in ABC can result in a significant decrease in radiation exposure to patients undergoing ureteroscopy. These minor adjustments in surgical practice may result in up to a 35% reduction in patient exposure.

158

SURGICAL CORRECTION OF VELOPHARYNGEAL DYSFUNCTION IN CHILDREN WITH 22Q11.2DS

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Purpose of study Up to 90% of patients with 22q11.2DS (22q) present with velopharyngeal dysfunction (VPD) and may require speech therapy and/or surgery. A recent systematic review found that no single surgical technique yielded better speech outcomes with fewer complications. This study aimed

to determine whether any pre-operative factors influence speech.

Methods used This 20 year retrospective study reviewed patients with a 22q diagnosis who underwent speech surgery at BC Children's Hospital. Improvements in speech score, categorized by the SLP-3 Scale, were compared against surgical technique, pre-operative closure anatomy, gap size, and developmental delay.

Summary of results Twenty-two patients met the inclusion criteria. Post-operatively, 15 had competent speech, 3 had borderline speech, and 4 had incompetent speech. There were no significant association between the improvement in speech outcomes and surgical technique, pre-operative closure anatomy, gap size, and developmental delay. There was no association between a patient's pre-operative anatomy and a surgeon's choice of technique.

Conclusions Acceptable speech can be attained for patients with 22q and no single pre-operative factor individually influences speech outcomes. Prior systematic reviews and our findings did not identify one surgical technique to be better at improving speech. Therefore, we suggest that a surgeon's choice of technique with which (s)he is most familiar may lead to a superior speech outcome.

159

A MODIFIED PHARYNGEAL FLAP TECHNIQUE FOR THE TREATMENT OF VELOPHARYNGEAL INCOMPETENCE

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10.1136/jim-2018-000939.158

Purpose of study Numerous surgical interventions are described for the management of velopharyngeal incompetence (VPI), though there is no definitive superior option. Our group previously described a novel approach for effectively managing VPI in children with 22q11.2 deletion syndrome (22qDS): a modified high pharyngeal flap with through-and-through dissection of the soft palate for flap inset. The purpose of this study is to determine the effectiveness of this surgical technique for treatment of VPI in non-22qDS patients. Here we report speech and surgical outcomes in a consecutive series of patients with severe VPI not associated with 22qDS, treated with our modified pharyngeal flap technique.

Methods used In this single surgeon retrospective case series, we explore outcomes in non-22qDS patients with severe VPI treated during the last six years with our modified pharyngeal flap. Preoperative velopharyngeal dynamics were assessed by videofluoroscopy or nasoendoscopy. A trained speech language pathologist conducted perceptual speech assessments using the SLP-3 scale with a minimum 6 month follow-up.

Summary of results Mean patient age was 6.7 years at the time of surgery (range, 3.8–16.7 years). All patients had severe VPI, with a mean preoperative speech score of 10.6 out of 13 (range, 7 to 13), which improved significantly to a mean postoperative score of 1.6 out of 13 (range, 0 to 7; $p<0.001$). Velopharyngeal competence was restored in 25 patients (83%), borderline competence in 3 patients (10%),

and VPI persisted in 2 patients (7%). Complications included one palatal fistula that required non-urgent revision, as well as one case of mild obstructive sleep apnea that did not require flap takedown. Mean skin-to-skin operative time was 74.9 min $\pm$ 12.4 (mean $\pm$ SD; range, 55 to 95) for patients undergoing isolated pharyngeal flap surgery (60%) and mean postoperative length of stay was 52.3 hours.

Conclusions The modified pharyngeal flap with through-and-through dissection of the soft palate allows direct visualization of flap placement. This leads to effective restoration of VP competency, independently of preoperative anatomy or etiology, with low complication rates, and short operative time.

160 OUTCOMES OF REVISION ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN ADOLESCENTS

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Purpose of study This study aims to analyze the outcomes of revision ACL surgeries in the pediatric population.

Methods used A retrospective study was performed on all revision ACL reconstructions performed at a single institution between 2009 and 2017. Patient demographic, injury, and operative data from the initial surgery and the revision were documented. Outcome measures included the Lysholm score, SANE score, Tegner activity score, satisfaction, visual analog score, HSS Pedi-FABS score, ability to return to the same level of sport, and any additional injury and/or surgery information. Outcomes and complications of the revision surgeries were compared to our institution's database of primary ACL reconstructions.

Summary of results Sixty revision ACL reconstructions in 57 patients were performed during the study period. Of these patients, 85% were available for a minimum 2 year follow-up and a mean follow up of 4.4 years. The mean age at the time of revision surgery was 17.0 years (range 12–20) compared to 15.4 years for the primary patients ($p<0.001$). A greater percentage of patients undergoing a revision procedure used an allograft compared with the primary cohort (65% vs 7%; $p<0.001$). A greater number of meniscus tears and cartilage injuries were documented in the revision cohort. Compared to the primary cohort, the SANE score, Lysholm score, and satisfaction were all lower in the revision cohort. Furthermore, these patients had a higher graft failure rate (21% vs 9%; $p=0.015$), and only 27% of revision patients returned to the same level of sport. When comparing revision procedures performed with autograft compared to allograft tissue, the autograft patients had higher Lysholm scores (91 vs 83; $p=0.045$) and trended towards a lower failure rate (11% vs 27%; $p=0.19$).

Conclusions Adolescent patients undergoing revision ACL reconstruction have more meniscus/cartilage pathology, poorer functional outcomes, higher graft failure rates, and lower return to sport than patients undergoing primary ACL reconstructions. Additionally, revision procedures performed with allograft tissue have lower Lysholm scores and a trend towards higher failure rates. When an ACL graft fails in a young patient, strong consideration should be given to using autograft tissue for the revision procedure

Poster Session

Adolescent Medicine and General Pediatrics

6:00 PM

Thursday, January 24, 2019

161 EMOTIONAL EATING, INCOME LEVEL, AND BMI IN CHILDREN

A Carnduff, E Williams, J Sawada, Y Lozano, S Harris, C Irani, E Medina, M Baum. Loma Linda University, Loma Linda, CA

10.1136/jim-2018-000939.160

Purpose of study This study's goal was to determine if emotional eating and/or income level correlated with unhealthy weight.

Methods used Children from the ages 8–16 years attended 'Operation Fit' after physician recommendation. This recommendation was based on risk for unhealthy weight (BMI>85th percentile). Operation Fit is a week long program, filled with nutritional and exercise orientated lessons. A pre-survey was completed on the first day of camp and a post-survey was completed at the end of camp. Both parents and children answered standardized questions concerning nutrition, exercise, and lifestyle practices. Children's BMI were collected. 787 children were included in this study.

Summary of results Logistical analysis were applied to evaluate connection between emotional eating and a child with unhealthy weight (BMI>85th percentile). The table 1 below shows results, indicating that there was statistical significance for emotional eating and unhealthy BMI. For females, a high BMI was seen in 69% ($n=258$; total $n=373$) of those who emotionally eat. In males, a high BMI was seen in 66% ($n=275$; total $n=414$) of those who emotionally eat. There was an increase in females with unhealthy BMI, but it was not statistically significant ($p=0.08$). A logistical analysis was also run between income level and emotional eating, but the results were not statistically significant.

Conclusions These results suggest that emotional eating in children can be associated with unhealthy BMI. These results have been found in adults, but to find them in children as well is surprising. With the statistical significance in mind, it may be beneficial for pediatricians to tailor prevention of obesity by including mental health hygiene. It may be of interest to investigate whether emotional eating is particularly aggressive in younger or older groups of children. As for the null significance of income level and unhealthy BMI, a preponderance of low income children enrolled in the program may have skewed results.

Abstract 161 Table 1

Parameter	P-Value
Emotional eating and unhealthy BMI	0.0423
Income level and BMI	0.8699
Emotional eating and income level	0.6460

162 A CODE TO PREVENTION: PROVIDING ONLINE RESOURCES FOR SUBSTANCE USE PREVENTION IN ADOLESCENTS IN THERMOPOLIS, WYOMING

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10.1136/jim-2018-000939.161

Purpose of study The use of addictive substances has serious consequences on the body and effective addiction prevention is key for reducing rates of substance use. Therefore, prevention must begin before addictions start, namely early adolescence. Rural communities may struggle with substance use due to limited access to resources and education. Thermopolis is a rural town of 2937 people located within Hot Springs County (HSC), WY, with high rates of methamphetamine use and a lack of a substance use prevention program for adolescents.

Methods used Community interviews and a review of demographics were done to identify a health domain of concern for HSC. A literature review was conducted to identify effective methods for substance use prevention in adolescents. Community partners were established with HSC Public Health and HSC High School via phone and in-person meetings. A prototype of a wallet-sized card was then developed with the intent of providing a cost-effective way to connect members of a rural community to national resources. The final prevention card prototype was then proposed to the community partners and chief of staff at HSC Memorial Hospital.

Summary of results Preliminary online research and community interviews indicated that substance use was an issue for HSC. The literature review revealed that online and interactive methods were effective in preventing increases in substance use in adolescents over time. The final prototype of the wallet prevention card is a three-paneled mini-brochure that contains QR codes to connect teens, parents, and teachers to interactive games, informational videos, and lesson plans on the National Institute on Drug Abuse website. Proposal of this design was approved by the community partners who additionally offered to provide future funding, support, collaboration for this project.

Conclusions The goal of the prevention card is to provide a cost-effective, simple, and efficient way to provide access to national resources to help parents, teachers, and teens become educated about substance use. With sufficient funding it will be possible to distribute these cards at HSC Public Health and HSC High School during counseling visits and interactive classroom sessions in order to provide access to resources as a means of introducing a sustainable substance use prevention program in HSC.

163 EVALUATING THE NEED FOR HOSPITALIZATION AFTER UNCOMPLICATED ENEMA REDUCTION OF INTUSSUSCEPTION IN THE PEDIATRIC POPULATION: A LITERATURE REVIEW

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10.1136/jim-2018-000939.162

Purpose of study The purpose of our research was to determine the need for hospitalization after successful enema reduction of uncomplicated intussusception by comparing the outcome in patients who were hospitalized and patients who were observed in the Emergency Department (ED) after reduction.

Methods used We performed a literature review using databases Pubmed and Google Scholar to find articles involving the recurrence of intussusception in pediatric patients after enema-reduction. Only studies of pediatric patients with intussusception which compared two groups: ED observation vs hospitalization were included in our analysis.

Summary of results Four studies fulfilled our inclusion criteria (see table 1). All of the studies were retrospective and included only patients with uncomplicated intussusception who had a successful enema reduction on the first attempt. In all of the studies, the average age of patients was between 11 months to 20 months. In majority of the studies, the rate of recurrence was between 7.8%–12.5% in both the hospitalized and ED groups. About half of the recurrences occurred within the first 48 hours after reduction (early recurrence). In majority of the studies, there were no significant differences in recurrence rates or adverse outcomes when comparing the 2 groups.

Conclusions When comparing hospitalization vs ED observation of patients with uncomplicated intussusception, our literature review shows no difference in outcome. A minority of patients had recurrences after discharge from the ED, but there were no serious complications when compared to the hospitalized group. our findings suggest hospitalization may be unnecessary. The limitations of studies included small number of patients and the retrospective nature. Further prospective studies are needed to identify risk criteria for those who may qualify for early discharge from ED vs those who require hospitalization.

164 IS BMI A PREDICTOR OF 'BODY POSITIVITY' IN CHILDREN?

¹E Williams, ¹A Carnduff, ¹YD Lozano, ¹J Sawada, ¹S Harris, ²C Irani, ¹E Medina, ¹M Baum. ¹Loma Linda University, Loma Linda, CA; ²Institute for Community Partnerships, Loma Linda, CA

10.1136/jim-2018-000939.163

Abstract 163 Table 1 Post-reduction outcome of intussusception ED stay vs. hospitalization

First Author, Year Published	N Subjects Hospitalized	N Subjects Observed ED	Average Hospitalized Stay (hours)	Average ED Stay (hours)	% Recurrence in Hospitalized Group	% Recurrence in ED Group	Average time of early recurrence in both groups	Average or range of time of late recurrence in both groups
Gilmore, 2011	10	43	33.7	7	0 (0%)	7 (12.5%); 2 while in ED	30 mins to 28 hours	4 to 27 months
Mallicote, 2017	79	68	31.7	4.9	11 (14%)	10 (15%)	18 hours	166 days
Bajal, 2003	27	51	22.7	7.2	4 (14.8%)	4 (7.8%)	5 hours	10.5 months
Chien, 2013	90	8	35.2	7.1	7 (7.8%)	0 (0%)	4 hours	8.9 months

Purpose of study In America, the prevalence of children and adolescents with obesity is 18.5%. In San Bernardino County schools, almost 40% of children are either overweight or obese. Studies have shown that overweight children tend to have lower self-esteem than their peers. As body dissatisfaction has been linked with unhealthy eating behaviors and disorders, in recent years there has been an increase in positive body image campaigns for children to develop body positivity, which encourages acceptance of all body shapes and sizes. This study evaluates if there is a correlation between BMI and taking pride in one's body.

Methods used Children ages 9–15 years old were referred from pediatric clinics in San Bernardino County. The children participated in Operation Fit, a day camp aimed at exposing kids at risk for unhealthy weight (BMI >85th percentile) to healthier lifestyle principles. BMI was measured on the first day of camp. They completed a Body Esteem Scale survey which included a question that asked 'whether or not they are proud of their body.'

Summary of results A logistic regression for a sample size of $n=411$ was used to determine if BMI was a predictor of body positivity. When all the variables were held constant, there was no relationship between BMI and taking pride in one's body ($p=0.47$). Gender, while nearly significant ($p=0.0631$), was not a good predictor of body pride.

Conclusions In our population, BMI and gender were not good predictors of body positivity. This seems contradictory to research that indicates that children of healthy weight have higher self esteem than children of unhealthy weight. Body image campaigns may be successful in conveying that body positivity is good, while body negativity is unhealthy. Choosing to take pride in one's body regardless of appearance pressures can create resiliency so children are better able to cope with negative influences. Additionally, body pride levels may be higher in children with unhealthy weight who also have parents/grandparents of unhealthy weight and many classmates of unhealthy weight. Further research is needed to determine what types of protective messaging is taught to children of unhealthy weight regarding self image.

Poster Session

Cardiovascular

6:00 PM

Thursday, January 24, 2019

165

THE TIMING OF ANTIBODY-MEDIATED REJECTION IN THE FIRST-YEAR AFTER HEART TRANSPLANTATION: DOES IT MAKE A DIFFERENCE?

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10.1136/jim-2018-000939.164

Purpose of study Antibody-mediated rejection (AMR) has recently been documented to have specific criteria in the 2011 ISHLT AMR biopsy-grading scale. AMR has been found to correlate with the development of cardiac allograft vasculopathy (CAV), primary graft dysfunction, and reduced survival.

Abstract 165 Table 1

Endpoints	AMR in the First-Month Post-HTx (n=9)	AMR at 2–12 Months Post-HTx (n=11)	P-Value
Subsequent 5 Year Survival	77.8%	81.8%	0.738
Subsequent 5 Year Freedom from CAV	100.0%	72.7%	0.116
Subsequent 5 Year Freedom from NF-MACE	88.9%	45.5%	0.038
Incidence of Recurrent AMR in the First-Year Post-HTx, %	0.0%	0.0%	1.000

The timing of AMR presentation i.e. whether AMR occurs early or late after heart transplantation (HTx) has not been firmly established. We chose to assess the timing of AMR and outcome after HTx.

Methods used Between 2000 and 2013, we assessed 20 HTx recipients who developed biopsy-proven AMR ≥ 1 in the first-month post-HTx ($n=9$) or 2–12 months post-HTx ($n=11$). Endpoints included subsequent 5 year survival, and subsequent 5 year freedom from CAV (as defined by stenosis $\geq 30\%$ by angiography) and non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke). Of interest was whether early AMR in the first month post-HTx led to increased recurrence of pathologic AMR in the rest of the first-year.

Summary of results The timing of AMR was the following: 45% of AMR occurred in the first-month post-HTx and 55% occurred between 2–12 months post-HTx. None of the patients with early or late AMR had recurrence of AMR in the first-year. In the long-term, late AMR was associated with significantly less freedom from NF-MACE. However, there was no difference in 5 year survival or 5 year freedom from CAV in patients with early or late AMR (see table 1).

Conclusions AMR in the first-month and in subsequent months (within the first year) post-HTx appears to have acceptable outcome. Late AMR may increase the risk for NF-MACE. More aggressive anti-humoral immunosuppression strategies may be warranted in this patient population.

166

TAKOTSUBO CARDIOMYOPATHY IN PATIENT WITH HYPOVOLEMIC SHOCK AND METHAMPHETAMINE USE

A Sandhu, K Doyle, F Joolhar, K Tangonan, T Win. Kern Medical, Bakersfield, CA

10.1136/jim-2018-000939.165

Case report Takotsubo cardiomyopathy, or broken heart syndrome, speculated to be due to release of catecholamines in response to extreme emotional insults has been reported throughout the literature in medicine. However large amounts of sympathetic activation and catecholamine release is not limited to realms of emotional triggers but can also be seen during times of severe hypovolemic shock, as well as in the presence of amphetamine ingestion, leading to similar cardiac findings on transthoracic echocardiogram as those seen in Takotsubo.

We present a case of a 62-year-old female with history of Chronic obstructive pulmonary disease, amphetamine abuse and an extensive psychiatric history who presented to the emergency department with hypotension and an acute kidney injury and initial urine toxicology positive for methamphetamine. Patient required fluid resuscitation and vasopressor support. Initial transthoracic echocardiogram done for cardiac murmur evaluation revealed preserved ejection fraction. Over the course of the admission patient was weaned off of vasopressors and transferred to the medical surgical floor. However, while on the floor, patient had an episode of non-sustained ventricular tachycardia and elevated troponin on labs. Electrocardiogram done did not show any ischemic changes, however, repeat transthoracic echocardiogram done showed reduced ejection fraction with typical finding of Takotsubo cardiomyopathy with apical ballooning present on imaging and akinetic chamber walls. Patient underwent cardiac catheterization which showed no significant atherosclerosis. Patient was discharged home on medication regimen targeting her congestive heart failure and repeat transthoracic echocardiogram showed improvement in the patient's ejection fraction. Takotsubo cardiomyopathy it seems is not a phenomenon limited to matters of a broken heart but can be seen in the patient population with an affinity for abusing illicit drugs, such as amphetamines as well as in extreme cases of hypovolemic shock. It becomes of the utmost important to keep this disease process as part of the differential diagnosis when approaching these patients.

167

STENOTROPHOMONAS MALTOPHILIA BACTEREMIA WITH SUSPECTED ENDOCARDITIS IN PATIENT WITH IMPLANTABLE CARDIOVERTER DEFIBRILLATOR AND CONGESTIVE HEART FAILURE SECONDARY TO AMPHETAMINE ABUSE

A Sandhu, A Heidari, K Doyle, K Tangonan, T Win, F Joolhar. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.166

Case report Multi drug resistant with the capacity to form a biofilm are just some of the characteristics of this aerobic, nonfermentive, Gram-negative bacterium known as *Stenotrophomonas maltophilia*. With a reputation of being a causative agent in difficult to treat infections which span across the spectrum of cellulitis to ophthalmitis to bacteremia, and being especially deadly in the immunocompromised population, this microbe is a noteworthy contender for the list of bacteria that clinicians need to be aware of when dealing with patients with indwelling catheters or implantable cardiac devices. We here report a case of a 23-year-old male with congestive heart failure with reduced ejection fraction and recent Implantable cardioverter defibrillator and peripherally inserted central catheter (PICC) for inotropic support with milrinone, who presented to the emergency department with episodes of intermittent chills and lab work positive for two blood cultures that grew *Stenotrophomonas maltophilia*. The culture and sensitivities revealed the microbe to be susceptible to Bactrim and Cefazidime and patient was started on the appropriate regimen. The PICC line was removed, along with the ICD to ensure complete resolution of the bacteremia and prevention of biofilm formation on the foreign objects. Transthoracic and Transesophageal echoes done did not show any vegetations on the leads or any valvular

involvement. Patient was continued on long term antibiotics and saw improvement in his symptoms. It therefore is of the greatest importance to be aware of this microbe when dealing with patients with multiple co-morbid conditions, immunocompromised state, and indwelling central venous catheters, to ensure timely initiation of appropriate antibiotic regimens to further prevent resistance and decrease the morbidity and mortality for the patient.

168

LONG-TERM OUTCOME OF HEART-KIDNEY TRANSPLANTATION IN AMYLOID PATIENTS

A Shen, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. *Cedars-Sinai Medical Center, Los Angeles, CA*

10.1136/jim-2018-000939.167

Purpose of study Heart transplantation in patients with amyloid light chain (AL) amyloidosis and transthyretin-related (TTR) amyloid has been controversial. In the advent of new treatments and bone marrow transplants, an increasing number of amyloid patients have received heart transplants. However, outcomes of dual-organ transplantation – namely, heart-kidney transplantation (HKTx) – in amyloid patients has not been studied. It is believed that kidney involvement with amyloid meant systemic disease and a contraindication to HKTx. Therefore, we sought to assess whether amyloid patients have good long-term outcome post-HKTx.

Methods used Between 2011 and 2014, we assessed 4 patients (2 AL, 1 TTR-wildtype (wt), 1 TTR-mutant (m)) who underwent combined HKTx for cardiac amyloidosis at our single center. A control HKTx population without amyloidosis was included (n=26). Endpoints included 4 year outcomes including survival, freedom from cardiac allograft vasculopathy (CAV) as defined by stenosis $\geq 30\%$ by angiography, freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke), and freedom from any-treated rejection, acute cellular rejection, and antibody-mediated rejection.

Summary of results None of the 4 amyloid patients who received a combined HKTx died after four years. HKTx amyloid patients had a higher rate of CAV development compared to the HKTx control but this was not statistically significant. There was no significant difference between the groups for any of the endpoints (see table 1).

Abstract 168 Table 1

Endpoints	AL/TTR Amyloid +HKTx (n=4)	HKTx Control (n=26)	Log-Rank P-Value
4 Year Survival	100.0%	80.8%	0.345
4 Year Freedom from CAV	75.0%	92.3%	0.265
4-Freedom from NF-MACE	100.0%	96.2%	0.695
4-Freedom from Any-Treated Rejection	100.0%	88.5%	0.476
4 Year Freedom from Acute Cellular Rejection	100.0%	96.2%	0.683
4 Year Freedom from Antibody-Mediated Rejection	100.0%	92.3%	0.568

Conclusions HKTx in amyloid patients has good long-term outcome. Therefore the need for a kidney in amyloid patients should not be a contraindication to heart transplantation. Larger numbers are needed to confirm these findings.

169 IS AMIODARONE TRULY A RISK FACTOR FOR PRIMARY GRAFT DYSFUNCTION IN HEART TRANSPLANTATION?

K Yabuno, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. *Cedars-Sinai Medical Center, Los Angeles, CA*

10.1136/jim-2018-000939.168

Purpose of study Primary graft dysfunction (PGD) after heart transplantation (HTx) is seen in approximately 10%–30% of patients immediately post-transplant. The cause of PGD is not clear but may include recipient, donor and peri-operative factors. Most recently, the presence of amiodarone at time of HTx has been associated with development of PGD. The mechanisms of this association are not clear. We sought to confirm this observation in a large single-center study.

Methods used Between 2010 and 2015, we assessed 364 HTx patients. We divided this cohort into those that were on amiodarone at the time of HTx (n=73) and those who were not on amiodarone (n=291). PGD was defined per the ISHLT PGD Grading Scale (mild, moderate, and severe PGD). Patients on amiodarone were further subdivided into those with high-dose (>200 mg daily, n=34) vs low-dose therapy (≤200 mg daily, n=37).

Summary of results Patients on amiodarone at the time of HTx did not appear to have increased risk of any grade of PGD vs those not on amiodarone. The incidence of PGD in the low-dose and high-dose amiodarone groups were similar (see table 1).

Conclusions Amiodarone use at the time of HTx (regardless of dose) does not appear to be a risk factor for the

development of PGD. Larger studies are needed to confirm these findings.

Poster Session

Gastroenterology

6:00 PM

Thursday, January 24, 2019

170 CEFDINIR INDUCED HEPATOTOXICITY

TS Matern, J Holt, G Chahal. *University of Nevada, Reno School of Medicine, Reno, NV*

10.1136/jim-2018-000939.169

Introduction Drug-induced liver injury is diagnostically challenging, as polypharmacy and novel medication use often makes it difficult to identify the culprit drug. Our research yielded only one case report in 2008 of Cefdinir-induced hepatotoxicity with actual pathologic confirmation of drug-induced cholestasis.

Case description The present case outlines a rare instance of Cefdinir-induced hepatotoxicity in a 50-year-old Hispanic male. The patient was hospitalized 11 days prior for septic pyelonephritis with associated perinephric abscess positive for group B strep. His infection was initially treated with IV Ceftriaxone; he was then switched to a 10 day course of oral Cefdinir. Following completion of antibiotics, the patient was readmitted for acute-onset jaundice with associated pruritus, diffuse right sided abdominal pain, and hepatomegaly. Blood cultures and CT imaging ruled out recurrent sepsis, pyelonephritis, or perinephric abscess. Liver enzymes were elevated with an ALT of 155, AST of 185, ALP of 1862, total bilirubin 11.7, conjugated bilirubin of 6.5, PT of 14.8, INR of 1.19, and PTT of 30. Of note, urine drug screen was negative, and acetaminophen level was unremarkable. Serology showed markedly elevated acute phase reactants with negative results for ANA, AMA, ALKMA, and ANCA. The patient was negative for HIV, as well as hepatitis A, B, and C.

Ultrasound, MRCP and ERCP showed no abnormalities that explained the patient's cholestasis. Liver biopsy revealed a mixed interface hepatitis consisting predominantly of neutrophils and eosinophils. These pathology findings, in conjunction with the onset of symptoms following Cefdinir use, supported the diagnosis of drug-induced cholestatic hepatitis. The acute hepatic injury observed in our patient was self-limited upon completion of antibiotics and administration of supportive therapy.

Discussion Although Cefdinir has only been implicated in drug-induced hepatotoxicity one other time, a comparison of the data from past literature supports Cefdinir as the culprit, as a similar pattern of LFT elevation and liver histological findings was observed. It is our hope that by identifying a second case of Cefdinir induced hepatotoxicity, we can now begin to describe the pattern and course of the associated liver injury, as well as the expected clinical outcome for affected patients.

Abstract 169 Table 1

Endpoints	Amiodarone at time of HTx (n=73)	No Amiodarone at time of HTx (n=291)	P-Value
Incidence of Primary Graft Dysfunction, %	6.8% (5/73)	4.8% (14/291)	0.554
Mild PGD, %	0.0% (0/73)	1.0% (3/291)	1.000
Moderate PGD, %	5.5% (4/73)	2.7% (8/291)	0.265
Severe PGD, %	1.4% (1/73)	1.0% (3/291)	1.000
Endpoints	High-Dose Amiodarone at time of HTx (n=34)	Low-Dose Amiodarone at time of HTx (n=37)	P-Value
Incidence of Primary Graft Dysfunction, %	5.9% (2/34)	8.1% (3/37)	1.000
Mild PGD, %	0.0% (0/34)	0.0% (0/37)	1.000
Moderate PGD, %	5.9% (2/34)	5.4% (2/37)	1.000
Severe PGD, %	0.0% (0/34)	2.7% (1/37)	1.000

Poster Session

General Internal Medicine and Aging

6:00 PM

Thursday, January 24, 2019

171

MALIGNANT CATATONIA: AN ELUSIVE AND PERPLEXING DIAGNOSISN Khan, A Sandhu, J Quinlan. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.170

Purpose of study Malignant catatonia is a rare disorder that presents with significant physiological manifestations of autonomic instability, coma, and death which requires urgent medical management. It can be mistaken for Neuroleptic Malignant Syndrome among other diseases and often is an elusive diagnosis.

Methods used Retrospective case report.

Summary of results A 20 year old African American male with a history of type II bipolar disorder presented with symptoms of catatonia and autonomic instability for 1 month. He had well controlled psychiatric symptoms off of medications for 1 year and then became suddenly mute and catatonic after moving from out of state. He was admitted to a local hospital, given a diagnosis of sepsis and thyrotoxicosis without improvement and he then presented to our hospital after his mother signed him out against medical advice. He had catatonia with mutism and catalepsy, brisk reflexes with sustained clonus in ankles, systolic blood pressure elevated to 210, tachycardia to 140's, and atrial fibrillation successfully treated with Digoxin. Workup resulted unremarkable MRI of brain, unremarkable cerebrospinal fluid for bacterial encephalitis, viral encephalitis, and autoimmune encephalitis. He was unsuccessfully treated empirically with 5 days of IVIG and Methylprednisolone for autoimmune encephalitis. He improved with Lorazepam 2 mg IV every 3 hours and Esmolol drip having intermittent verbalization, increased facial expressions, and ability to eat a limited diet. Psychiatry was consulted and recognized Malignant Catatonia and recommended transfer for definitive treatment with electroconvulsive therapy. An accepting facility was found however transfer was made complicated by court order given patients inability to consent, unsafe transfer due to patient's overall medical condition, and pending bed availability. Patient's mother then signed patient out against medical advice to take him to another facility despite having explained the risks of transfer.

Conclusions This case illustrates the delay in recognition of Malignant catatonia due to the multiple confounding symptoms, associated severe medical complications and resulting treatments, logistical and legal challenges for obtaining appropriate control of the disease, and the importance of Malignant catatonia as a medically significant differential diagnosis.

172

CATASTROPHIC TRACHEOESOPHAGEAL PERFORATION AS A RESULT OF ESOPHAGEAL RADIATIONN Khan, C D'Assumpcao, K Doyle, K Tangonan. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.171

Purpose of study Radiation therapy is often used in extra-nodal AIDS-associated Non-Hodgkin's lymphoma (NHL) as adjuvant to chemotherapy. Esophageal perforation is a rare but serious complication of esophageal carcinoma radiation. There have been reports of fistula formation, thoracic fluid collections, infections, and less often massive hemorrhage. Reported here is a fatal case of irradiated esophageal NHL complicated by spontaneous tracheoesophageal rupture.

Methods used Retrospective case report.

Summary of results 37 year old male with AIDS and associated primary diffuse large B cell NHL of the distal esophagus status post rituximab and radiation 1 month prior presented in cardiorespiratory arrest after having sudden onset profuse hemoptysis and hematemesis immediately after having used the restroom at home. CPR was immediately initiated and patient underwent failed cricothyrotomy and then successful rapid sequence intubation with difficulty. Patient had return of spontaneous circulation after 16 min and then unstable ventricular tachycardia with successful electrical cardioversion. On physical exam patient had blood in the oropharynx and nares, pale skin and mucosa, absent brainstem reflexes, myoclonic jerks, with GCS of 3T. CT angiogram of the chest revealed a large tracheoesophageal fistula with communication of the mediastinal soft tissues, bilateral dense consolidations of upper and lower lobes of the lung, and diffuse thickening of the esophageal wall. Gastroenterology deemed esophageal stent placement not possible given friable mucosa. Patient remained in intensive care for 3 days with no neurological improvement after rewarming from therapeutic hypothermia, discontinuing sedation, and EEG showing post-anoxic myoclonus status indicating a very poor prognosis. Per family wishes, patients was made comfort care and declared deceased on day 3 of admission.

Conclusions Catastrophic tracheoesophageal perforation with massive aspiration is the cause of death. It is suspected the mucosa was made friable by radiation therapy of primary large B cell esophageal NHL. Bearing down in the restroom may have perforated the friable mucosa between the trachea and esophagus. The risk to succumbing to this fatal complication should be discussed with patients when considering esophageal radiation therapy.

173

RECURRENCE OF EPENDYMOMA AFTER A DECADEH Saab. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.172

Case report Ependymomas are tumors that arise from the ependymal cells that line the ventricles for the brain and central canal of the spinal cord. Although these neuroectodermal tumors are the most common brain tumors and primarily present as intramedullary lesions, they rarely manifest as an extramedullary primary cord tumors. We present a case of a 47 year old Caucasian male who presented in 2006 with bilateral lower extremity weakness and paresthesia and was found to have six lesions after a lumbar laminectomy of L2-L5, one of which was found to be a myxopapillary ependymoma. He later presented again on April 2018 with similar symptoms and was found via an MRI of the lumbar spine to have two intradural masses

at T9 with compression of the spinal cord causing suspicion of recurrence of his extramedullary myxopapillary ependymoma. T8–10 laminectomy and gross tumor resection was accomplished and pathology report confirmed recurrence.

174

A CASE OF HEPATITIS C: TWO DECADES OF WAITING FOR GODOT OR CURE

HK Sandhu, A Heidari, D Mahoney, R Johnson. *Kern Medical – UCLA, Bakersfield, CA*

10.1136/jim-2018-000939.173

Purpose of study Treatment of hepatitis C has evolved drastically over last several years. Response rate has improved from less than 20% in early 1990s to over 90% recently. Treatment modalities have evolved from barely tolerability with serious adverse reaction to almost well tolerated treatment with minimal side effects. We are describing a case of chronic hepatitis c that failed treatment twice 20 years prior; the patient returned and was placed on a direct acting anti-viral agent.

Methods used Retrospective case report.

Summary of results A 56 years old Hispanic female presented to our hepatitis clinic 22 years ago with diagnosis of hepatitis C. Her viral load was over one million copies. She had no clinical evidence of cirrhosis and only risk factor was exposure to reused needles for medical purposes in Mexico before her immigration to US. Liver biopsy showed heavy portal lymphoid infiltrates, fatty changes, and hepatocytolysis. Her genotype was 1a and treatment was started with non-pegylated Interferon alpha 2a three times per week for 24 weeks. She failed treatment with viral load of over one million at the end of therapy. After one and half year she was started on combination of interferon 2b 3 times a week with daily ribavirin for 48 weeks. Before end of treatment course she developed severe neutropenia and therefore, treatment was stopped. Her viral load was 43 000. Liver biopsy showed grade 3 inflammation with stage 4 fibrosis. She was lost to follow up but came back to our clinic 15 years later. Her viral load was less than a million and her fibrosis score (FibroSure) came back as F3 and A3. She had negative screening for hepatocellular carcinoma with ultrasound and AFP. She was placed on combination treatment of Glecaprevir plus Pibrentasvir for 12 weeks duration. She has had no side effects to this point. The goal is to reach sustained virologic response or SVR, 12 weeks after completion of her treatment. **Conclusions** In the era of direct acting agents, treatment of hepatitis C is in its golden time. There should be more public education to encourage patients with previous failed attempts that the wait is over and cure is in reach.

175

INTRACELLULAR CYTOKINE SIGNALS AS BIOMARKERS OF DEPRESSION IN OLDER ADULTS

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10.1136/jim-2018-000939.174

Purpose of study To examine whether lipopolysaccharide-induced (LPS) expression of intracellular cytokines (ICCs) in peripheral blood mononuclear cells (PBMCs) is a sensitive

measure of inflammation that can be correlated to depressive symptoms in older adults.

Methods used This was a cross-sectional, secondary analysis of data from the Sleep Health Aging Research (SHARE) project. Our analysis included 180 Los Angeles community-dwelling older adults (>60 years old) with proportionate representation from high and low socially isolated groups. Depressive symptoms were measured using the 10-item Center for Epidemiological Studies-Depression Scale (CES-D 10). PBMCs were isolated from each participant, and LPS-induced expression of interleukin (IL)–6 and tumor necrosis factor (TNF)– α in PBMCs was measured using flow cytometry. Circulating inflammatory markers in plasma including soluble TNF receptor 2 (sTNFR2), IL-6, and C-reactive protein (CRP) were also measured. After adjusting for covariates, multivariate linear regression was used to test the associations between inflammatory markers and depressive symptoms.

Summary of results Positive correlations, although not statistically significant, were observed between depressive symptoms and LPS-induced expression of pro-inflammatory cytokines: Δ TNF- α (adjusted β =0.040, p =0.57), Δ IL-6 (adj. β =0.082, p =0.25), Δ TNF- α +IL-6 (adj. β =0.078, p =0.270). Non-significant negative correlations were found between depressive symptoms and circulating inflammatory markers: sTNFR2 (adjusted β =–0.022, p =0.79), IL-6 (adjusted β =–0.089, p =0.26), CRP (adjusted β =–0.13, p =0.094).

Conclusions Although the observed correlations were not statistically significant, in contrast to circulating inflammatory markers, the correlation of ICCs with depressive symptoms was in an expected direction, i.e., higher ICC expression correlating with higher depressive symptom severity. Inflammation measures via LPS-induced ICC expression may serve as more sensitive biomarkers of depressive symptoms in older adults and require further research.

176

REFRACTORY-PERSISTENT HEPARIN INDUCED THROMBOCYTOPENIA

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10.1136/jim-2018-000939.175

Introduction Heparin induced thrombocytopenia (HIT) is a pro thrombotic reaction caused by platelet activating antibodies that recognizes heparin-platelet factor 4 complex. Delayed onset HIT is characterized by a late nadir due to persistent platelet-activating IgG antibodies. It begins 5 or more days after heparin is discontinued with complications like thrombosis up to 3 weeks after exposure to heparin. In 50% of cases of typical HIT, the platelet count can decrease to <20,000/ μ L. Most cases respond to cessation of heparin and administration of non-heparin anticoagulant, but there are cases of persistent HIT, defined as thrombocytopenia due to platelet activation/consumption for more than seven days despite standard therapy. These patients are at high risk for thrombotic events, which may result in limb-loss and mortality. We present a case of delayed-refractory-HIT successfully managed with combination treatment of steroids and intravenous immunoglobulins.

Methods Retrospective case study.

Case summary 66 year old Hispanic Female with fracture secondary to trauma two weeks prior, on deep venous thrombosis(DVT) prophylaxis with low molecular weight heparin came with dyspnea. She was diagnosed to have DVT and bilateral pulmonary emboli. She had a platelet count of 17,000/ μ l. Heparin was discontinued due to high clinical suspicion for HIT and Argatroban was started. Confirmatory serotonin release assay was positive for HIT. Patient continued to have platelet count persistently less than 20,000/ μ l until day 10 of discontinuation of heparin. She was subsequently given total 3 doses of intravenous immunoglobulin (IVIG) on day 11, 12, 18 and solumedrol on day 17 with gradual improvement to 87,000/ μ l.

Conclusion Most cases of HIT respond to cessation of heparin and use of an alternative non-heparin anticoagulant, but there are cases of persistent HIT with high risk for thrombotic events resulting in limb-loss and mortality. IVIG has been proposed as an adjunct therapy for these refractory cases based on its ability to saturate Fc γ RIIa receptors on platelets, thus preventing HIT antibody binding and platelet activation. We demonstrate here successful use of IVIG and one dose of solumedrol in rapidly correcting the refractory thrombocytopenia.

177 CALCIPHYLAXIS OF MITRAL VALVE WITH INFECTIVE ENDOCARDITIS

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10.1136/jim-2018-000939.176

Case report

Introduction Calciphylaxis in end stage renal disease (ESRD) is well studied but there is limited data for calciphylaxis leading to valvular heart disease complicated by infective endocarditis (IE). ESRD is more common than rheumatic fever as etiologic factor for valvular calcification, thickening, stenosis or regurgitation, which is prominently seen in mitral or aortic valve in 40%–60% patients. ESRD patients who develop mitral annular calcification (MAC) are also at increased risk for IE with vascular access a significant risk factor.

Method used Retrospective case study.

Case summary 47 year old hispanic female with ESRD on hemodialysis was diagnosed with septic thrombophlebitis 4 days after placement of the right internal jugular (IJ) tunneled catheter. She had multiple skin lesions on abdomen, lower extremities secondary to calciphylaxis. Ultrasound showed occlusive thrombus in right IJ vein and Right IJ catheter was subsequently removed. Blood cultures and cultures from right IJ catheter tip grew methicillin resistant staphylococcus aureus(MRSA). Transesophageal echocardiogram showed moderate mitral annular calcification, massive amount of calcium causing severe mitral valve stenosis with valve area of 1 cm² and multiple small, mobile tissues density masses attached to the posterior leaflets. It also showed anteriorly directed regurgitant jet consistent with posterior leaflet pathology. Coronary angiography showed angiographically normal coronary arteries. She was treated for infective endocarditis and transferred to another facility for mitral valve replacement.

Conclusion ESRD patients on dialysis have increased risk of calciphylaxis causing valvular heart disease. It also carries increased risk of IE, thromboembolism and arrhythmias. Prevention and management of risk factors in dialysis patients is important since there is limited data to show benefit of management after onset of valvular heart disease. Once disease has progressed, patients with valvular calcifications carry a poor short and long term survival despite corrective valve replacement surgeries. Current guidelines also recommend antibiotic prophylaxis against IE in dialysis patients with mitral annular calcifications.

178 PAINLESS PAPULE TO MERKLE CELL CARCINOMA

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10.1136/jim-2018-000939.177

Introduction Merkel cell carcinoma(MCC) is a tumor of Merkel cells found in basal layer of epidermis, hair follicle. It is also associated with sensory neurites in dermal papillae with controversial origin as totipotent stem cell with neuroendocrine features acquired during malignant transformation. Incidence is 0.7 per 1 00 000 which increases with age but is also higher in young immunocompromised. Merkel cell Polyoma Virus (MCPvY) which is part of human skin genome has prevalence of 79% in patients with MCC. Integration of viral genome into tumor genome suggests viral proteins as oncogenic drivers in MCPvY positive MCC. Somatic mutations in tumor suppressor genes have been implicated for MCPvY negative MCC. MCC can be asymptomatic, localized skin lesion or as metastatic disease with diffuse lymphadenopathy and has been found to have increased risk of associated salivary, biliary tree and Non Hodgkin lymphomas within first year of diagnosis.

Methods Retrospective case study.

Case summary 64 y/o Hispanic female came to hospital with abdomen pain and 6 month history of painless papule on left thigh that progressed in size 2 months prior to presentation with unsuccessful incision and drainage. She had a shave biopsy of lesion which showed Malignant small blue cell tumor, also known as MCC. Imaging showed adenopathy along left pelvic wall, periaortic area and enlarged necrotic pelvic lymph nodes varying 4–6 cm in dimension. Patient had positive MCPvY oncoprotein antibody titer of 23900 STU with normal reference range of 0–74 STU. In interim patient was started on chemotherapy with cisplatin and etoposide followed by immunotherapy with Avelumab with regression of skin lesion.

Conclusion MCC is a rare carcinoma that can have unusual presentation as persistent painless papule to metastatic disease. Treatment varies from resection for stage 1 to chemotherapy with adjuvant immunotherapy with monoclonal antibodies to programmed cell death protein 1 (PD-1) as preferred therapy for patients with advanced metastatic MCC. Newer targeted therapies with tyrosine kinase inhibitors and somatostatin receptors are also used. MCPvY oncoprotein tumor antibody can be used as marker of tumor burden to monitor disease progression after appropriate treatment.

Poster Session

Genetics

6:00 PM

Thursday, January 24, 2019

179

THE MRNA TARGETS OF IRE1 DURING UNFOLDED PROTEIN RESPONSE

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10.1136/jim-2018-000939.178

Purpose of study The unfolded protein response is triggered by stress from improperly folded proteins in the ER. There are three associated pathways, with Inositol-requiring-1 (IRE1) being the most evolutionarily conserved. IRE1 has two isoforms – IRE1 α and IRE1 β . IRE1 α is ubiquitously expressed in mammalian cells, while IRE1 β is exclusively found in gastrointestinal and lung cells. IRE1 cleaves XBP1, which is ligated in the cytoplasm to generate an active transcription factor and executes cellular stress responses. IRE1 also cleaves mRNA targets in a process known as regulated IRE1-dependent decay of mRNA (RIDD) and has roles in maintenance of ER homeostasis and initiation of cell death. Improper UPR activation has been appreciated in inflammatory processes and many autoimmune disorders (i.e. atherosclerosis, SLE).

The mRNA targets of IRE1 during the UPR are unknown. We hypothesized that mRNAs targeted by IRE1 would degrade at a faster rate than nontarget mRNA.

Methods used This study utilized a 0 to 12 hour time course using HCT-116 cells, a colon cancer cell line. There were 4 time points (0, 2, 6, 12 hours), and the cells were split into four groups – 1.) control group treated with DMSO (vehicle control), 2.) treatment with 500 μ M thapsigargin (a chemical activator of the UPR), 3.) 4 μ g/mL of actinomycin D (chemical inhibitor of transcription), and 4.) both 500 μ M thapsigargin and 4 μ g/mL actinomycin D. RNA was collected from all 16 samples and used to generate mRNA sequencing libraries. Activation of the UPR with thapsigargin treatment was confirmed with an XBP1 splicing assay and inhibition of transcription with actinomycin treatment was confirmed by measuring XBP1 abundance by RT-qPCR.

Summary of results Data from the time course experiments is pending.

Conclusions The data from these time course experiments will identify mRNAs that are significantly down-regulated upon thapsigargin treatment, independent of new transcription initiated by the UPR to resolve the induced protein stress. The dependence of down-regulation of these mRNAs on Ire1 activity will be confirmed by using an Ire1 inhibitor. Together, these data will identify mRNAs whose down-regulation is dependent on Ire1 activity during the UPR.

180

CRISPR/CAS9-BASED GENE THERAPY FOR INHERITED VISUAL DISORDERS

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Purpose of study Usher syndrome type II is characterized by congenital sensorineural hearing loss and retinitis pigmentosa leading to progressive vision loss. This project targeted *USH2A*, the most commonly mutated gene in Usher syndrome, and investigated the use of CRISPR/Cas9-based gene editing as a viable therapeutic approach for retinal degeneration. The *USH2A* protein, or usherin, is required for maintenance of photoreceptors. Our study determined the efficacy of delivering CRISPR therapy via an adeno-associated viral (AAV) vector to post-mitotic human photoreceptor cells.

Methods used Two guide-RNA sequences were selected to direct the CRISPR/Cas9 editing system to the *USH2A* gene. These guides and the Cas9 genome were each inserted in a plasmid under the rhodopsin kinase promoter. All plasmids were packaged using the AAV2 capsid variant, 7 m8. The constructs were then administered to post-mortem human explant retinas and retinal organoids. Two weeks after administration, cells were dissociated and sorted to determine retinal cell transduction efficiency. The DNA sequence itself will be evaluated by PCR to determine the percentage of cells which were successfully targeted by the Cas9 double stranded DNA break.

Summary of results Results are pending, but the AAV vector is expected to transduce roughly 50%–60% of photoreceptors, and 5% or less of all other retinal cell types. Based on similar studies in the literature, we expect to see the desired CRISPR DNA edits in up to 10% of photoreceptors. We also expect that one guide-RNA will perform better than the other and will be used in future investigations.

Conclusions This study looked at the effectiveness of targeting CRISPR/Cas9 to *USH2A* by analyzing the products of non-homologous end joining in photoreceptors. Future directions include using this system to deliver a repair template in order to correct the most common mutation in *USH2A*. By presenting a clinically-relevant system for testing gene editing in the context of human photoreceptor cells in the lab, future researchers will be able to move toward testing these methods for therapeutic use in murine and human subjects. This has the potential to improve vision outcomes in patients affected by Usher syndrome, many of whom have few treatment options for their retinitis pigmentosa.

Poster Session

Health Care Research

6:00 PM

Thursday, January 24, 2019

181

EVALUATION OF THE NUTRITIONAL STATUS OF PEDIATRIC PATIENTS IN SOROTI, UGANDA

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10.1136/jim-2018-000939.180

Purpose of study According to the Uganda Health and Demographic Survey of 2016 (UHDS 2016), the frequency of severe malnutrition (-3 SD or less) in the sub-region surrounding Soroti is 3.3% stunting, 0.4% underweight, and 0.3% wasting. The aim of this research is to quantify the magnitude of discrepancy between the anthropometric Z-scores of pediatric patients (ages 6 months to 5 years) at Soroti Regional Referral Hospital (SRRH), and those recorded in UHDS 2016. We assessed demographics, food and water security, and the patient's reason for admission.

Methods used Anthropometrics assessed were height, weight, sex, age, mid upper-arm circumference (MUAC), and bipedal edema. We use these measurements to calculate Z-scores, a validated rapid nutritional assessment technique. A survey of patient pathology, demographics, and food security was conducted at SRRH in July 2018. Data collected is compared with corresponding statistics from UHDS 2016.

Summary of results Data was gathered for 99 patients. Severe stunting was seen in 25.6% of patients, severe weight deficiency was seen in 24.7% of patients, and severe wasting was seen in 19.1% of patients. 74% of guardians said their children were missing key foods, the most common of which were milk, eggs, and meat. 50% of patients were concerned that their drinking water was unclean, and 34% reported a history of typhoid. The median family income was 41,000 UGX (14.15 CAD) per month, and the median family size was 8 (4 adults, 4 children). It is important to note that 41,000UGX is well below the UNDP International Poverty line.

Conclusions Severe malnutrition is a significant concern at SRRH, and is in need of systemic addressing. Patients from families earning less than 41,000 UGX per month are more often stunted and underweight.

182

STRUCTURAL AND MECHANICAL CHANGES OF SOFT AND FIRM POLYURETHANE STENTS: A BENCHTOP STUDY

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10.1136/jim-2018-000939.181

Purpose of study Ureteral stents help relieve obstruction and maintain drainage. However, chronic indwelling stents carry complications including fragmentation, migration and encrustation. Other than indwelling time, factors contributing to stent encrustation are unknown. The purpose of this study is to compare the risk for encrustation and force required for removal in soft, firm, multi-length, and fixed length stents in a controlled artificial urine bath.

Abstract 182 Figure 1 Firm multi before vs after

Methods used Twenty four stent coils (6 firm multi-, 6 soft multi-, 6 firm fixed, 6 soft fixed length) were bathed in an *in vitro* artificial urine solution for 15 days at human body temperature to simulate a rapid encrustation model. The urine bath was exchanged every 3 days and the length and diameter of the stents were measured. The force required for stent removal from a ureteral benchtop model was measured using a force gauge before and after the urine bath. Mann-Whitney U test was used for statistical analysis with $p < 0.05$ considered significant.

Summary of results After 15 days, all stents showed evidence of encrustation on gross evaluation and SEM. The mean force required for stent removal after the urine bath was 0.664N (firm fixed), 0.549N (firm multi), 0.502N (soft fixed), 0.475N (soft multi). Firm stents required significantly more force for removal than soft stents prior to urine bath ($p < 0.001$) and after the urine bath ($p = 0.01$) regardless of whether these were fixed or multi-length. Soft stents increased in both length (9.5 to 12.7 cm; $p < 0.001$) and diameter (1.4 to 3.3 mm; $p < 0.001$) while firm stents only increased in diameter (1.4 to 2.3 mm; $p < 0.001$).

Conclusions Signs of stent encrustation occurred as early as 15 days. While firm stents required more force for removal, soft stents showed significant spatial changes. These should be considered at the time of stent selection to optimize patient comfort and quality of life.

183

ARE THERE BENEFITS TO ANIMAL ASSISTED THERAPY IN PEDIATRIC CANCER PATIENTS?

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Purpose of study Research studies have explored the benefits of animal-assisted therapy (AAT) in certain patient populations but there has been little research on the effectiveness and safety of AAT in pediatric oncology patients. The objective of this study was to evaluate the safety and benefits of AAT in pediatric cancer patients.

Methods used We performed a comprehensive literature review using search engines, Pubmed, Cochrane and google scholar. Only studies of pediatric oncology patients published in English that included both a patient-reported outcome and an assessment of a quantitative health impact were included.

Summary of results Our initial search on the topic of AAT yielded 68 articles. Of those, 10 studies were on pediatric

Abstract 183 Table 1 Impact of animal assisted therapy in pediatric patients with cancer

First Author and Year	Number of participants and age in AAT group	Description of Control Group	Frequency of AAT	Duration of Follow-up	Outcomes/Variables measured and how they were measured	Health Impact in AAT group vs Controls
McCullough A, 2018	n=60; Age: 3–17 years	n=46; Age 3–17 years No AAT	24 min session, once a week	4 months	Parental and Patient Stress/ Anxiety, BP, HR	Patients: Anxiety decreased in in both groups (P=,0.001), Parents: Anxiety decreased in AAT group (p=0.008)
Chubak J, 2017	n=19; Age: 7–18 years	n=19; Age: 7–18 years Pre and Post AAT	One-time 20 min session	4 months	Patient emotional distress and behavior. Provider and staff survey	Patient Emotional Distress Decreased (p=0.005), Overall positive feedback from staff
Silvia N, 2018	n=24; Age: 6–12 years	n=24; Age: 6–12 years; Pre and Post AAT	Three 30 min sessions per week	4 weeks	Patient HR, BP, Pain, Stress, Mood, and Caregiver	In patients: pain decreased (p=0.046), better mood (p=0.041), stress decreased (p=0.005). In caregivers: anxiety decreased (p=0.007), stress decreased (p=0.006)

HR=heart rate, BP=Blood Pressure, RR=Respiratory rate

oncology patients but only 3 of the 10 studies, included a quantitative outcome analysis and included perspectives from the patients and caregivers. See table 1 below for a summary of the studies. All of these studies excluded patients who required isolation or those with severe immunosuppression. The hospitals had a safety AAT protocol in place and the intervention consisted of visit(s) between a therapy trained dog team and each patient. Anxiety and fear was measured using standardized scales. In 2 of 3 studies, AAT provided immediate benefits, such as decreased anxiety, fear, and pain but sustained benefits were not measured. In the other study, care-takers and staff in the AAT group reported reduced stress. There were no adverse health effects such as zoonotic infections as a result of AAT.

Conclusions Although there is paucity of literature on the impact of AAT in pediatric cancer patients, our review provides beginning evidence that AAT can be used as adjunctive treatment to reduced stress and/or pain in a subset of pediatric cancer patients. In addition, AAT is well accepted by staff and care-takers. Larger prospective controlled trials are need to substantiate the benefits of AAT in pediatric cancer patients.

184

FOLLOW-UP ASSESSMENT OF THE SICKLE CELL DISEASE SCREENING PROGRAM IN THE INDIGENOUS THARU POPULATION OF NEPAL

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10.1136/jim-2018-000939.183

Purpose of study Sickle cell disease (SCD) is an inherited blood disorder that is found in regions with malaria and is associated with increased morbidity and mortality. Members of the indigenous Tharu ethnic group of the Terai region of Nepal suffer a high prevalence of SCD. Early screening of SCD reduces morbidity and mortality by increasing access to vaccinations, antibiotic prophylaxis, comprehensive care and education. There have been recent efforts to increase SCD screening in Nepal. A group of medical students from the University of British Columbia

conducted a screening program in a small region of Dang, Nepal in 2015, where 2899 individuals were screened and 271 were screened as positive. Following this, a local health post was provided with the necessary resources to conduct SCD screening independently. Our study followed up with the local health post to evaluate how effective the local health post has been in screening the Tharu population from 2015–2018.

Methods used We obtained SCD screening statistics from the local health post. The health post kept detailed records regarding the individuals that were screened, their results and their follow up treatment. SCD screening statistics for 2015, 2016, 2017 and up to August 2018 have been provided.

Summary of results SCD screening statistics indicate that 3825 individuals have been screened in the period of 2015 – August 2018. The total patients screened for each year has been 2899 (2015), 144 (2016), 668 (2017), 90 (2018). Over the course of 2015 – August 2018, 373 patients screened positive and 9 were diagnosed with SCD.

Conclusions There are various potential causes that may contribute to the large decrease in patients screened per year. One potential cause is the saturation of the screening program in the local Tharu population, such that most individuals have been screened. Other causes include inaccurate data collection and lack of education prompting individuals to get screened. Future directions should include studies to elucidate the causes of decreased SCD screening in the region. This will lay the foundation for future interventions, including additional screening programs at more locations and increased community education regarding SCD.

185

EVALUATION OF DIGITAL ANGLE MONITOR TO IMPROVE ULTRASOUND SKILLS IN ANESTHESIOLOGY RESIDENTS: A PILOT PROJECT

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10.1136/jim-2018-000939.184

Purpose of study Ultrasound use has expanded dramatically over the last decade. A difficult component of ultrasound training is understanding the ultrasound plane's relation to the body. Currently, instruction of the proper ultrasound probe angle with the skin is commonly based on crude probe movements (e.g. tail up/tail down). Adding a real-time digital angle monitor to the ultrasound probe would remove this subjectivity and allow for more precise probe manipulation. This study sought to evaluate if addition of a digital angle monitor to an ultrasound probe would improve the time to image acquisition and image quality for selected ultrasound scans. This study was a pilot project seeking to evaluate the utility of this tool to then facilitate future projects to improve both diagnostic and procedural ultrasound.

Methods used CA-1 anesthesiology residents at a single institution, after IRB approval, were randomized into either a digital angle monitor cohort or a non-digital angle monitor cohort. Each participant was given a handout instructing them on how to obtain 6, standard point of care ultrasound views on an ultrasound simulator (CAE Vimedix). The angle monitor cohort received an additional handout explaining the angle monitor, how to interpret it, and the optimal angle for image acquisition. Time to image acquisition was recorded with a maximum of 60 s. Image quality was graded using a scoring scale of 1 (poor) – 5 (best); scores of 1–2 were considered failure while scores of 3–5 were considered passing.

Summary of results Preliminary results of this ongoing study demonstrate that residents who had the digital angle information demonstrated a strong correlation between time to image acquisition and image quality while the non-digital angle group demonstrated no correlation.

Conclusions The addition of a digital angle monitor allows novice ultrasound users to acquire higher quality images in a shorter amount of time, thus overcoming at least some of the learning curve associated with ultrasound imagining. When learners are provided with additional information on obtaining optimum image quality they will be able to master this skill faster. Further studies assessing these applications are currently ongoing.

Poster Session

Immunology and Rheumatology

6:00 PM

Thursday, January 24, 2019

186

DIAGNOSTIC CHALLENGES IN ANTI-MDA5 ASSOCIATED CLINICALLY AMYOPATHIC DERMATOMYOSITIS

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10.1136/jim-2018-000939.186

Case report Introduction: Anti-MDA5 Associated Clinically Amyopathic Dermatomyositis (CADM) is challenging to diagnose. This rare disease is characterized by rapidly progressive, life-threatening interstitial lung disease and fevers. Muscle involvement is typically minimal to none posing a diagnostic

dilemma. Recognizing the disease's subtle cutaneous and articular manifestations while keeping a high index of suspicion is required in making this diagnosis.

Case description A 58-year-old male presented with 1 week history of arthritis, rash, dyspnea and high fevers. CT chest demonstrated airspace consolidations. Broad-spectrum antibiotics were ineffective raising concern for an underlying autoimmune etiology. He had hand joint synovitis, ragged cuticles, dilated capillary loops, hypoxic respiratory failure, and numerous erythematous skin lesions over hand joints. Skin biopsy demonstrated subtle vacuolar/interface change compatible with dermatomyositis. Left upper deltoid biopsy was nonspecific showing atrophy with diffuse MHC1 staining potentially suggestive of partially treated inflammation. Initial myositis panel was positive for MDA5 antibody by line immunoassay but not immunoprecipitation. Pulse dose steroids, cyclophosphamide and IVIG therapy were given to no avail. The patient ultimately died after 28 days in the hospital. A repeat myositis panel returned 2 months later demonstrating a positive MDA5 antibody by immunoprecipitation therefore confirming the suspected diagnosis. Autopsy was notable for acute lung injury with diffuse alveolar damage and muscular atrophy without evidence of myositis. Chronic pulmonary changes were conspicuously absent.

Discussion Diagnosing Anti-MDA5 Associated CADM is challenging, especially in the face of rapidly progressive lung disease and a potential amyopathic picture. Our patient's case illustrates how initial disease presentation can mimic infection and how diagnosis may potentially be delayed by ambiguous results of antibody testing and turnaround time. Relying on clinical intuition and searching for subtle extrapulmonary features are key for suspecting the disease and initiating empiric therapy. This case highlights the importance of having a high index of suspicion for Anti-MDA5 Associated CADM in the correct clinical setting.

187

GRANULOMATOSIS WITH POLYANGITIS PRESENTING AS NEW ONSET SCLERITIS AND HEMOPTYSIS

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10.1136/jim-2018-000939.186

Case report Introduction: ANCA associated Vasculitis is a rare group of disorders characterized by small vessel inflammation leading to occlusion, ischemia and organ dysfunction. Varied clinical presentation can be observed such as scleritis, hemoptysis, dyspnea, pulmonary nodules with cavitation and renal involvement.

Case presentation A 41-year-old male presented to emergency department with complaints of fever, productive cough, malaise and dyspnea for three week. He endorsed progression of symptoms and associated new onset hemoptysis, pleuritic chest pain and bilateral ocular erythema and pain for three days. On examination he was tachypneic with pulse oxygen 90% and bilateral erythematous scleral injection. Chest x-ray revealed multiple pulmonary nodules confirmed with CT chest with contrast. He was empirically initiated on antibiotics and antifungal therapy pending microbiology, TB, coccidioidomycosis serology results and further immunological work-up. Without significant clinical improvement on empiric treatment and negative microbiology results he was initiated on IV steroid.

Bronchoscopy showed hemorrhage in the right upper lobe, bilateral alveolar infiltrates, BAL negative for AFB, coccidioidomycosis and cytology negative for malignancy. Serum ANA, Anti-DsDNA and complement levels were normal. Serum anti-myeloperoxidase antibody returned positive. He was diagnosed with granulomatosis with polyangiitis and started on Rituximab IV and long-term prednisone regimen with significant clinical improvement.

Discussion As inflammation and multiple organ dysfunctions occur in patients with vasculitis rendering the patient immunocompromised allowing otherwise subclinical diseases potential to evolve into severe systemic diseases. A Case report noted underlying diagnosis of vasculitis leading to disseminate coccidioidomycosis. In patients, like in our case, living in endemic coccidioidomycosis regions it is important to have a broad approach to diagnosis. Premature exclusion of diseases thought to rarely occur in a certain area or vice versa can lead to misdiagnosis and improper treatment.

Poster Session

Infectious Diseases

6:00 PM

Thursday, January 24, 2019

188 A CASE OF SCALP ABSCESES IN AN IMMUNOCOMPETENT NEONATE CAUSED BY *MORGANELLA MORGANII*

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10.1136/jim-2018-000939.187

Summary of case A 3 week-old infant, born near-term, presented to the emergency department with swollen lesions on her head that developed and enlarged over 5 days. 4 days prior to admission the patient had presented to the ED for an evaluation of the scalp lesions. A non-contrast CT of the head showed a cephalohematoma. No further interventions were done and the patient was discharged home. On the day of admission, the lesions were larger and had purulent green drainage. An MRI of the head showed thinning and erosion of the parieto-occipital calvarium with no extension beyond the bone. Bacterial cultures of the drainage isolated *M. morganii*. Empiric cefepime and vancomycin were started, and a 14 day course of cefepime and clindamycin was given, with clindamycin to cover for any possible *Staphylococcus aureus*, including MRSA, that may not have grown in the cultures but which are typical pathogens of soft tissue infections. The infant responded to antibiotic therapy well, and was discharged home.

Discussion *Morganella morganii* is a gram-negative bacillus that causes fatal infections in immunocompromised hosts, such as premature newborns. However, full term neonatal infection with *M. morganii* is rare and one review found only 15 cases of neonatal sepsis and no case of scalp abscesses as in our patient. In these cases, the most common presenting features were fever, perinatal depression and respiratory distress. One neonate presented with fever, anorexia and vomiting, and was later found to have a brain abscess. 36% mortality was

reported. Early identification and proper antibiotic use resulted in full recoveries. Our patient had early identification of *Morganella* due to aggressive culturing before empiric antibiotics were utilized. We believe early appropriate antibiotics lead to avoidance of serious complications such as sepsis, brain abscess or death. Given the lack of immunocompromised state we believe this child may have had complications of trauma from birth (cephalohematoma) as a possible contributory factor. This case demonstrates that a high index of suspicion to culture may yield positive results in neonatal cutaneous *Morganella Morganii* infections.

189 PSEUDOMEMBRANOUS AND OBSTRUCTIVE ASPERGILLUS TRACHEOBRONCHITIS

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Objectives Aspergillus tracheobronchitis (ATB) is an unusual form of pulmonary aspergillosis. Delayed antifungal intervention is associated with high mortality; therefore, early recognition and diagnosis is crucial for patient survival. With an increased number of immunocompromised patients in the United States, it is an important diagnosis to be considered.

Methods In this case, we report a 66-year-old female with a history of kidney transplantation on chronic anti-rejection treatment who presented with dysphonia and dysphagia secondary to aspergillus infection extending from the supraglottis to the mainstem bronchus.

Results We review in detail the presentation, diagnosis, medical management, and surgical approach used in this case and discussed in the literature. The presented patient was successfully treated with a combination of prolonged antifungal medication, surgical debridement, and tracheostomy for airway protection. We review current literature regarding classification of ATB into obstructive, pseudomembranous, and ulcerative forms. Pseudomembranous and obstructive forms of ATB are seen in this case and are associated with high mortality.

Conclusion We report successful treatment of pseudomembranous and obstructive aspergillus tracheobronchitis in a solid organ transplant recipient. ATB is a rare opportunistic infection requiring a multidisciplinary team; in this case otolaryngology, pulmonology, critical care medicine, transplant nephrology, infectious disease, and eventually speech and language pathology. As the number of immunocompromised patients continues to rise, it is vital that the otolaryngology community remains attune to opportunistic infections affecting the upper aerodigestive tract.

190 MULTIFOCAL OSSEOUS COCCIDIOIDOMYCOSIS MASQUERADING AS MULTIPLE MYELOMA

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Purpose of study Coccidioidomycosis is an endemic fungal infection in the southwest United States that primarily manifests in the lung but can disseminate to bone and other tissues. Multiple Myeloma is a neoplastic proliferation of plasma

cells that notoriously presents as lytic bone lesions. This is a rare case of disseminated osseous coccidioidomycosis (cocci) that initially mimicked multiple myeloma.

Methods of study Retrospective case report.

Summary of results A 35-year-old African American homeless, cachexic man presented to our hospital following an assault to his neck. MRI of spine showed osteolytic lesions involving almost every vertebral body as well as extension into the spinal canal. MRI brain showed multiple destructive calvarial lesions as well as extension to soft tissues of the scalp and dura. His bone survey showed numerous lesions on multiple bones outside spine and skull. Plasma cell dyscrasia was suspected when his total protein/albumin ratio was 8.6/3.0 ng/dl. However, SPEP, UPEP and beta-2 microglobulin were inconclusive. His chest x-ray showed upper lobe cavity leading to further investigation. Patient later revealed he had a biopsy of his back before he left against medical advice from an outside hospital recently. It was found that he had a CT guided biopsy of his thoracic spine which showed fungal elements consistent with spherules with endosporeulation consistent with disseminated cocci. His cocci serology was positive with complement fixation titers of 1:256. Liposomal amphotericin B was started with subsequent clinical and serological improvement. He was discharged with daily outpatient infusion therapy in our infusion center. One week after his discharge he developed spontaneous pathological C5 body fracture and underwent C5 corpectomy with C4-C6 anterior fusion. Histopathology of C5 confirmed disseminated cocci without any malignancies. Unfortunately, he left against medical advice postoperatively.

Conclusion Disseminated osseous coccidioidomycosis can mimic primary or metastatic malignancy with osteolytic appearance. Bone biopsy should be considered for differentiation.

191 CONCOMITANT BACTEREMIA, UTI AND MENINGITIS IN A 15-WEEK-OLD

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10.1136/jim-2018-000939.190

Case report A 15-week-old ex-34 week preterm infant presented with fussiness, decreased appetite and home temperature of 37.7°C. Patient has been healthy since treatment of a right atrial thrombus and MSSA endocarditis at DOL 9 two weeks of gentamicin and six weeks of nafcillin.

On exam, patient was afebrile, well-appearing, and fussy but consolable with soft, flat fontanelles, and normal capillary refill. Due to the endocarditis history, baseline CBC, CRP and blood cultures were obtained with anticipatory guidance to return if temperature exceeded 38°C. Baseline WBC count was 18 600 (68% segs and 2% bands), and CRP was 1.766. Within 24 hours, blood cultures grew gram-positive cocci. Upon readmission, patient was febrile to 40°C, fussy and inconsolable with a supple neck, slightly bulging anterior fontanelle, mild subcostal retractions, no adenopathy and mild hypotonia. A full sepsis workup revealed a WBC count of 1900 (31% segs and 24% bands) and CRP of 8.489. Echocardiogram showed no residual thrombi.

Empiric vancomycin and ceftriaxone were initiated until blood, urine, and CSF cultures grew *S. agalactiae* sensitive

to ampicillin, which was then administered for three weeks.

This case demonstrates the rare occurrence of concomitant ultra-late-onset (>90 days) GBS bacteremia, UTI, and meningitis in a 15-week-old. At this age, UTI is the most common cause of fever, with concomitant meningitis affecting <1%. In patients who do not have prior infection or meet high-risk criteria for febrile protocols, home supportive treatment with or without antibacterial therapy is standard care. This case represents a diagnostic challenge inherent to preterm infants with immature immune systems, who don't mount full febrile responses despite bacteremia, resulting in minimal utility of febrile protocols for bacteremia risk stratification. Although elevated CRP has a greater sensitivity than elevated WBCs in severe bacterial infection, CRP elevations lag behind subtle warning signs, including fussiness and decreased feeding, potentially leading to delays in diagnosis and treatment. This case illustrates the importance of subtle signs and physical exam findings in suspecting bacteremia to quickly discover and treat concomitant infection, as traditional markers of infection are not always prominent at illness onset in preterm infants.

192 COCCIDIOIDOMYCOSIS CHORIORETINITIS

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10.1136/jim-2018-000939.191

Case report 27 year old Filipino man presented to Kern Medical with decreased vision in his left eye, low back pain, weakness in his lower extremities, and masses in his paraspinal, supraclavicular, and submandibular regions. Thoracic and abdominal CT demonstrated multiple abscesses with involvement of the left supraclavicular lymph nodes and a left paraspinal abscess extending from T7-T12 with penetration and subsequent osteomyelitis of the T12 vertebra. Whole body bone scan also showed increased uptake of left fibular and tibial regions, left frontal lobe, and xiphoid process. Incision and drainage of the paraspinal abscess and subsequent staining of the aspirate indicated the presence of double walled spherules with endosporeulation. Serological immunodiffusion showed IgM and IgG reactivity with a complement fixation titer of $\geq 1/512$. The patient was placed on liposomal amphotericin B for his extraocular disease.

The patient started to complain of floaters in his left eye, which progressed until he complained of a total loss of vision in this eye. Ophthalmologic examination discovered 'puff balls' in the vitreous overlying the posterior pole in this eye only. The right eye did not have any abnormal findings. He was discharged from the hospital and referred to a retinal specialist as an outpatient. On examination he had normal visual acuity in the right eye, with light perception vision only in the left eye. Anterior segment exam did not reveal an active anterior uveitis. In the left eye there were found to be significant vitreous opacities. A large, white subretinal lesion was present in the temporal macula. There was significant traction associated with this lesion and a combined tractional/exudative retinal detachment was present, extending inferiorly. Given the history of concurrent coccidioidomycosis infection, the patient was diagnosed with a coccidiomycosis associated

chorioretinitis. He was started on intravitreal amphotericin B deoxycholate 5 mcg/0.1 mL every three days in addition to his systemic treatment.

193 DISSEMINATED COCCIDIOIDOMYCOSIS OF THE THYROID, CENTRAL NERVOUS SYSTEM, AND BONE

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Introduction Coccidioidomycosis is endemic to the Southwestern United States and Northern Mexico. Dissemination occurs in 1% of symptomatic patients, with most common sites being the nervous system, bones, joints or skin. Dissemination to the thyroid is extremely rare, with less than ten cases reported in the English literature since 1979.

Case report A 53-year-old Hispanic female with past medical history of Diabetes mellitus type 2 and Hypertension presented with altered mental status, worsening headaches, subjective fevers, photophobia, and neck stiffness. Magnetic resonance imaging of the brain demonstrated a prior lacunar infarct in the left basal ganglia. Coccidioides (Cocci) serology of the cerebrospinal fluid showed positive immunodiffusion (ID) IgG and complement fixation (CF) of 1:4. Serum Cocci serology demonstrated positive ID IgG, ID IgM, and CF of 1:256. Patient was discharged on oral Fluconazole 1000 mg daily. One month later, patient presented with deteriorating mentation; neuroimaging revealed patchy meningitis of the basal cisterns and an acute lacunar infarct of the left caudate nucleus. Computed tomography angiography demonstrated a heterogeneous thyroid gland with a 5 mm hypodense nodule in the left thyroid lobe. Ultrasound showed a heterogeneous thyroid, an avascular exophytic solid nodule measuring 1.7 × 0.95 × 1.1 cm in the left thyroid lobe, and an ill-defined isoechoic 1.3 × 0.8 × 1.1 cm mass with internal calcifications in the left side of the isthmus. Due to concern for a neoplastic lesion, fine needle aspiration (FNA) was performed. Biopsy showed no evidence of malignancy. However, fungal stain was consistent with Coccidioides spherules with endosporeulation. MRI of the spine also demonstrated dissemination to the cervical spine. Patient was treated with fluconazole 1000 mg PO daily indefinitely and amphotericin B infusions three times per week for twelve weeks.

Conclusion Although uncommon, fungal infections should be in the differential diagnosis of a focal thyroid nodule or swelling, especially when located in areas endemic to certain fungal infections. FNA of the thyroid is an effective diagnostic tool to establish the diagnosis.

194 EROSIIVE VULVOVAGINITIS ASSOCIATED WITH BORRELIA BURGDOERFERI INFECTION

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Case report We describe a case of acute erosive vulvovaginitis associated with infection by the Lyme spirochete, *Borrelia burgdorferi* (Bb). The patient is a 57-year-old woman

Abstract 194 Figure 1 *Borrelia* spirochete in stratum spinosum. Dieterle silver stain, 1000X

who had been diagnosed with Lyme disease based on serological testing and systemic symptoms consistent with tick-borne disease, and she was being treated with oral antibiotics. She presented with a painful genital lesion. Histological examination was not characteristic of any typical pattern found in erosive vulvar conditions. However, Dieterle staining for spirochetal infection demonstrated visible spirochetes throughout the stratum spinosum and stratum basale, and immunostaining for Bb antigens was positive. A vaginal culture yielded motile spirochetes, and polymerase chain reaction (PCR) testing identified the cultured spirochetes as *B. burgdorferi sensu stricto*. PCR amplification for *Treponema pallidum* and *T. denticola* gene targets was negative, and the patient had negative syphilis serology. Her lesion improved with additional systemic and topical antibiotics. Bb has been cultured from vaginal and seminal secretions of Lyme disease patients. The presence of active infection in an erosive genital lesion provides corroborative evidence that sexual transmission of Lyme disease may be possible. Spirochetal infection with Bb should be considered in cases of genital ulceration that have no identifiable etiology.

195 GROUP A STREPTOCOCCUS PUERPERAL SEPSIS AFTER SPONTANEOUS ABORTION

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Background Group A streptococcal (GAS) puerperal sepsis is a serious and life threatening condition that affects 3 cases per 1 00 000 population worldwide. The incidence has decreased but at one time it was the leading cause of maternal death. This is a case of GAS sepsis post abortion associated with use of a sex toy.

Case presentation Patient is a 44 year old African American female with multiple spontaneous abortions and a stillbirth, who presented to the emergency room with fever, diarrhea and abdominal pain. She had a spontaneous abortion 3 days prior and on arrival was febrile at 102.4F. CT scan showed a

retro uterine abscess measuring $7 \times 4.2 \times 5.4$ cm. Ultrasound was negative for retained conception products. Blood cultures were obtained and due to a penicillin allergy she was started empirically on Vancomycin and Meropenam. However, six out of the eight blood culture bottles grew Group A *Streptococcus*.

On further questioning, patient confirmed vaginal use of dildo a day after her spontaneous abortion while she still had vaginal abortive secretions. This led to the hypothesis of group A strep ascending infection from vaginal canal to produce endometritis with further complication to a retro uterine abscess with adjacent enterocolitis and septicemia.

Her abscess was drained by interventional radiology. The fluid gram stain showed many white blood cells with no organisms and cultures did not grow any organism. Cytology of the fluid also showed polymorphonuclear cells. Blood culture sensitivities returned and her antibiotic regimen was changed to Levofloxacin 750 mg daily to finish a 3 weeks course.

A repeat CT scan indicated a decrease in size of the abscess a week post discharge. Her work up for multiple spontaneous abortions and stillbirths were also negative. A follow up clinic visit was made for continuous monitoring of patient.

Conclusion Group A streptococcus is a life-threatening infection that can lead to maternal mortality if not treated. Clinicians should be aware of any routes of infection introduction along with treatment possibilities to prevent maternal mortality.

196

CONCOMITANT CENTRAL NERVOUS SYSTEM TOXOPLASMOSIS AND SERONEGATIVE DISSEMINATED COCCIDIOIDOMYCOSIS IN A NEWLY DIAGNOSED ACQUIRED IMMUNE DEFICIENCY SYNDROME PATIENT

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Purpose of study Opportunistic infections are a major cause of morbidity and mortality in acquired immune deficiency syndrome (AIDS). We describe a fatal case of disseminated coccidioidomycosis (Cocci) and central nervous system (CNS) toxoplasmosis in a newly diagnosed AIDS patient.

Case description 33 year-old Hispanic male with no medical history presented to an outside hospital with headaches and was diagnosed with a 2.7 cm ring enhancing intracranial lesion in the right temporal lobe. He was transferred to our facility for neurosurgical intervention. Post-operatively, he was febrile and transferred to the medicine team. He was screened and diagnosed with AIDS with CD4 of <20 . Antiretroviral and CNS toxoplasmosis treatments were started. Comprehensive screening in AIDS host, including cocci serology, was negative except high IgG titers for toxoplasmosis. Histopathology of the brain lesion confirmed the diagnosis. Further investigation revealed that the patient was made aware of HIV diagnosis two years prior but remained in denial. He was discharged after fever resolved but was readmitted one week later with persistent fevers and was found to have a new left upper lobe infiltration. Broad-spectrum antibiotics plus fluconazole were started and he was placed on air born precautions to rule out tuberculosis. Cocci serology was again negative. His condition deteriorated with hypoxemia and development of diffuse

miliary pattern revealed by CT of the chest. Bronchoscopy was arranged but hypoxemia worsened and prompted intubation. Bronchoalveolar lavage after intubation showed spherules and blood culture grew fungus resembling *Coccidioides immitis*. Antifungal treatment was changed to liposomal amphotericin B but he developed severe acute respiratory distress syndrome (ARDS), went into cardiac arrest, and passed away.

Conclusion Defects in the IL-12/IFN- γ pathway and T-helper 17-mediated response are associated with increased severity of coccidioidomycosis. In HIV hosts, negative serology can be seen in up to 1/3 of cases. Therefore, other diagnostic modalities should be initiated promptly and simultaneously. Fungemia and ARDS are both associated with very high mortality in coccidioidomycosis.

Poster Session

Morphogenesis and Malformations

6:00 PM

Thursday January 24, 2019

197

QUANTIFYING BIREFRINGENCE IN DUCHENNE MUSCULAR DYSTROPHY ZEBRAFISH MODEL

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Purpose of study Duchenne muscular dystrophy (DMD) is a severe form of muscular dystrophy characterized by a deletion mutation of dystrophin that is inherited in an X-linked recessive manner. Dystrophin-deficient muscle undergoes progressive degeneration, leading to muscle atrophy and dysfunction. Zebrafish (*D. rerio*) have highly conserved genomic and structural similarities with mammals and have emerged as useful tools to model disruption in sarcomere assembly, congenital myopathies, and muscular dystrophies.

Birefringence assay is a rapid, non-invasive approach that utilizes the light scattering property of the pseudo-crystalline array of muscle sarcomeres, widely used to assess the integrity of muscle tissues in translucent Zebrafish embryos early in development. *DMD*^{-/-} zebrafish exhibit myofiber degeneration with repeated cycles of regeneration which appear as dark patches under polarized light, wild-type fish display bright birefringence without patches of lesions. We set out to develop a method that employs the use of gray value measurements of muscle birefringence as a surrogate for severity of muscle lesions.

Methods used Zebrafish embryos were collected at 4 days post fertilization, heads were removed for genotyping, tails were fixed in 4% paraformaldehyde (PFA). A maximum of 5 tails of the same genotype were mounted in 0.025% phosphate buffered saline with Tween (PBST). Two polarizing filters, one placed under the sample at the base of the microscope, the second filter set directly on the objective lens were used to visualize muscle lesions. Images were acquired using Olympus Cellsens Dimensions software. Pictures were analyzed using Image J Software for quantification of gray values.

Summary of results $DMD^{+/+}$ Zebrafish had gray values of 145.7 ± 14.8 , $DMD^{-/-}$ 100.2 ± 41.85925 , t-Test p-value (0.001). Our results show $DMD^{-/-}$ were 31% less bright compared to age-matched wildtype fish. Additionally, $DMD^{-/-}$ zebrafish had highly variable gray values, this is expected since the pattern of lesion development varies from animal to animal.

Conclusions Differences in brightness levels between DMD mutants and wildtypes demonstrates severity of lesions could be quantified using gray value measurements. Decreased gray values are associated with increased severity of lesions.

Poster Session

Neonatology General

6:00 PM

Thursday January 24, 2019

198 TIMING OF SURGICAL LIGATION FOR PATENT DUCTUS ARTERIOSUS IN EXTREMELY IMMATURE INFANTS

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10.1136/jim-2018-000939.197

Purpose of study The optimal management of a patent ductus in extremely premature infants born at gestational age ≤ 25 weeks is controversial. The timing and indication for surgical ligation is unclear. Therefore, we evaluated the effect of timing of surgical ligation for PDA on mortality in infants born at ≤ 25 weeks.

Methods used We performed a review of medical records of neonates born at gestational age ≤ 25 weeks between Jan 2010 through July 2016. We excluded infants with congenital malformations. We analyzed the effect of timing of ligation on percent mortality adjusting for severity of illness using SNAPPE-II (at initiation of treatment) and CRIB-II (at birth) scores. Descriptive statistics and chi-square were calculated using SPSS, v25 (IBM). Logistic regression was performed to ascertain the impact of infant's age at the time of surgical ligation on the likelihood of death.

Summary of results A total of 135 infants ≤ 25 weeks gestation were included, of which 86 underwent surgical ligation only and 49 underwent ligation following failed indomethacin treatment. There was no statistical difference in the mean age of ligation between the non-survivors (9.5 ± 9.7 d) and survivors (13.5 ± 10 d) independent of severity of illness. The factors contributing to the decision regarding the timing of ligation in these cohorts are unclear.

Abstract 198 Table 1 Logistic regression showing likelihood of mortality with different variables

Variable	Odds Ratio (95% C.I.)	p value
Age at ligation	0.948 (0.867–1.036)	0.238
SNAPPE-II	1.009 (0.951–1.071)	0.767
CRIB-II	1.049 (0.908–1.211)	0.518

Conclusions There was no difference in mortality in infants based on age at which surgical ligation was performed, independent of severity of illness.

199 SURGICAL TREATMENT OF PDA IS ASSOCIATED WITH INCREASED MORTALITY COMPARED TO MEDICAL TREATMENT IN EXTREMELY LOW BIRTH WEIGHT INFANTS

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10.1136/jim-2018-000939.198

Purpose of study Lack of evidence to support appropriate treatment including no intervention for patent ductus arteriosus (PDA) in infants ≤ 29 weeks makes it difficult to interpret the role of the PDA amongst those infants that do not ultimately survive.

Methods used We performed a retrospective review of medical records of deaths of 57 neonates born at gestational age ≤ 29 weeks between January 2010 and July 2016 who carried a diagnosis of PDA. We divided them into groups without any treatment, those receiving medical treatment (including indomethacin), those undergoing ligation. We then did a subgroup analysis after excluding infants with genetic and cyanotic heart disease, and those ≤ 27 weeks.

Summary of results A total of 57 infants less than 29 weeks gestation did not survive. 13 (23%) infants died due to BPD, 15 (26%) due to NEC, 11 (19%) from IVH, 11 (19%) from genetic/cyanotic congenital heart disease, and 7 (12%) died from sepsis. In this group, an average of $45\% \pm 6.2\%$ of infants dying from NEC, BPD, or IVH were ligated. After excluding genetic anomalies, cyanotic congenital heart disease, and infants ≥ 27 weeks, effect size increased slightly to an average of $52\% \pm 10.6\%$ of infants dying from BPD, NEC, and IVH and were surgically ligated.

Conclusions In our cohort of fifty-seven infant deaths of gestational age ≤ 29 weeks, a large percentage of deaths from BPD, NEC and IVH were associated with surgical ligation. Effect size increased when excluding genetic anomalies, congenital heart disease, and older preemies, confirming increased mortality in micropremies undergoing ligation versus medical treatment.

200 UTILITY OF PROBIOTICS IN MANAGEMENT OF COLIC IN INFANTS: A COMPREHENSIVE LITERATURE REVIEW

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10.1136/jim-2018-000939.199

Purpose of study Colic in newborns has been associated with maternal depression, cessation of breastfeeding and child abuse. Therefore, early intervention to reduce symptoms is crucial. The use of probiotics in treatment of colic in infants remains controversial. The objective of this study was to evaluate the effect of probiotics on colic in infants.

Methods used We performed a comprehensive literature search through variety of search engines including, PubMed, Google

Abstract 200 Table 1 Effect of probiotic use in colic

Author, Year	Age Range of Participants	# Subjects Probiotics vs Controls*	Outcome	Probiotics Group: Experienced Outcome	Placebo Group: Experienced Outcome	P-Value
Baldassare 2018	30–90 days	27 vs 26	Crying Reduction >50% at 21 days	26 subjects (96.3%)	17 subjects (65.4%)	<0.05
Fatheree 2017	3 weeks-3 months	11 vs 5	Reduction in cry/fuss time at 42 days	Baseline Average: 275 mins Day 42 Average: 94 mins	Baseline Average: 283.5 mins Day 42 Average: 29 mins	0.19
Chau 2015	3 weeks-6 months	24 vs 28	Crying Reduction >50% at 21 days	17 subjects (70.8%)	6 subjects (21.4%)	0.035
Pärty 2015		13 vs 15	Crying reduction >50% at 28 days	4 subjects (31%)	0 subjects (0%)	<0.05
Mi 2015		20 vs 19	Crying reduction >50% at 28 days	20 subjects (100%)	3 subjects (15.7%)	<0.05
Sung 2014		67 vs 60	Reduction in daily cry/fuss time at 30 days	27 subjects (40%)	29 subjects (48%)	0.23
Szajewska 2013		40 vs 40	Crying Reduction >50% at Day 21	39 subjects (97.5%)	15 subjects (37.5%)	<0.001
Savino 2010	2–16 weeks	25 vs 21	Crying Reduction >50% at Day 21	24 subjects (96%)	15 subjects (71.4%)	0.036

*Number of subjects included in the final analysis

Scholar and Cochrane. Only randomized controlled studies were included in our analysis.

Summary of results Eight studies satisfied our inclusion criteria (see table 1). Participants were healthy full-term infants diagnosed with colic if they cried more than 3 hours/day for at least 3 days/week. Infants were predominantly breastfed. Probiotics were given daily for at least 21 days in most of the studies and the most common probiotic used was *L. reuteri*. The outcome was typically measured by a questionnaire or interview with parents. Some studies examined the fecal flora and showed increased lactobacillus in the probiotic group. In majority of the studies, crying time and the proportion of infants crying decreased within 21 days in both groups but was more significant in the probiotic group. There were no serious adverse events. The limitations of the studies included different methods of assessment, small sample size to separate the effect on breastfed and formula fed infants, and not taking into account other variables, such as maternal diet or other exposures.

Conclusions Our review suggests probiotics may lead to decreased crying in some infants with colic. Compared to placebo, the effect of probiotics was less significant after a few weeks, pointing toward the self-limited nature of colic. Larger prospective placebo controlled trials that control for different variables are warranted.

201

HEALTHCARE PROVIDER ATTITUDES TOWARDS AND KNOWLEDGE OF BUBBLE CONTINUOUS AIRWAY PRESSURE (BCPAP) TO TREAT NEWBORNS IN NAKURU, KENYA

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10.1136/jim-2018-000939.200

Purpose of study bCPAP is a safe, low-cost therapy for respiratory distress that improves neonatal outcomes in low resource settings, however successful implementation depends on the acceptance of this technology by local healthcare providers. The aim of this study was to investigate the baseline experience and knowledge regarding bCPAP in the newborn unit (NBU) in the Provincial General Hospital (PGH) in Nakuru, Kenya at the onset of a local quality improvement initiative to increase bCPAP use.

Methods used A written survey was distributed in person to providers in the NBU by the nurse in charge or the head of pediatrics beginning 12/2017 and ending 2/2018. The target population was all nurses (n=17) and pediatricians (n=3) on staff at PGH. Consulting nurses, physicians, and student doctors from Egerton University were asked to respond if they were in the NBU at the time of the survey administration.

Summary of results 38 survey responses were collected including 16 nurses and 3 physicians from PGH (95% response rate). The remaining responses were from 9 consultants and 10 student doctors. 68% of providers had used bCPAP and 55% had some formal training on bCPAP. Doctors were not more likely to have had bCPAP training compared to nurses (p=0.69). Of those that had used bCPAP at PGH, 38% had no formal training. 95% desired more training on site with bedside teaching being the most preferred training modality. 82% felt bCPAP was safe and 90% thought bCPAP could prevent death. 95% were happy that bCPAP was available in the NBU. 95% percent named signs of respiratory distress that might indicate need for bCPAP, 82% identified a normal newborn respiratory rate, and 47% percent identified an abnormal oxygen saturation. 40% named potential complications of bCPAP. 47% of nurses correctly identified the maximum recommended bCPAP pressure to reach without consultation with a physician.

Conclusions Healthcare providers in the NBU at PGH feel positive about bCPAP. Formal training on the use of bCPAP is needed and should include bedside teaching as this was the modality most desired by providers.

202

LUMBAR PUNCTURE BETWEEN TWO ACADEMIC NEONATAL INTENSIVE CARE UNITS

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Purpose of study Traumatic and unsuccessful LPs are difficult to interpret, leading to repeat procedures and potentially unnecessary antibiotic use. Little is known whether success with LPs vary in regard to level of training or between

Abstract 202 Table 1 Characteristics of LPs at two centers

	Center 1 n=506	Center 2 n=348	p=
Birth weight, g Median (IQR)	2920 (1780)	3140 (1168)	0.0225
Gestational Age, weeks, Median (IQR)	38 (7)	39 (5)	0.0454
DOL at LP Median (IQR)	5 (26)	2 (11)	<0.001
Successful LP (%)	35%	50%	<0.001
Traumatic LP%	40%	41%	0.834
Antibiotic Days Median (IQR)	7 (4)	8 (4)	0.464

varying medical centers. The purpose of this study is to determine differences in rate of success in performing LPs between two academic centers and its impact on the duration of antibiotic therapy.

Methods used A 5 year retrospective chart review was conducted in all patients who had a lumbar puncture between January 2011 to December 2015 at two academic affiliated Neonatal Intensive Care Units (NICU). Center 1 was a tertiary NICU with pediatric residency training program and Center 2 was a community NICU.

Summary of results A total of 854 LPs were performed; 506 in Center 1 and 348 in Center 2. There was a trend towards fewer LPs over 5 years (170, 203, 216, 143, 122, respectively). Over half of the LPs were performed by Residents in

Center 1, whereas Physician Extenders performed 81% of the LPs in Center 2. There was a statistically significant difference in the birth weight and gestational age in infants at the two centers. The rate of successful LPs was higher at Center 2, yet there was no difference in the rate of traumatic LPs and median number of antibiotic days between the two centers.

Conclusions There were fewer successful LPs at the center with a pediatric residency training program. Residents may have fewer exposures to LPs which may lead to poor LP results. Despite a difference in success rate, there was no difference in the amount of traumatic LPs nor in the antibiotic days among the centers. LP results were only one of many pieces of information that were used to dictate antibiotic therapy, but may not have changed the clinical decision for treatment.

203

COST OF NEONATAL RESUSCITATION

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10.1136/jim-2018-000939.202

Abstract 203 Table 1 Breakdown of costs for all infants <35 weeks of gestation (per patient)

	Mean (US \$)	Standard error (US \$)	Median (US \$)	IQR (US \$)
Hospital fees	\$32	\$1	\$37	\$18-38
Professional fees	\$137	\$5	\$79	\$78-153
Equipment	\$81	\$3	\$87	\$14-106
Pharmacy	\$71	\$12	\$0	\$0-0
Total cost	\$321	\$18	\$210	\$111-283

Abstract 203 Figure 1 Costs of neonatal resuscitation by gestational age

Purpose of study There is a paucity of data in the literature regarding neonatal resuscitation costs. The objective of this study is to estimate the costs of resuscitation for newborns less than 35 weeks.

Methods used Single center, retrospective study to determine the variable costs of resuscitation for inborn neonates less than 35 weeks from 2015–2017 (n=401). The total cost (2017 U.S. dollars) was limited to the initial stabilization period. Adjusted means and standard errors (SE) were determined using a generalized linear mixed-effects model with log link function and gamma distribution. The multivariable model included maternal and infant characteristics.

Summary of results The overall mean cost (SE) was \$321 (SE \$18). As gestational age increases, the cost of resuscitation decreases (figure 1). Professional fees and equipment accounted for the majority of costs (table 1). In the adjusted analysis, vaginal delivery was the only statistically significant factor associated with 23% lower costs (effect size 0.77, 95% CI 0.66, 0.90).

Conclusions As expected, cost of resuscitation is inversely correlated with gestational age. After adjusting for gestational age and birthweight, only mode of delivery is statistically significant in impacting the difference in costs.

Poster Session

Neonatology – Perinatal Biology

6:00 PM

Thursday January 24, 2019

204 INVESTIGATION OF A NITRIC OXIDE MEMBRANE TRANSFER IN MYOMETRIAL CELLS

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Introduction Premature failure of uterine relaxation resulting in the delivery of an underdeveloped (>37 weeks) fetus is the leading cause of newborn mortality worldwide. Despite significant efforts from the scientific and medical community, the majority of spontaneous preterm labor (PTL) cases remain unanswered. Gamma-glutamyl transpeptidase (GGT), classified as a hydrolase, is a critical enzyme in regulating cellular levels of glutathione and maintaining cellular redox homeostasis. S-nitroso-glutathione (GSNO) is a glutathione analog that shares nearly identical chemical properties. One notable difference between the two structures is the addition of a nitric oxide group to the thiol group on GSNO. By replacing glutathione with GSNO and manipulating the oxidative stress pathway, we can exploit this mechanism to introduce Nitric Oxide (NO) into myometrial cells to induce relaxation.

Methods used A Photon Technology International (PTI) microscope was used to be able to detect if GGT successfully cleaved the GSH analog. 4-amino-5-methylamino-2',7'-difluoro-fluorescein diacetate(Daf-FM), was introduced into the system to detect concentration of NO by reacting with NO to emit fluorescence. The PTI microscope quantified the fluorescence emitted from the reaction between Daf-FM and NO. Acivin, an irreversible inhibitor of GGT, was used as a control

experiment to attenuate the effects of GGT in the presence of GSNO.

Summary of results Human telomerase reverse transcriptase (hTERT) cells were treated with 100 μ M daf-FM and 100 μ M GSNO and showed significant increase in fluorescent levels upon treatment of GSNO. hTERT cells were treated with 100 μ M acivicin to inhibit GGT activity and fluorescent intensities was observed to have significantly decreased upon treating the cells with the inhibitor.

Conclusions GSNO treatment of myometrial smooth muscle cells shows intracellular nitric oxide content. The treatment of myometrial smooth muscle cells with the specific inhibitor of GGT revealed that the inhibitor interferes with the ability of nitric oxide to enter the cell.

205 VAGUS NERVE STIMULATION PARADOXICALLY INCREASES MICROGLIAL ACTIVATION IN A NEONATAL RAT INFLAMMATION MODEL

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Purpose of study Premature infants have poorly developed immature immune systems and are at increased risk of infection after birth. Systemic infection can lead to sepsis which kills 40%–50% of infected infants. Paradoxically, treatments targeted at reducing infection are not very effective in reducing mortality. As inflammation-mediated dysregulation of autonomic control causes breathing pathophysiologies that impair long-term outcomes, treatments targeting inflammation may prove to be more successful. Vagus nerve stimulation (VNS) is a treatment that has shown potential to reduce inflammation.

Methods used Microglia are central nervous system immune cells that respond to inflammation by producing pro- and anti-inflammatory cytokines. Several studies have shown that microglia morphology changes from a resting/ramified state to an amoeboid/simplified profile when activated. We used the microglia-specific immunohistochemical marker, Iba1, to stain microglia in brainstem regions of 10–14 day old rat pups that are important for cardiorespiratory control in response to LPS, a glycoprotein found in the coat of *E. coli* that increases neuroinflammation, as well as microglia exposed to LPS and then subsequently treated with VNS for 30 min using 1.75 mA at 25 kHz. We then used Sholl analysis to quantify the arborization of microglia using the following parameters: maximum intersections, number of primary branches, radius of maximum intersections, and ramification index.

Summary of results We found the VNS treatment group, when compared to the LPS-only group, had a statistically significant decrease in both ramification index (p=0.004) and maximum intersections radius (p=0.033) while a statistically insignificant difference in maximum intersections (p=0.375) and primary branches (p=0.180).

Conclusions We hypothesized VNS treatment would attenuate LPS-induced activation in microglia cells found in the hypoglossal motor nucleus. Our results are surprising in terms of the microglia because we see VNS may actually increase microglial activation. This suggests that microglia are responding in a more complex manner than merely inactivated/activated with the stimulation parameters used in these experiments.

Poster Session

Neonatology – Pulmonary

6:00 PM

Thursday January 24, 2019

206

COMPARISON OF THE EFFICACY OF ELECTRO-ACUPUNCTURE ON ACUPOINTS ST36 AND GB34 IN BLOCKING PERINATAL NICOTINE-INDUCED OFFSPRING LUNG INJURY

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Purpose of study Perinatal nicotine exposure affects developing lung adversely, and there is no effective intervention. Recently, we have demonstrated that electroacupuncture (EA) applied to maternal *Zusanli* (ST36) acupoint blocks nicotine-induced pulmonary phenotype in exposed offspring. However, mechanism underlying this effect and specificity of benefit to ST36 are not established. Therefore, we compare effects of EA via ST36 and *Yanglingquan* (GB34), since both acupoints are known to affect HPA axis.

Methods used 24 pregnant rat dams were randomly divided into four groups: saline (S), nicotine (N), nicotine +ST36 (n+ST36), and nicotine +GB34 (n+GB34). Nicotine was administered s.c. (1 mg/kg), once daily, and EA was applied to bilateral ST36 or GB34 from embryonic day 6 to postnatal day 21. Maternal and offspring HPA axes, offspring lung morphometry (radial alveolar count and mean linear intercept), key lung developmental markers [PPAR γ , β -catenin, and glucocorticoid (GC)], and corticosterone (CORT) in serum of offspring were detected; HPA axis (pituitary ACTH and serum CORT levels) in mother was determined.

Summary of results With perinatal nicotine exposure, alveolar count decreased, but mean linear intercept increased; whole lung PPAR γ protein levels decreased, and β -catenin, GC and CORT levels increased, all these changes consistent with previously described nicotine-induced phenotype. Maternal pituitary ACTH and adrenal MC₂R levels increased. In n+ST36 group, all nicotine-induced changes in lung morphometry, signal transduction markers, and maternal HPA axis were blocked. In contrast, there was no effect of n+GB34 on nicotine-induced changes in any of the marker examined, both in offspring and mother.

Conclusions EA applied to ST36 provides effective protection against perinatal nicotine-induced lung injury, which is likely mediated via modulation of maternal and offspring HPA axes. In contrast, EA applied via GB34 is completely ineffective.

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207

IMPACT OF HIGH FLOW NASAL CANNULA WEANING ON CLINICAL OUTCOMES OF PRETERM INFANTS AT A HIGH ALTITUDE CENTER

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Purpose of study High Flow Nasal Cannula (HFNC) is a widely used modality to wean-off CPAP and has an established safety record in preterm populations. There is no evidence to date that using HFNC to wean off CPAP allows a faster wean to room air at sea level neonatal intensive care units (NICU). However, there are no published data on the effect of HFNC as a secondary respiratory support modality at high altitude. This is important because studies show that the incidence of bronchopulmonary dysplasia (BPD) is higher in infants admitted to NICUs at high altitude, albeit the cause is not fully elucidated. Core aims of this quality improvement (QI) study implementing an original HFNC Weaning Algorithm was to reduce the total duration of respiratory support by 5 days and the rate of bronchopulmonary dysplasia (BPD) by 5% in one year. Other aims included decrease time to first oral feeding, and reduction in length of stay (LOS) of preterm infants in a Level IV NICU situated at 5200'.

Methods used Our Respiratory Quality Improvement (QI) Team developed HFNC weaning guidelines for infants born less than 34 weeks gestation in December 2017. After multi-disciplinary team education, the project was implemented in March 2018 and used PDSA methodology to follow the process. Outcomes of infants born the year preceding this QI intervention were used as controls.

Summary of results The Control group comprised 113 infants. Thirty seven infants have been discharged in the HFNC Group thus far. There was 73% compliance with following the proposed guidelines. Baseline characteristics were similar between groups. Table 1 depicts the outcome metric results in the two study groups. Per proposed Qi goals, all aims of the study were reached or surpassed in the first 6 months of this QI intervention. For some outcomes statistical significance was not reached, possibly due to small sample.

Conclusions Preliminary results support a more consistent approach to weaning on HFNC support, leading to better clinical outcomes in preterm infants.

Abstract 207 Table 1 Outcomes

	Control	Intervention	p value
Days on respiratory support $\pm$ SD	41.5 $\pm$ 35.8	34.2 $\pm$ 28.5	0.21
Day to first oral feed $\pm$ SD	28.4 $\pm$ 25.5	20.2 $\pm$ 16.1	0.05
BPD	63 (55.7%)	18 (48.6%)	0.56
Length of stay in days $\pm$ SD	57.6 $\pm$ 31.4	47.5 $\pm$ 23.0	0.03

Poster Session

Nephrology and Hypertension

6:00 PM

Thursday January 24, 2019

208 ACUTE TUBULAR DYSFUNCTION WITH LOWER DOSES OF CISPLATIN

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10.1136/jim-2018-000939.207

Purpose of study Cisplatin is a cancer chemotherapeutic agent widely used for the treatment of many solid-organ cancers however its clinical use is complicated by its dose-related variety or renal injury. Nephrotoxicity due to cisplatin is manifested as progressive renal impairment, salt-wasting, a fanconi-like syndrome, hypomagnesemia. One study suggested that decrease in GFR and magnesium concentration happens after doses higher than 50 mg/m² body surface area per dose. Another study reported renal damage occurs when approximately 500 mg of cumulative drug had been administered.

Methods used Retrospective case study.

Summary of results 63 year old Caucasian female with stage IIIc endometrial carcinoma completed 9 cycles of 40 mg/m²/week cisplatin chemotherapy with radiation presented to the emergency department with intractable nausea and vomiting which started after completing her 7th cycle of cisplatin. On presentation, her vitals were stable, physical exam was remarkable for orthostatic hypotension and a resting tremor in both upper extremities. Her labs were significant for potassium of 2.5, chloride of 89, bicarbonate 33, creatinine of 0.74, magnesium levels <0.3 and calcium of 5.4. She received fluids and electrolyte replacement. However patient continued to have low level of serum magnesium, potassium, phosphorus and calcium despite adequate IV replacements indicating urinary losses. Her 24 hour urine electrolytes and amino acid analysis showed increase excretion of magnesium, potassium, sodium and elevated levels of multiple amino acids. Once her nausea was controlled she was switched to oral supplementation of magnesium, potassium, and calcium. Daily serum levels of potassium, phosphorous and calcium were stable, however, magnesium levels continued to be low. Patient was clinically stable and was subsequently discharged home with a plan for daily IV infusions of magnesium at an infusion center with close monitoring of serum electrolytes.

Conclusions Long-term effects of cisplatin toxicity may lead to subclinical and/or permanent reduction in GFR. Clinician should monitor the renal function closer as tubular dysfunction can occur after only 360 mg and hypomagnesemia can occur if only 120 mg of cumulative drug is administered.

Poster Session

Surgery

6:00 PM

Thursday January 24, 2019

209 A METHOD FOR QUANTIFYING FACIAL NERVE ANATOMY

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10.1136/jim-2018-000939.208

Purpose of study Electromyography facial nerve (FN) mapping has allowed surgeons to visualize *in-vivo* FN patterns preoperatively. These maps are a valuable data source to investigate FN anatomy in relation to disease pathologies such as vascular anomalies (VAs). However, current methods of describing FN pattern have been limited to categorizing FNs into types based on FN branch anastomoses. In this work, we aim to create a method to quantify *in-vivo* FN patterns.

Methods used Seattle Children's Hospital pediatric patients with VAs who had FN map photographs from 2000–2018 were queried. An image analysis code was developed using MATLAB to digitize FN branches and anatomical reference points into a Cartesian coordinate system. The images were standardized and aligned such that the Frankfort horizontal served as the x-axis. A radial grid, with an origin set at the FN pes anserinus and radii (R₁, R₂, and R₃) with increasing values, was overlaid on the image. The Euclidean distance from the superior EAC to the FN pes anserinus was computed. Next, Euclidean distances, arc distances, and angles between adjacent FN branches at R₁, R₂, and R₃ were calculated. FN curvature was measured by calculating the differences between the angles of adjacent FN branches from R₁ to R₂, R₂ to R₃, and R₁ to R₃. Each distance measurement was divided by the horizontal distance of the EAC to the oral commissure to yield a unitless proportional distance.

Summary of results The MATLAB program was used to analyze 23 FN maps. The mean proportional Euclidean distance between the superior EAC and the FN pes anserinus was 0.35 (σ=0.13). The mean proportional Euclidean distance, proportional arc distance, and angle at R₁ were 0.29, 0.30, and 45.8°, respectively (σ=0.17, 0.18, and 31.4°, respectively). The mean differences in adjacent branches' angles between R₁ to R₂, R₂ to R₃, and R₁ to R₃ were -5.5°, -6.5°, and -12.0°, respectively (σ=11.7°, 9.2°, and 18.5°, respectively).

Conclusions In comparison to each quantitative measurements' means, the standard deviations were proportionally large. This suggests the method of quantification was able to detect variations in FN patterns. The utility of this method will allow future quantification of FN pattern abnormalities associated with FN VA pathologies and may serve to help guide in surgical planning.

210

MYOPIA AND GLAUCOMA: AN ASSESSMENT OF IMAGING TOOLS TO IDENTIFY THE DIFFERENCES AND ROLE OF PARAPAPILLARY ATROPHY IN DIAGNOSIS

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10.1136/jim-2018-000939.209

Purpose of study Optical Coherence Tomography (OCT) is an imaging tool that allows visualization of the retinal layers. One of the areas identified on such scans corresponds to Parapapillary Atrophy (PPA), which can be divided into alpha, beta, and gamma PPA. We will examine beta and gamma PPA in this project. PPA refers to the physiological process and corresponding area of thinning of the retinal nerve fiber layer and retinal pigment epithelium that lies adjacent to the optic nerve head. The role of beta and gamma PPA in clinical diagnosis of glaucoma remains unclear. This study sought to determine if beta and gamma PPA areas correlated with onset or diagnosis of glaucoma, especially in myopes who have longer axial lengths and for whom pathology such as tilting and torsion of the optic nerve head often confounds accurate detection of glaucoma.

Methods used Cross sectional data for 158 glaucoma patients (mean age 65.5, 95% CI 63.1–67.2 years) and 20 nonglaucomatous patients (mean age 61.4, 95% CI 54.4–68.5 years) were included. Beta and gamma PPA areas, disc area, clinical disc margin, and Bruch's Membrane Opening Area were manually delineated on individual OCT ONH B-scans. Univariable and multivariable analyses were used to assess whether beta and gamma PPA area can be used to differentiate between healthy and glaucoma eyes, while also adjusting for age and axial length.

Summary of results Both beta PPA and gamma PPA were larger in glaucoma patients (mean 0.98, 95% CI 0.89–1.06 and mean 0.16, 95% CI 0.13 to 0.20, respectively) as compared to the nonglaucomatous controls (mean 0.66 mm², 95% CI 0.55–0.76 mm² and mean 0.08 mm², 95% CI 0.02 to 0.14 mm²), respectively), though the difference in gamma PPA was not statistically significant. Larger beta PPA was associated with age, race, BMO area, axial length, and MD. Larger gamma PPA was associated with BMO area, AL. The area under the Receiver operating curves (95% CI) for differentiating between healthy and glaucoma eyes was 0.58 (0.47, 0.69) for beta PPA and 0.53 (0.41, 0.64) for gamma PPA.

Conclusions Beta PPA was weakly associated with diagnosis of glaucoma after adjusting for age and axial length.

211

AN INVESTIGATION AND RANKING OF RESIDENT WELL-BEING ASSESSMENT TOOLS

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10.1136/jim-2018-000939.210

Purpose of study Residency is a challenging time for physicians in training. The long work hours, coupled with many responsibilities residents are given puts a lot of stress on them. This has led to undesirable consequences for a large number of residents, including burnout, depression, malpractice suits, and others that reduce the quality of their well-being. Many physicians are not always comfortable with talking about these issues so this lack of well-being is not

Abstract 211 Table 1

Parameter	0	1	2
Designed for medical professionals	No	Physicians in general	Sub-specialty specific
Validation	None	Non-medical	Medical
Estimated completion time		5–10 min	>10 min
Number of domains of well-being	<2	2–4	>4

assessed very well, especially for residents. There are many tools that can be used to assess resident well-being, but not much research has been done into which tool would work. The following is a comparative study of well-being assessment tools.

Methods used An exhaustive literature review was performed to identify validated tools. Key phrases such as 'physician well-being tests', 'resident quality of life' and 'medical well-being assessment tools' were used in the search. These tests were summarized, given an estimated time of completion, and pros and cons from the published results were also collated. Tools that have been assessed in surgeons and surgical residents were also identified.

Summary of results The tools were evaluated and ranked on the measured parameters. Refer to the attached table 1 for these parameters.

Conclusions The Well-being index from Mayo Clinic is the best option for assessing resident well-being. A prospective evaluation of the high scoring tools is proposed and will be measured by clinical specialty in students, residents, and practicing physicians.

212

DOXYCYCLINE REDUCES SCARRING BY MODULATING COLLAGEN ARCHITECTURE

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Purpose of study Scarring impacts hundreds of millions of patients every year. However, few effective treatments exist. Doxycycline, an antibiotic with known anti-fibrotic properties, has not been explored as an anti-scarring agent. We reveal that local doxycycline treatment reduces skin scarring without sacrificing scar strength.

Methods used Mice underwent dorsal stented excisional wounding and doxycycline and PBS (control) solutions were injected into the wound base. Wounds were harvested on day 15 for tensile strength and histologic analysis. Scar thickness was quantified by averaging 27 dermal thickness measurements from H and E-stained sections at varying scar depths. A MATLAB algorithm was used to quantify aspects of collagen structure (e.g., branching) from picrosirius red-stained images. The relative contribution of *En1* +fibroblasts (EPFs, responsible for murine dorsal scarring) was determined by histologic analysis of wounds in *En1*^{Cre};R26^{mTmG} mice. Statistical comparisons were made using unpaired t-test of doxycycline- versus PBS-treated wounds.

Summary of results Treatment with 2 mg/ml doxycycline reduced scar thickness by 25% compared to PBS (*p<0.001). Notably, ultimate tensile strength was comparable between doxycycline- and PBS-treated wounds (n=19, p=0.438).

Doxycycline-treated wounds had significantly reduced picro-red, scar-like collagen (* $p=0.004$) and increased picro-green, favorable collagen (* $p=0.011$). Picro-green fibers also demonstrated significantly increased branching (* $p=0.044$) and were less uniformly aligned, resembling unwounded skin collagen. Scarring fibroblasts (EPFs) were significantly reduced with doxycycline treatment, demonstrated by a 33.7% decrease in GFP signal in *En1^{Cre};R26^{mTmG}* mouse wounds (* $p=0.021$).

Conclusions We report that locally administered doxycycline significantly reduces scar burden without compromising wound strength. These findings may be explained by doxycycline's effects on scarring fibroblasts, as well as favorable collagen architecture that mimics the 'basketweave' appearance of unwounded skin. Due to doxycycline's widespread use and established safety profile, we favor rapid transition to clinical studies.

213 OUTCOMES OF PATIENTS WITH UNRESECTABLE ARTERIOVENOUS MALFORMATIONS: A 27-YEAR CHART REVIEW

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10.1136/jim-2018-000939.212

Purpose of study Arteriovenous malformations (AVMs) are vascular lesions characterized by abnormal connections between arteries and veins, progressive ectasia, high flow, and dysfunction. Curative treatment requires complete excision of the AVM, but some are unresectable and require life-long management. This study aims to determine the patterns of management that contribute to positive long-term outcomes for patients with unresectable AVMs.

Methods used A 27 year retrospective chart review (1991–2018) of patients with unresectable AVMs seen at our centre was conducted. Data collected included: demographics, AVM characteristics, clinical presentation, investigations, treatment modalities, outcomes, and complications.

Summary of results We identified 12 unresectable AVMs amongst 78 AVMs from 3273 patients with vascular anomalies. Five pediatric and 7 adult patients received care from on average 4 different medical specialties. Average length of follow-up was 5 years (ranged 1–12 years). Adult patients had more severe presenting symptoms such as ulceration, pain, and functional impairment compared to pediatric patients. There were 49 courses of treatment among all 12 patients (average 4 per patient): endovascular (24), surgical partial resection (14), and combination (11). Treatment indications included AVM progression, cardiac stress, bleeding, pain, wounds, cosmetic deformity, and symptom prevention. 60% of treatments improved symptoms, 30% resulted in no change, and 10% worsened symptoms. 13 out of 49 treatment courses resulted in a complication such as skin breakdown or significant perioperative or postoperative bleeding.

Conclusions Patients with unresectable AVMs were able to achieve positive outcomes through endovascular therapy and partial resection aimed at symptom alleviation and prevention. Regardless of symptom severity, small changes in symptoms initiated action from the medical team. Future work should be aimed at studying a larger population of patients with unresectable AVMs to better understand the patterns of management and outcomes.

214

UTILIZING TRAINED MEDICAL STUDENT EVALUATORS FOR ROBOTIC ANASTOMOSIS COMPETENCY EVALUATION OF THE VESICO-URETHRAL ANASTOMOSIS

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10.1136/jim-2018-000939.213

Purpose of study The robotic anastomosis competency evaluation (RACE) provides feedback on the vesico-urethral anastomosis (VUA) of a robotic prostatectomy. Expert surgeons were used in its validation but take extended time to complete tasks, limiting the usefulness of RACE. Crowdsourced evaluators provide rapid evaluations, but there remains skepticism due to their lack of medical knowledge. We compare trained medical students to experts to determine their reliability as evaluators.

Methods used Five medical students (two 2nd and three 4th year students) and 3 experts (150–500 cases) evaluated 30 VUA videos performed by 20 different surgeons with expertise ranging from resident to faculty using RACE. Medical students were trained by an expert (AJH) using a sample case video. Medical student scores were compared to expert scores using Bland-Altman analysis and intra-class correlation (ICC) assuming a 2-way mixed model.

Summary of results Medical students had higher ICCs than experts for absolute agreement (0.849 vs. 0.415) and for consistency (0.895 vs. 0.744) (both $p<0.001$). Averaged scores by medical students compared to averaged scores by experts resulted in ICC 0.702 for absolute agreement and 0.825 for consistency (both $p<0.001$). Medical students completed tasks faster than experts, taking 2.6 (range 1–3) days to complete video analysis versus 8.66 (1–11) days for experts. A Bland-Altman plot displayed a mean positive bias of 1.18 ($p=0.007$), indicating that medical students score slightly higher than experts on average. With lower RACE score cases, there is less consistency in grading by medical students relative to experts. However, with higher RACE scores, the variability in score differences between students and experts are minimal indicating greater consistent agreement on high quality VUAs.

Conclusions Medical students display a greater agreement in RACE scores in absolute scores and variability relative to experts. Medical students assign higher RACE scores in general compared to experts but improve in agreement with experts on cases with high RACE scores. Although medical students provide variable scores for lesser quality VUAs, they may serve as useful evaluators for high-quality VUAs.

215

THE EVOLUTION OF THE SURGICAL RECONSTRUCTIVE LADDER

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10.1136/jim-2018-000939.214

Purpose of study The main goal of reconstruction in the realm of surgery has been to restore form and function to patients. Traditionally the reconstructive ladder has provided plastic surgeons a stepwise guideline for reconstruction. This includes healing by secondary intention, direct tissue closure, local tissue transfer, distant tissue transfer, and free tissue transfer. As medicine has modernized, advanced therapies have been developed that offer additional steps in the reconstructive ladder to

incorporate a more holistic patient based approach. The new reconstructive pathway aims to incorporate innovative technology while examining economics of care and assessing care efficiency in order to better serve patients. This study describes the evolution of the reconstructive ladder, and present strategies for practitioners to move forward into a holistic care model of wound reconstruction.

Methods used A detailed literature review was performed, focusing on novel and innovative methods of wound reconstruction. Once the data on various advances were collected, each was analyzed for their potential benefit to reconstruction methods, considering the effectiveness, innovation, and how realistic the method appeared.

Summary of results Within the literature, there seemed to be patterns that suggest three major categories that many experts project for the future of reconstructive surgery. The first of these are the rapid growth technologies that help the surgeon and medical team see the body in a 3D space to better understand the topology and underlying anatomy of their patients seen in 3D simulations, 3D printing, and CAD/CAM. Next, is the use of stem cells or early progenitor cells like adipose derived stem cells, keratinocytes, and mesenchymal stem cells to help expedite the healing process. Lastly, the increasing use and development of new forms of allotransplants as seen as more and more organs and body parts are being transplanted that have never been done before.

Conclusions Though lots of work needs to be done until many of these tools become commonplace, there are many exciting developments in the field of reconstructive surgery that may contribute to the reconstructive ladder of the future.

216

FEMORAL BONE MINERAL DENSITY CHANGES AFTER PRIMARY HIP REPLACEMENT: AN EVALUATION OF THREE DIFFERENT TYPES OF HIP ARTHROPLASTY

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Purpose of study The aging population's demand for hip arthroplasty is compounded by a decreasing ratio of hip specialists to patients. These trends underscore the importance in maximizing implant longevity and ultimately decreasing morbidity. The loss of periprosthetic bone mineral density (BMD) following total hip arthroplasty (THA) may increase the rate of failure of THA. We evaluated 3 hip replacement stems (Omni Apex Modular, Omni Apex Arc, and Corin Cormet Resurfacing) and their respective effects on femoral BMD. The null hypothesis is that these three implants have the same effect on post-op BMD.

Methods used This study enrolled 116 total patients (31 Arc, 45 Modular, and 40 Resurfacing). All patients had a diagnosis of primary osteoarthritis. Patients with prior surgery or metabolic bone disease were excluded. Patients were followed from pre-operation to five years post-op, with DEXA scans taken at each annual follow-up visit. A Gruen ruler was digitally superimposed onto each DEXA scan to separate the femur into statistically comparable 2 cm zones. These zones were then compared across prosthetic groups.

Summary of results Potential confounders of age, BMI, and gender were accounted for. Of the 116 patients enrolled in

the study, 96 patients completed a post-op DEXA scan (27 Arc, 38 Mod., and 31 Res.); 69 patients completed their 2 year DEXA scan (16 Arc, 30 Mod., 23 Res.); and 48 patients completed their 5 year DEXA scan (13 Arc, 23 Mod., and 12 Res.). Patients with an Arc stem showed a mean -0.6% change at 2 years, and a -5.6% change in BMD at 5 years. Patients with a Modular stem showed a -6.4% change in BMD at 2 years, and a -5.4% change in BMD at 5 years. Patients with a Resurfacing stem showed a +2.5% change in BMD at 2 years, and a +8.5% change in BMD at 5 years. One-way ANOVA across all three implants at 5 years revealed a p-value of 4.1⁻¹⁰.

Conclusions The p-value is much lower than our α -level of 0.05, and thus we reject the null hypothesis. Resurfacing stem shows a positive impact on proximal femur BMD for the duration of the 5 year study. The Arc and Modular stems are less effective in mitigating BMD loss. While Resurfacing arthroplasties may have beneficial effects on BMD, this should be weighed against advantages of longer stem arthroplasties.

217

APPLICABILITY OF CALCANEAL APOPHYSEAL SCORE FOR BONE AGE ASSESSMENT FOR PATIENTS WITH CEREBRAL PALSY

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Purpose of study Correlation of bone age with growth velocity is clinically important for measuring skeletal maturity and predicting remaining growth in pediatric patients. Nicholson et al JBJS 2015 describes a reliable correlation between chronologic age (CA), peak height velocity (PHV), and calcaneal apophyseal ossification score (CAS) in typically developing children. CAS correlation is potentially of great clinical utility in CP population, where standard evaluation includes foot XR, but has not yet been validated.

Methods used Multiple raters recorded bilateral CAS for a cohort of 426 CP patients with appropriate XR. Contralateral CAS in bilateral CP and affected vs unaffected sides in patients with unilateral disease was compared using T-tests. Data was stratified and analyzed.

Summary of results Within the cohort (192 female, 234 male; age 5-18, mean 11.11), measurements were highly reliable between observers (ICC=0.926) and between time points for the same observer (ICC=0.915). No statistically significant side-to-side difference was found ($p>0.05$), nor mean CA per CAS compared to Nicholson ($p>0.34$); however there was a significant increase in standard deviation in CP population ($p<0.000005$).

Conclusions There does not appear to be a meaningful difference in the relationship between CAS and CA between children with and without cerebral palsy. CAS can be used in a GMFCS 1-3 population without adjustment for laterality or GMFCS. However, using a single CAS to estimate a CP child's chronologic age or time until PHV has less precision than in a typically developing population subjected to serial annual radiographs.

Abstract 217 Figure 1

218 A NEW RADIOGRAPHIC MEASUREMENT FOR QUANTITATIVE ANALYSIS OF FOREFOOT SPLAY IN CHILDREN WITH PERSISTENT IDIOPATHIC TOE WALKING

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Purpose of study Children with persistent idiopathic toe walking (ITW) beyond age six may develop ankle contractures and skeletal foot deformities that continue into young

adulthood. Forefoot deformities have not been systematically studied.

Methods used We performed a retrospective review of two groups of patients – those with typically developing (TD) feet (23 patients, mean 10.9, range 8–17 years) and those with diagnosed persistent ITW (71 patients, mean 10.4 years, range 5–19 years). Standardized AP weight-bearing foot XR were evaluated for inter-metatarsal angle and the forefoot splay index (FSI), a novel measurement defined as the ratio of the forefoot width (FF) to the hindfoot width (HF).

Abstract 218 Figure 1

Summary of results The ITW group had a statistically significant increase in forefoot splay compared with the TD group (FSI=1.75 vs 1.56; $p<0.0001$). Measurement of FF, HF, and FSI were highly reliable between observers (ICC=0.92–0.96) and between time points for the same observer (ICC=0.95–0.96). The ITW group had greater inter-metatarsal angles for each of the five inter-metatarsal angles than the non-ITW group. All five measures demonstrated good intra-rater reliability (ICC >0.80).

Conclusions Children and young adults with ITW have forefoot splay that can be radiographically quantified with FSI and inter-metatarsal angles. The newly described FSI is a simple measurement with a high inter- and intra-rater reliability, allowing for better characterization of the skeletal development of children with persistent ITW.

219 LONG-TERM CLINICAL, RADIOLOGICAL, AND HISTOLOGICAL FOLLOW-UP AFTER COMPLEX VENTRAL INCISIONAL HERNIA REPAIR USING UBM BIOLOGICAL GRAFT REINFORCEMENT

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Purpose of study Complex ventral incisional hernia repair represents a challenging clinical condition in which biologically-derived graft reinforcement is often utilized, but little long-term data inform that decision. This study evaluates the clinical, radiographic, and histological outcome of complex incisional hernia repair using UBM reinforcement with 12–70 months of follow up.

Methods used A single arm, retrospective observational study of all ventral incisional hernia repairs utilizing UBM reinforcement over a six-year time frame by a single surgeon was performed. Patients were assessed in long term follow up clinically and with the Carolina Comfort Scale. A subset of patient was assessed with abdominal wall ultrasound or CT scan. Three patients had abdominal wall fascial biopsies years after the incisional hernia repair with UBM graft, and the histology is analyzed.

Summary of results 64 patients underwent repair of complex incisional hernias with UBM graft reinforcement by a single surgeon. 42 patients had concomitant procedures including large or small bowel resection, excision of infected mesh, evacuation of abscess or hematoma, cholecystectomy, or panniculectomy with abdominoplasty. 16 patients had ostomies at the time of repair. Median follow-up time is 36 months, with a range of 12–70 months. Nine patients (14%) have required surgical repair of a recurrent hernia, and a tenth patient has a recurrence that is managed non-surgically, for a total recurrence rate of 15.6% over the entire time frame. Median time to recurrence was 32 months, and a Kaplan-Meier freedom from recurrence curve is depicted. 28 patients have undergone ultrasound or CT assessments of the abdominal wall which demonstrate radiographic fascial integrity 12–70 months after repair.

Conclusions In 64 patients undergoing complex ventral incisional hernia repair with UBM reinforcement all have experienced successful resolution of complex clinical conditions and 15.6% of these repairs have recurred at a median follow-up of 3 years. Three full-thickness biopsies of the repaired fascia years later shed light on a promising remodeling response which may signal strength and durability comparable to native fascia.

220 SUSTAINED RELEASE OF SILENCING RNA USING HYDROGELS FOR APPLICATION IN INTIMAL HYPERPLASIA

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Purpose of study Anastomotic restenosis following prosthetic vascular grafting is a well described phenomenon. Thrombospondin – 2 (TSP2), an anti -angiogenic protein secreted by vascular smooth muscle cells, has been identified as a target for knockdown in attempt to treat this condition. Beginning with click-alginate gels, the goal of this work was to develop a clinically suitable hydrogel vehicle for perivascular anti-TSP2 siRNA elution in order to prevent anastomotic restenosis following prosthetic vascular grafting.

Methods used All hydrogels were prepared as a 20% w/v solution in 1X PBS. Anti-TSP2 siRNA was incubated with Jet-PEI; this complex was dissolved within the hydrogel matrix, which was then incubated in serum free DMEM for 4 hours to 1 week. This solution was then applied to human aortic smooth muscle cell cultures. TSP2 knockdown was measured 48 hours later cells using qRT-PCR.

Summary of results Knockdown of TSP2 using click-alginate gel was unsuccessful. Through dose dependent experimentation with heparin, it became clear that the anionic nature of the alginate gel interfered with transfection through the target cell membrane using a cationic lipid reagent. Moving forward, a robust, biodegradable, cationic gel such as click-gelatin would be the ideal candidate. Preliminary data confirms successful TSP2 knockdown. The next steps include the investigation of click-gelatin as a suitable sustained release model *in vivo*, which could indicate click-gelatin as a promising target for application in the practical reduction of intimal hyperplasia.

Conclusions Click-alginate gel is not a suitable vehicle for sustained release siRNA delivery *in vitro*. This is most likely due to the profound anionic nature of alginate gel, which interferes with transfection of human aortic smooth muscle cells using Jet-PEI transfection reagent. Lastly, gelatin, a neutral to cationic polymer, is a promising candidate for this application, given its modifiable properties and clinical applicability.

221 SAFE USE OF PERIOPERATIVE CEFAZOLIN IN PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY: A REVIEW

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Purpose of study Cefazolin (Ancef) is the most frequently prescribed antibiotic for surgical site infection prophylaxis in the perioperative setting. However, many practitioners believe administration of cefazolin is contraindicated in patients with a history of penicillin allergy due to the potential for cross-reaction secondary to the beta-lactam ring common to both molecules. In this literature review, we explore when it is appropriate to use cefazolin in patients with a history of penicillin allergy.

Methods used PubMed, EMBASE, and SciFinder databases were searched for the chemical structures of clinically relevant beta-lactam antibiotics and studies published from January 2008 – September 2018 describing beta-lactam antibiotic use in patients who reported history of penicillin allergy.

ChemDraw version 17.1 was used to qualitatively compare the antibiotic chemical structures in question.

Summary of results The R1 side chain of penicillin and cefazolin was found to be significantly different. This finding suggests that cefazolin can be administered in select patients with a history of penicillin allergy. We propose recommendations and specific situations where it is appropriate to do so.

Conclusions These guidelines contribute to current antibiotic stewardship practices and address unnecessary substitution of cefazolin for later-generation antibiotics, which are associated with higher costs, increased risk of complications, and the potential for emergence of multidrug resistant organisms.

222

DYSPHAGIA IN CHILDREN AFTER CONGENITAL CARDIAC SURGERY: A SYSTEMATIC REVIEW

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Purpose of study As the morbidity and mortality of congenital cardiac surgery has improved, attention to postoperative feeding outcomes has become increasingly important[SF1]. While centers have embarked on various strategies to achieve oral feeding post-operatively, there is still wide variability in common practice.

Methods used The literature was searched using the MEDLINE, EMBASE, and CINAHL databases for publications up to March 2018. All papers discussing pediatric patients with congenital heart defects, surgical intervention, and swallowing dysfunction were reviewed in a systematic fashion. Exclusion criteria were non-English publications, only >18 year old patients, and no outcome data regarding feeding or swallowing.

Summary of results In total, 19 studies were included[SF1]. Of these, 6 studies focused on dysphagia specifically, but notably included heterogenous assessment methods and outcomes. 9 studies discussed vocal fold dysfunction (VFD). Among those, only 5 assessed swallowing function discreetly and none found dysphagia in more than half of the patients with VFD. There were 5 studies evaluating feeding disorders in general, and only 1 study evaluated long-term results greater than 2 years.

Conclusions The available data on dysphagia after congenital cardiac surgery is heterogenous and sparse. In particular, there is a lack of common outcomes that are reported. Additional studies that focus on dysphagia in this population are needed to better isolate the risk factors and to develop comprehensive postoperative feeding strategies. A consensus of standardized, trackable outcomes will provide the basis for evidence driven feeding programs in this fragile population.

223

SHOULDER AND ELBOW FUNCTION FOLLOWING THE SUPINATION-EXTERNAL ROTATION PROTOCOL IN CHILDREN WITH BIRTH RELATED BRACHIAL PLEXUS INJURIES: A PILOT STUDY

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Purpose of study Birth-related brachial plexus injuries (BRBPI) occur in approximately 1 of 1000 live births. Consensus

regarding the optimal management of birth-related brachial plexus injuries (BRBPI) has not been achieved with various treatments including physiotherapy, occupational therapy, and surgery. Our group developed a protocol that repositions the shoulder into supination and external rotation (Sup-ER), which restores supination and external rotation by two years of age. However, the longer-term outcomes of the Sup-ER splint have not been reported.

Methods used This cross-sectional cohort study examined 16 children older than 4 years of age with severe BRBPI who were treated with the Sup-ER splint. Shoulder and elbow function were measured by the Axillary, Back, and Cranial loops and a modified Mallet scale. Additionally, the passive and active range of motion of internal rotation, external rotation, supination, pronation, elbow flexion and elbow extension, as well as internal and external rotation strength were examined.

Summary of results All functional and active movements were statistically significantly lower in the affected arm compared to the unaffected arm, except for elbow flexion. Passively, there were statistically significant differences between the affected and unaffected arms in all movements except for internal rotation and supination. Strength in internal and external rotation was weaker in the affected arm, with internal rotation having a relatively larger strength deficit.

Conclusions Despite statistical differences in the anatomic ranges of motion between the affected and unaffected arms, the ranges in both arms were within functional limits. Overall, the Sup-ER protocol has been effective in restoring elbow and shoulder function in children with BRBPI.

Adolescent Medicine and General Pediatrics II Concurrent Session

8:00 AM

Friday, January 25, 2019

224

ASSESSING NUTRITIONAL INTAKES IN CHILDREN WITH NEPHROTIC SYNDROME

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Purpose of study Information regarding nutrition management of childhood nephrotic syndrome (NS) is limited. Based on risks of disease-related edema and corticosteroid side-effects, our NS clinical pathway incorporates standardized recommendations for daily energy, sodium (Na), calcium (Ca) and Vitamin D (VitD) along with food intake records. This study compares actual dietary intakes of patients with NS to our pathway's nutrition recommendations.

Methods used Our retrospective study included incident NS patients (1–17 years) treated with prednisone (60 mg/m²/day) seen from Feb 2013-May 2018 who completed a valid 3 day food record 4 weeks post-diagnosis. Intake information was analyzed using esha™ Food Processor program. Pathway recommendations for daily energy requirements were based on height, weight, age and gender using a sedentary activity factor. We recommended a daily Na intake of 1 mg/1 calorie of