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Clinical Research
Plenary Session
SSCI Young Investigator Award Finalists
SSCI Young Investigator for General
Medicine
SSCI Poster Award Finalists
SAFMR/SSCI/ Young Faculty Award
SAFMR/SSCI/ Trainee Research Award
8:00 AM
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429 PERIPHERAL SELECTION FOR TYROSINE AND
AGAINST THREONINE IN ABSENCE OF CENTRAL
PREBCR CHECKPOINT SELECTION

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10.1136/jim-2016-000393.429

Purpose of Study We sought to identify selection pressures on the amino acid content of the center of the immunoglobulin antigen binding site in the IgM repertoire created in the absence of bone marrow selection by the surrogate light chain (SLC), which is composed of $\lambda 5$ and VpreB. Lack of any of the preBCR components causes incomplete block in B cell development marked by passage of cells with untested receptor activity that can occupy peripheral compartments by time.

Methods Used We cloned, sequenced and analyzed μ heavy chain transcripts from immature, transitional, follicular, mature, and marginal zone B cells from mice genetically deficient for $\lambda 5$ and compared the amino acid composition of the third Ig heavy chain complementary determining region (CDR-H3) to wild type. We focused on CDR-H3 position 101 which is critical for antigen binding. We also evaluated B cell apoptosis by flow cytometry and serum dsDNA binding titers by ELISA.

Summary of Results In WT mice, SLC selection promotes the presence of tyrosine at position 101. In the absence of $\lambda 5$, immature B cells express threonine, valine and leucine more frequently. With development, however, there is a progressive increase in the presence of tyrosine, with a complementary loss of threonine, valine and leucine. The mechanism of selection appears to be apoptosis, which is greatly increased in the developing B cells in the $\lambda 5$ deficient mice. In spite of the partial correction of the repertoire, the presence of charged CDR-H3s remains high, and the mice express dsDNA binding IgM.

Conclusions The SLC serves as an invariant antigen to select the amino acid composition of μ heavy chain. In the absence of $\lambda 5$, and thus without SLC selection, the unselected repertoire demonstrates an altered pattern of amino acid usage at specific positions at the center of the antigen binding site. Peripheral selection can ameliorate, but not fully correct the repertoire. SLC selection acts to prevent autoreactivity

430 HIV RISK BEHAVIORS AMONG IMMIGRANT LATINO YOUTH: A PUBLIC HEALTH PRIORITY

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Purpose of Study HIV/AIDS disproportionately affects Latino youth in the US. Structural inequalities render immigrants more vulnerable to HIV. We compared rates of HIV sexual risk behaviors (HRB) among Latinos who immigrated at age 12 or younger (children migrants, CM) and those who did after age 12 (young adults migrants, YAM) and explored the association between acculturation strategies and HRB.

Methods Used We collected demographic, migration, acculturation strategies and sexual behaviors history (condom use, transactional sex, sex while intoxicated and sex with multiple partners) in a convenience sample of HIV (-) Latinos ages 18–29 in Atlanta. Acculturation was measured based on the *Bidimensional Acculturation Scale*. Socio-demographic and migration characteristics were summarized by descriptive statistics. Univariate and multivariable logistic regression models were applied to explore the effects of acculturation and age at migration on occurrence of HRB.

Summary of Results We enrolled 132 subjects [60% male, mean age 23 years (SD: 3.4)], 96% of them were Mexican. Ninety four percent of CM had a high school education or higher compared to 62% of YAM ($p < 0.001$). Fifty five percent of CM lived with their parents, compared to 15%

of YAM ($p < 0.001$). Moreover, 79% of YAM had an undocumented immigration status, compared to 41% of CM ($p < 0.001$). YAM engaged in HRB significantly more than CM (73% vs. 53%, $p = 0.02$) and these differences were driven primarily by poor condom use (56% vs. 31%, $p = 0.009$) and having sex with a commercial sex worker (13% vs 0% $p = 0.001$). CM utilized assimilation and integration strategies (both $p < 0.05$), while YAM adopted primarily the separation strategy ($p < 0.001$); which was more frequently seen in participants who engage in HRB. Multivariate analysis showed that odds of HRB were two and three times more likely in males and when living with someone other than parents, respectively (both $p < 0.05$). Undocumented immigration status and using separation strategies had borderline significance for HRB (both $p < 0.1$).

Conclusions YAM engage in HRB more than CM, notably males and those living outside the parental household. Scaling up PrEP, improving condom use amongst recently immigrated undocumented Latino male youth and curtailing their social isolation are critical in decreasing HIV risk.

431 TEMPORAL TRENDS AND CLINICAL OUTCOMES IN PATIENTS WITH UNCONTROLLED DIABETES AND RELATED COMPLICATIONS

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Purpose of Study Patients with uncontrolled diabetes are frequently hospitalized with life threatening complications such as ketoacidosis, hyper-osmolarity and diabetic coma. There is paucity of data with respect to contemporary trends in management and outcomes of uncontrolled complicated diabetes mellitus related hospitalizations.

Methods Used We analyzed the 2003 to 2011 Nationwide Inpatient Sample databases to examine the temporal trend and in-hospital mortality in patients presenting with uncontrolled complicated diabetes mellitus aged ≥ 18 years in the United States. All patients with primary diagnosis of uncontrolled complicated diabetes mellitus were identified using ICD-9 CM codes- 250.02–250.03, 250.10 -250.13, 250.20 -250.23 and 250.3.

Summary of Results From 2003 to 2011, the number of patients admitted with the primary diagnosis of uncontrolled complicated diabetes mellitus increased from 171,408 to 216,965 (ptrend < 0.001). During the study period, in-hospital mortality decreased from 0.8% to 0.4% (adjusted odds ratio [per year] 0.90; 95% confidence interval 0.89 to 0.91; ptrend < 0.001). The average hospital charges increased from \$14,370 to \$22,897 (ptrend < 0.001), whereas the average length of stay decreased from 3.9 to 3.4 days (ptrend < 0.001).

Conclusions Although the number of hospitalizations with primary diagnosis of uncontrolled diabetes mellitus increased by approximately 26.5% between 2003 and 2011, there have been favorable trends in the clinical outcomes of these patients, with a decrease in risk-adjusted in-hospital mortality.

431A CHARACTERISTICS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WHO ARE READMITTED WITHIN 30 DAYS FOLLOWING AN ACUTE EXACERBATION

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Purpose of Study The Hospital Readmissions Reduction Program targets Medicare patients with congestive heart failure, acute myocardial infarction, pneumonia, and COPD and penalizes hospitals which have an increased 30-day readmission rate. Approximately 20% of patients with acute exacerbations of COPD are readmitted within 30 days. Analysis of these readmissions can help hospitals and clinicians identify patients at risk for readmission and identify possible deficiencies in the patient care.

Methods Used We retrospectively reviewed medical records of patients with acute exacerbations of COPD who were readmitted to the hospital within 30 days of discharge. We collected information on patient demographics, on comorbidity, on laboratory and radiographic information, and on management; based on record review we identified the clinical diagnosis which best explained the readmission.

Summary of Results We identified 27 admission-readmission hospitalization events in 16 patients with acute exacerbations of COPD between 1/1/2011 and 12/31/2015. The mean age was 73.4 ± 6.9 ; 66.7% were men. These patients had frequent comorbidities, including CAD (40.7%), HTN (96.3%), DM (33.3%), and CKD (25.9%). The initial chest x-rays were clear in 81.5%, showed infiltrates in 11.1%, and showed cardiomegaly in 14.8%. Nineteen percent of the admissions required mechanical ventilation. The length of stay for the index hospitalization was 4.7 ± 2.5 days; 92.6% of patients were discharged home. Most patients (61.5%) were readmitted with an acute exacerbation of COPD within with an average interval of 15 ± 8.4 day since discharge. Following the second hospitalization more patients (25.9%) were discharged to nursing facilities. These patients had a mean of 2.7 ± 1.9 hospitalizations for all causes during the 12 months prior to their index admission.

Conclusions Patients with acute exacerbations of COPD who require readmission within 30 days are older, have frequent comorbidity, have short lengths of stay during the index admission, and are discharged home following hospitalization. The time interval before readmission provides adequate time for clinic follow-up. These patients are easily identified by their past history of frequent admissions.

431B IMPACT OF DIAGNOSIS AGE ON QUALITY OF LIFE AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Purpose of Study Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder disproportionately affecting minority women of child-bearing age. However, 15–20% of all patients with SLE are diagnosed as children. This study compares the health-related quality of life (HRQOL) in childhood-onset SLE (cSLE) to HRQOL in adult-onset SLE (aSLE).

Methods Used Data was collected as part of an ongoing SLE longitudinal registry at MUSC, including demographics, clinical disease manifestations and patient-reported responses to the Short Form-36 (SF-36) v2 questionnaire. For this study, two SF-36 questionnaires were analyzed from each patient. Scores were analyzed across eight physical and mental health domains including physical functioning, role physical, bodily pain, social functioning, mental health, role emotional, vitality, and general health. SF-36 scores were then compared between cSLE patients, defined as diagnosed prior to age 18 years, and aSLE patients.

Summary of Results aSLE patient (n=323) and cSLE patients (n=9) were similar in racial (68.4% black) and gender (94.0% female) distribution. Mean normalized scores for all eight of the SF-36 domains were higher for cSLE patients compared to aSLE patients, with statistical significance found in two domains: physical functioning (52.1 ± 6.1 cSLE vs 38.8 ± 12.4 aSLE, $p=0.0016$) and role physical (50.1 ± 7.1 cSLE vs 38.6 ± 12.5 aSLE, $p=0.0067$). We did not find significant differences in SF-36 scores based on race, gender or disease-specific manifestations such as renal disease.

Conclusions These findings suggest that having been diagnosed at an earlier age and having lived most of their life with a systemic autoimmune disease may contribute to the higher health-related quality of life reported by patients with cSLE. Of interest, the contrast between cSLE and aSLE patient scores was greatest within the physical functioning and role physical domains despite the limited sample size of cSLE patients with completed questionnaires.

431C ACTIVATION OF NRF2 ATTENUATES MIR-21 AND RESTORES SMAD7 EXPRESSION IN ALCOHOL-EXPOSED LUNG FIBROBLASTS

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Purpose of Study We previously determined that alcohol exposure inhibits Nrf2, the master transcription factor that activates anti-oxidant responses, and induces transforming growth factor- β 1 (TGF β 1) in the lung and in lung fibroblasts with pathophysiological consequences. Further, treatment with the Nrf2 activator sulforaphane attenuates alcohol-induced TGF β 1 expression in lung fibroblasts. However, the mechanisms by which alcohol and Nrf2 modulate TGF β 1 are unknown. Several microRNAs (miRs) have been shown to regulate gene expression through suppression of gene transcription and down-regulation of a target gene. miR-21 has been shown to target Smad7, a TGF β 1 inhibitor. We hypothesized that alcohol induces TGF β 1 expression through upregulation of miR-21 and

subsequent suppression of Smad7 in lung fibroblasts. In addition, we predicted that activating Nrf2 with sulforaphane attenuates this effect through down-regulation of miR-21 expression, which in turn restores Smad7 expression.

Methods Used Mouse primary lung fibroblasts (PLFs) were cultured \pm alcohol (60 mM) \pm sulforaphane (5 mM). miR-21 expression was analyzed at 24 hours. In parallel, Smad7 gene and protein expression were analyzed at 24 and 72 hours, respectively. In parallel, 3T3 NIH lung fibroblasts were transfected with Nrf2 silencing RNA (or appropriate controls) and treated with sulforaphane. Smad7 gene expression was analyzed at 24 hours.

Summary of Results Alcohol exposure increased miR-21 expression in PLFs and decreased Smad7 gene and protein expression. In contrast, sulforaphane attenuated miR-21 expression and increased Smad7 expression in alcohol-treated cells. Interestingly, Nrf2 silencing inhibited the effect of sulforaphane on Smad7 gene expression.

Conclusions Alcohol inhibits Nrf2 activity and in parallel (or as a consequence) induces miR-21 and suppresses Smad7. We speculate this is at least one mechanism through which alcohol induces TGF β 1. It appears that alcohol-mediated induction of miR-21 and Smad7 is attenuated by sulforaphane via a Nrf2 signalling pathway. These findings provide a potential mechanism by which treatment with Nrf2 activators such as sulforaphane could limit injury and/or promote repair in the lungs of individuals with alcohol use disorders.

432 THE EFFECTS OF ANIMAL ASSISTED THERAPY ON PEDIATRIC RESIDENTS

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10.1136/jim-2016-000393.435

Purpose of Study Physician burnout increases during training and is linked to poorer patient outcomes and physician depression / suicide. Effective, low risk, low cost wellness intervention strategies are critical to improve trainees' learning environment and mood. This study sought to determine if canine assisted therapy mitigates resident burnout, depression, and anxiety on inpatient rotations.

Methods Used In this single-center, cross-over randomized trial, 21 pediatric residents on six different inpatient teams participated in an 8-week study. Three teams participated in weeks 1–4 (Phase I), and three teams participated in weeks 5–8 (Phase II). Residents were exposed to certified therapy dogs for 1–3 hours each weekday during weeks 3–4 and 5–6. No dogs were present during weeks 1–2 and 7–8.

The Maslach Burnout Survey (MBS, components A, B, and C) and State-Trait Anxiety Inventory (STAI) were administered anonymously on day one and every other week thereafter. The Beck Depression Inventory (BDI) was administered on day 1 and weekly thereafter.

Paired Student t-tests compared the changes between baseline scores vs. weeks with dogs present / not present respectively and changes between the weeks with dogs present / not present.

Summary of Results Depression (BDI, $p=0.0022$), anxiety (STAI, $p=0.0094$), and burnout (Maslach B, $p=0.0447$) significantly increased from baseline in weeks in which there was no dog present but not in weeks in which there was a dog present ($p=0.0827$, 0.5255 , and $p=0.0581$, respectively). There was a significant decrease in depression (BDI, $p=0.0114$) and burnout (Maslach A, $p=0.0102$) in weeks with a dog compared to weeks without a dog.

Conclusions Pediatric residents on inpatient rotations showed decrease in depression, anxiety, and burnout scores in weeks when they were exposed to therapy dogs as compared to weeks in which they were not. Thus, animal therapy is a reasonable approach to mitigate resident burnout with minimal risk of harm, particularly considering the low cost, low time commitment, and the precedent of therapy animals in hospitals for patient care.

433 LEFT VENTRICULAR FALSE TENDONS ARE ASSOCIATED WITH LEFT VENTRICULAR DILATION AND IMPAIRED LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION

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10.1136/jim-2016-000393.436

Purpose of Study Left ventricular false tendons (LVFTs) are chord-like structures that traverse the LV cavity and are generally considered to be benign. However, they have been associated with arrhythmias, left ventricular hypertrophy and LV dilation in some small studies. Our objective was to evaluate the relationships of LVFTs with LV structural and functional changes assessed by echocardiography.

Methods Used We retrospectively evaluated echocardiographic and clinical parameters of 126 patients identified as having LVFTs within the past 2 years at a large tertiary care university medical center and compared them to 85 age and sex-matched controls without LVFTs.

Summary of Results There were no significant differences in age (52 ± 2 vs 54 ± 2 years), sex (55 ± 5 vs 59 ± 4 % men), race (36 vs 23% white), systolic blood pressure (SBP, 131 ± 2 vs 132 ± 2 mmHg) or body mass index (BMI, 31 ± 1 vs 29 ± 1 kg/m²) between controls and patients with LVFTs, respectively. Patients with LVFTs had much more prevalent heart failure compared to controls (43% vs 21%, $p=0.001$). Patients with LVFTs had more LV dilation and reduced LV ejection fraction (18% lower) compared with controls (all $p < 0.05$). Patients with LVFTs also had more severe diastolic dysfunction (52% vs 37% with grade II-III diastolic dysfunction, $p=0.03$) and higher E/e', an indicator of LV end-diastolic pressure (12.4 ± 0.6 vs 10.5 ± 0.4 , $p=0.02$). After adjustment for age, sex, race, BMI and SBP, insertion of LVFTs into the basal and middle LV segments was associated with reduced LV systolic function ($p < 0.01$) and LVFTs in the middle LV were associated with LV dilation ($p < 0.01$). LVFTs located in the apex were not associated with LV systolic dysfunction or dilation.

Conclusions Our findings suggest LVFTs may not be benign variants and LVFTs located in the basal and middle LV may have more deleterious effects. Further prospective

studies should be performed to determine their pathophysiological significance and if they play a causal role in LV dysfunction.

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434 PROPHYLACTIC DEXTROSE GEL DOES NOT PREVENT NEONATAL HYPOGLYCEMIA: A PILOT STUDY

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10.1136/jim-2016-000393.437

Purpose of Study Transient neonatal hypoglycemia (TNH) affects ~15% of all deliveries and ~50% of at-risk newborns. Current standard of care treatment for at-risk newborns with asymptomatic TNH despite feeding is intravenous dextrose. Dextrose gel applied to the buccal mucosa is a promising alternative route that has been shown to reverse pre-existing hypoglycemia and decrease NICU admission. We wondered if prophylactic 40% dextrose gel would reduce TNH and reduce the rate of NICU admissions for treatment of TNH.

Methods Used This quasi-experimental study allocated asymptomatic at-risk newborns born at Harris Health Ben Taub Hospital to prophylactic dextrose gel based on the researchers' availability; other at-risk newborns served as controls. Newborns had to have ≥ 1 inclusion criteria based on the hospital's Hypoglycemia Protocol: 1) prematurity (35 weeks 0 days-36 weeks 6 days), 2) small (birth weight <2500 g) or 3) large for gestational age (>4000 g), or 4) infants of diabetic mothers. After an initial feed, 0.5 ml/kg 40% dextrose gel (Insta-Glucose) was rubbed into the buccal mucosa, and blood glucose (BG) was checked 30 min later. The Wilcoxon rank-sum test was used to compare groups in terms of the first BG and other quantitative variables while Fisher's exact test was used for categorical variables. A multivariable linear regression model was used to compare groups' first BG after adjusting for at-risk category.

Summary of Results 222 subjects were enrolled (74 prophylactic and 148 controls). The first BG was not different between prophylactic and control infants (51.8 ± 16.8 vs 52.4 ± 14.8 mg/dL, $p=.54$). After adjusting for the 4 at-risk categories, the first BG was not different between prophylactic and control infants ($p=.58$). The NICU admission rate for TNH was 13% in both groups.

Conclusions To our surprise, prophylactic dextrose gel did not increase initial BG or reduce NICU admission for TNH in at-risk newborns. Perhaps the sample size was too small, the gel should have been given before feeding, or BG was checked too soon to show a beneficial effect of prophylactic dextrose gel. Alternatively, exogenous glucose may have minimal effect on glucose homeostasis during the first few hours after birth, and may be primarily regulated by counterregulatory mechanisms.

435 ENVIRONMENTAL OR NASAL CANNULA OXYGEN (ECO) FOR PRETERM INFANTS RECEIVING OXYGEN THERAPY: A RANDOMIZED CROSS-OVER PILOT TRIAL

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Purpose of Study Preterm infants have frequent episodes of intermittent hypoxemia due to pulmonary disease and immature respiratory control. Servo-controlled oxygen environment (OE) may decrease episodes of hypoxemia by providing a more stable hypopharyngeal inspired O_2 concentration compared to nasal cannula (NC).

Methods Used This was a single center randomized cross-over trial with a 1:1 parallel allocation of infants to the order of testing each of the two interventions. Preterm infants on supplemental O_2 via OE or NC with flow rates ≤ 1.0 L/kg/min were randomized using sequentially numbered sealed opaque envelopes. Infants crossed-over every 24 hours for 96 hours. Data were collected using ixTrend software to electronically capture real time numeric and waveform data from patient monitors. A sample size of 25 infants was required to determine if OE decreased episodes of intermittent hypoxemia ($SpO_2 < 85\%$ for ≥ 10 seconds) by at least 20%, with a standard deviation of 0.5, a power of 80%, and a two tailed type I error rate of 0.05. Numeric data were analyzed using MATLAB.

Summary of Results Twenty five infants with a mean gestational age of $27\ 0/7 \pm 2$ weeks and a birth weight of 933 ± 328 g were studied at 37 ± 26 postnatal days. The number of episodes of intermittent hypoxemia per hour was 4.7 ± 3.1 in the OE group versus 5.4 ± 2.6 in the NC group ($p=0.05$). When the proportion of time with intermittent hypoxemia was expressed as a ratio, using OE as the baseline, the difference was significant [NC/OE, 1.551 ± 1.2 ; $p=0.03$]. Infants on OE had a lower proportion of time with $SpO_2 < 85\%$ compared to infants on NC ($p=0.02$) [Figure 1]. The proportion of time with $SpO_2 < 91\%$, $> 95\%$, and 91 to 95% did not differ significantly between groups (all $p > 0.05$). SpO_2 stability was compared using the coefficient of variation of the SpO_2 and did not differ between groups [4.4% in OE versus 4.9% in the NC; $p=0.07$].

Conclusions In preterm infants receiving supplemental O_2 , servo-controlled oxygen environment decreased intermittent hypoxemia compared with nasal cannula.

436 DOSE-RESPONSE RELATIONSHIP BETWEEN EARLY ENTERAL VITAMIN D SUPPLEMENTATION AND NEURODEVELOPMENTAL OUTCOMES AT 2 YEARS OF AGE: FOLLOW-UP DATA FROM A RANDOMIZED TRIAL IN EXTREMELY PRETERM INFANTS

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Purpose of Study Extremely preterm infants (≤ 28 weeks gestation) depend on external sources of vitamin D. It is

Abstract 436 Table 1 Baseline characteristics and outcomes

	Placebo Group (n=25)	200 IU Group (n=20)	800 IU Group (n=19)	p
Gestational age (GA), median (IQR)	26 (24–26)	25 (24–27)	25 (24–26)	0.37
Birthweight, mean±SD	770±207	778±176	743±215	0.76
Adjusted GA at follow-up, median (IQR)	23 (22–25)	22 (21–25)	23 (22–25)	0.14
Use of asthma medications up to 3 months prior to follow-up visit, n/N (%)	11/25 (44)	9/20 (45)	8/19 (42)	0.79
Use of supplemental oxygen up to 3 months prior to follow-up visit, n/N (%)	2/25 (8)	2/20 (10)	0/19 (0)	0.78
Cognitive score, median (IQR)	90 (80–100)	90 (71–100)	95 (80–100)	0.61
Language score, median (IQR)	79 (74–91)	81 (66–91)	86 (77–91)	0.40
NDI, n/N (%)	13/25 (52)	9/20 (45)	6/19 (32)	0.14

unknown if early vitamin D supplementation in these infants reduces neurodevelopmental impairment (NDI). We hypothesized that cognitive scores at 2 years of age are 10 points higher in extremely preterm infants supplemented early with enteral vitamin D.

Methods Used The early vitamin D trial was a blinded randomized controlled trial in which 100 extremely preterm infants were randomly assigned to receive placebo, a vitamin D dose of 200 IU/day, or a vitamin D dose of 800 IU/day since day 1 of enteral feeding until day 28 (NCT01600430). Infants who participated in the trial were included in this study if they had a 2-year follow-up evaluation. The primary outcome was cognitive score at 22–26 months corrected age. Secondary outcomes included NDI (cognitive score <85, gross motor function \geq 2, blindness, or deafness), and use of asthma medications or supplemental O₂ after NICU discharge.

Summary of Results Of a total of 79 infants eligible for follow-up, 64 had 2-year outcome data (81%). Baseline characteristics and outcomes of these infants are shown in Table 1. The incidence of NDI was 44% (ranged from 32% in the 800 IU group to 52% in the placebo group). The mean cognitive score was 88±14 and did not differ across subgroups.

Conclusions This is the first pilot study reporting 2-year outcomes after early vitamin D supplementation in extremely preterm infants. Cognitive scores were not significantly higher in infants supplemented with vitamin D, but our analysis was underpowered to detect a 5-point difference. A non-significant dose-response relationship between vitamin D and NDI was found.

437 MATERNAL NUTRIENT RESTRICTION IMPAIRS CARDIOMYOCYTE DEVELOPMENT AND FUNCTION IN GUINEA PIGS AND HUMANS

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10.1136/jim-2016-000393.440

Purpose of Study Maternal nutrient restriction (MNR) during pregnancy and lactation increases offspring susceptibility to cardiometabolic disease. The purpose of this study is to examine the effect of MNR on cardiac development and function in guinea pigs and human adolescents.

Methods Used Pregnant guinea pig sows were provided a 30% reduced calorie diet until mid-gestation, followed by a 10% reduced calorie diet until 35 days post-parturition when they were transitioned to full calorie diet. Control pregnant sows were provided a full calorie diet. Late gestation fetal and 28-day-old neonatal hearts were harvested. Myocardial morphology and cardiomyocyte (CM) number and function were characterized using immunohistological and biomolecular techniques. CM-specific gene expression was analyzed by qPCR. Cardiac morphology and function were examined by echocardiography in 386 human adolescents with/without a history of fetal growth restriction.

Summary of Results MNR resulted in significant growth restriction in guinea pig offspring. After correction for total body weight, hearts exhibited disproportionate growth restriction in MNR fetuses (0.72±0.05 vs 0.59±0.03 %body weight, $p<0.05$). Histological examination of cardiac cross sections showed a disorganized architecture characterized by increased collagen deposition and aberrant cell cycling. CM number was significantly reduced in MNR fetuses (510±29 vs 625±38 cells/hpf, $p<0.01$) and neonates (525±12 vs 675±20 cells/hpf, $p<0.01$) as compared to controls. Ki-67 positive cells were significantly increased (12.5±1.5 vs 4.8±0.6 %positive CM/hpf, $p<0.01$) in MNR fetuses and neonates as compared to controls. However, MNR neonates were unable to significantly expand CM number as compared to controls (15±16 vs 50±23 mean difference cells/hpf, $p<0.01$). Fetal and CM-specific gene expression were perturbed in MNR fetuses and offspring. Corollary studies in 386 human adolescents revealed a U-shaped relationship between Ponderal Index and left ventricular mass independent of current BMI ($p=0.035$).

Conclusions MNR disproportionately affects heart development by reducing CM number and altering cardiac architecture. These effects may have lifelong implications and predispose growth restricted infants to premature cardiac dysfunction as evidenced by our human data.

438 PRO-INFLAMMATORY SIGNALING BY PLATELET-ACTIVATING FACTOR CONTRIBUTES TO BRONCHOPULMONARY DYSPLASIA

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10.1136/jim-2016-000393.441

Purpose of Study Platelet-activating factor (PAF) is a highly potent lipid inflammatory mediator known to cause airway inflammation and injury. Our objective is to investigate the role of PAF in the pathogenesis of BPD and its potential as therapeutic target.

Methods Used **A:** Newborn C57BL/6 mice (WT) (n=12) were exposed to either 21% or 85% oxygen from P3–14 (BPD model) after which the lungs were harvested and processed for mRNA analysis. **B:** Gene-targeted mice using PTAFR KO (without PAF receptor; decreased PAF signaling), PAF-AH KO (without PAF acetylhydrolase which breaks down PAF; increased PAF signaling), and WT control were utilized in the BPD model (n=12/group). At the end of exposure, pulmonary function testing (PFT) was done using flexiVent. Half of the pups were processed for lung histology/morphometry and the other half for bronchoalveolar lavage (BAL) and mRNA analysis. BAL cytokines were analyzed using a multiplex ELISA kit. **C:** Mouse macrophages (RAW 264.7) were treated with PAF antagonist CV6209 or media control and exposed to either 21% or 85% oxygen for 24 h. Cells were then harvested and processed for mRNA analysis.

Summary of Results **A:** Hyperoxia increased mRNA of the PAF receptor (PTAFR) and the rate-limiting enzyme of PAF synthesis phospholipase A2 (PLA2G2E), indicating increased PAF synthesis and tissue sensitivity by elevated receptor expression. CXCL1 (AKA KC/GRO), a neutrophil chemokine, was also increased. **B:** Hyperoxia-induced alveolar simplification was decreased in PTAFR KO compared to WT, while it was exaggerated in PAF-AH KO, as indicated by higher mean linear intercept (MLI) and lower number of septal branches/junctions in PAF-AH KO, and lower MLI and higher septation in PTAFR KO. Hyperoxia increased mRNA of PTGS2 (COX2 gene), CXCL1, and IL6 in PAF-AH KO while these changes were muted in PTAFR KO. Hyperoxia-induced increases in CXCL1 protein was markedly higher in BAL from PAF-AH KO, while there were no increases in PTAFR KO. **C:** CV6209 blocked the hyperoxia-induced increase in CXCL1 mRNA. **Conclusions** PAF contributes to the pathogenesis of BPD and regulates pro-inflammatory signaling in BPD through CXCL1. PAF is a potential target for therapy in BPD.

439 IMPAIRED ADIPONECTIN SECRETION ALONG WITH ADAPTATIONS AT TARGET TISSUES CONTRIBUTE TO INSULIN RESISTANCE OF PREMATURITY

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10.1136/jim-2016-000393.442

Purpose of Study Insulin resistance and the resulting hyperglycemia are highly prevalent in premature infants. Adipose tissue secretes adiponectin, sensitizing target tissues, primarily skeletal muscle and liver, to the actions of insulin. The impact of premature birth on adiponectin secretion and the effects at target tissues is unknown

Methods Used Eleven baboons were delivered prematurely by C-section at 125 d gestational age (GA) or term (185 d GA) and sacrificed immediately after birth (GA controls) or at 14 days. A hyperinsulinemic-euglycemic clamp was performed on day of life (DOL) 5 and 14 to evaluate tissue responses to insulin. Total and high molecular weight (HMW) adiponectin were measured by ELISA. Adipocyte mRNA expression of key adiponectin signaling proteins [insulin receptor (INSR), IRS-1, Akt, and PPAR γ] was measured by RT-PCR. Adiponectin receptors, (AdipoR1/AdipoR2), and downstream molecules APPL1 and APPL2 were measured in skeletal muscle and liver by western blot.

Summary of Results Total and HMW adiponectin were significantly reduced in preterm baboons at DOL14 (29% and 19% of term baboons respectively p<0.05). Insulin sensitivity (M value) was significantly lower in preterm baboons as compared to term (18.8 \pm 2.8 vs 13.7 \pm 1.3 respectively, p<0.05). Adipose tissue mRNA expression of PPAR γ and INSR was decreased in preterm baboons (54% and 71% of term baboons respectively, p<0.05) whereas Akt and IRS-1 were similar. AdipoR1 protein content was 3.9 fold higher in skeletal muscle of preterm baboons when compared to term (p<0.05). APPL1 protein content was 3.2 fold higher in preterm muscle and 1.9 fold higher in the preterm liver compared to term (p<0.05).

Conclusions Decreased serum adiponectin contributes to insulin resistance of prematurity. Impaired adiponectin secretion is due to down-regulation of intracellular adipocyte signaling molecules (PPAR γ and INSR). Up-regulation of adiponectin receptors and downstream molecules (APPL1) in preterm baboon muscle and liver are likely compensatory mechanisms providing evidence of adaptations by target tissues to mitigate the impact of decreased adiponectin secretion.

Allergy, Immunology, and Rheumatology I Concurrent Session 2:00 PM Sunday, February 12, 2017

440 ROLE OF NATURAL SELECTION OF D β SEQUENCE IN PREVENTING HYDROPHOBIC AMINO ACID EXPRESSION IN CDR β 3

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10.1136/jim-2016-000393.443

Purpose of Study Diversity of the T cell receptor is mainly developed through V(D)J rearrangement and N addition during TCR development. The product of V(D)J rearrangement is the CDR β 3, a region of high variability that recognizes antigen and includes all of the D gene. The D β sequence is highly conserved across various species, from

trout to mouse to humans. This suggests that there are some natural constraints on the TCR; these constraints are thought to limit deleterious T cells from reaching the periphery. We hypothesize that alterations from the preferred germline sequence to one that codes for previously under-represented amino acids will alter T cell repertoire, development and function.

Methods Used In order to test our hypothesis, mice were generated with an alteration in their D β gene segments. The alterations are a D β 2 KO and a replacement of the D β locus with a hydrophobic D_H (D β YTL). Both developing thymocytes and mature splenic T cells were sorted from these mice by flow cytometry. RNA from the thymocytes was extracted and the VDJ-beta genes were sequenced using primers to the VB13-1 and to the VBC1. In frame sequences were analyzed using IMGT junction analysis program. Ovalbumin immunization was used to interrogate the antigen specific response of the altered T cells.

Summary of Results We have data comparing the T cell repertoires of WT and altered D β mutants. When compared to WT mice, the mutant hydrophobic D β mice have an altered T cell repertoire in both CDR β 3 amino acid composition and CDR β 3 length and these differences can be attributed to the changes in the germline sequence. Changing the Db also changes the total T cell number in both developing and mature T cells, with an altered Db being selected against. The altered Db mice also have reduced antigen specific recognition after OVA immunization.

Conclusions The D β germline sequence affects the TCR repertoire. There is a preferred set of amino acids that is available to the TCR that is encoded in the germline sequence. This preference was developed over millions of years of evolution and deviations from this preferred sequence has significant effects on both the TCR repertoire and function.

441 EFFECTIVENESS OF ROMIPILOSTIM IN REFRACTORY IMMUNE THROMBOCYTOPENIA ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J Teerakanok, A Adiga, K Nugent. *Texas Tech University Health Sciences Lubbock, Texas, Lubbock, TX.*

10.1136/jim-2016-000393.444

Case Report Immune thrombocytopenia (ITP) is frequently associated with systemic lupus erythematosus (SLE), but less than 5% of patients have severe thrombocytopenia. Most patients respond to corticosteroids or second-line therapy (azathioprine, cyclosporine, rituximab, intravenous immunoglobulin (IVIG), but some patients may require thrombopoietin-receptor agonists.

Our patient was 19-years-old woman; she was diagnosed with SLE in March 2015 because of acute liver failure, anemia, thrombocytopenia (52,000/ μ L), positive ANA, anti-dsDNA, SS-A, SS-B, and hypocomplementemia. She was treated with intravenous methylprednisolone (IVMP) and was discharged with oral prednisolone. In June 2015, she presented again with petechiae on her face and legs and bleeding per gum and vagina; her initial platelet count was 5,000/ μ L. Bone marrow biopsy showed normocellular

marrow with megakaryocytic hyperplasia consistent with ITP. She was treated with IVMP, IVIG 1 g/kg, RhoGAM 1 dose, rituximab weekly, romiplostim 125 mcg 2 doses, and platelet transfusions. Despite this treatment her platelet count stayed below 50,000/ μ L. She was discharged on oral prednisolone with a platelet count of 44,000/ μ L. Azathioprine 50 mg daily was started in August 2015. However, she came back 2 weeks later with hematemesis and a platelet count of 6,000/ μ L. She was treated with IVMP 1 g for 4 days and then oral prednisolone, IVIG 1 g/kg (2 doses), azathioprine, and platelet transfusions. Her platelet count ranged between 10,000–50,000/ μ L. She was discharged after bleeding stopped on prednisolone 60 mg/day and azathioprine. Romiplostim 125 mcg was given in the clinic the next day with a platelet count of 9,000/ μ L. One week later her platelet count increased to 150,000, and she received another dose in the following week. Since then her platelets have stayed above 100,000/ μ L; prednisolone was tapered down and azathioprine was stopped.

Thrombopoietin receptor agonists, such as eltrombopag and romiplostim, have been successfully worked in the management of ITP, but there are limited data regarding their use in refractory ITP associated with SLE. Our case report suggests that romiplostim is a good treatment option for ITP associated with SLE that is refractory to conventional therapy.

442 CHRONIC NONBACTERIAL OSTEOMYELITIS OF THE MANDIBLE IN AN 8 YEAR OLD FEMALE

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10.1136/jim-2016-000393.445

Case Report Introduction: Chronic nonbacterial osteomyelitis (CNO) is an uncommon condition which can present a significant diagnostic challenge to providers. It is defined as an aseptic inflammatory bone disorder and has been classified as a pediatric rheumatologic disease. It typically manifests as swelling and localized bone pain, and often appears without the generalized symptoms that one would expect in infectious osteomyelitis. A history in patients of comorbid autoimmune disease or a family history of autoimmune diseases is commonly observed. We report a case of biopsy proven CNO of the mandible in an 8 year old female.

Case Presentation An 8 year old previously healthy female presented with a 10 day history of swelling localized to the left mandible. The patient had received a 3 day course of amoxicillin-clavulanate followed by extraction of a local primary tooth believed to be a cause of her swelling. Following tooth extraction, the patient was switched to clindamycin and swelling and tenderness persisted without improvement. Of note, the patient had no history of fever since onset of symptoms. In our emergency department a CT of her jaw demonstrated cortical destruction and periosteal reaction within the left mandible. Inflammatory markers were only mildly elevated. She was initially treated while inpatient for suspected infectious osteomyelitis with IV ampicillin-sulbactam, without significant improvement observed. A biopsy of the area of interest demonstrated fibro-osseous proliferation, consistent with CNO. In light

of this, the patient was placed on a course of oral steroids and meloxicam with gradual improvement thereafter. As part of her ongoing workup we plan to obtain a bone scan to evaluate for any multifocal disease.

Discussion The differential diagnosis of CNO is broad, and often this can contribute to diagnostic delay. In establishing a diagnosis of CNO, ruling out infectious osteomyelitis and malignancy are critical. Close followup is needed after diagnosis in order to monitor for potential progression to multifocal disease. As with other rheumatologic conditions, early diagnosis and aggressive treatment can contribute to improvements in disease course and outcomes, and thus increased awareness of this disease is needed.

443 AN UNUSUAL CAUSE FOR CRYOGLOBULINEMIA: ROCKY MOUNTAIN SPOTTED FEVER

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10.1136/jim-2016-000393.446

Case Report Cryoglobulinemia and associated vasculitis has been seen in several conditions, including infections, medications, malignancies, and connective tissue disorders. Early diagnosis is key to preventing long-term sequelae, but due to vague symptoms and the likelihood for more common diseases, it remains a difficult diagnosis to make.

A 62-year-old male initially presented for complaints of severe headache, fevers and new lower extremity rash. He spends much of his time outside, including hunting, but denies any known recent tick bites. Initial admission to local hospital lead to a diagnosis of Rocky Mountain spotted fever (RMSF) with initial titers being highly suggestive at 1:1024. A seven day course of doxycycline was initiated. Despite appropriate treatment, he did not improve, and developed oropharyngeal pain, edema, and persistent rash now involving his abdomen. He was re-admitted to his local hospital, where he was found to be hypotensive with acute kidney injury (AKI) and significant oropharyngeal ulceration. Workup was initiated to evaluate for an underlying explanation. His respiratory status rapidly declined, and he was subsequently intubated and transferred to a higher level of care. Methylprednisolone was initiated to help with his pulmonary status, and his rash was noted to have mild improvement. Hepatitis panel and human immunodeficiency virus (HIV) antibody were negative. Send-out labs done during initial hospital stay showed positive cryoglobulins. Rheumatoid factor was elevated and his C3 and C4 complements were low. It was thought that his cryoglobulinemia was secondary to his RMSF and was already on steroids for other reasons. His hospital course was quite extensive, including tenuous respiratory status, decreased renal function and hypervolemia requiring hemodialysis, and infection. However, he slowly improved and was discharged on prednisone. In his outpatient rheumatology follow up, he was transitioned to azathioprine, without improvement, and later changed to rituximab.

Mixed cryoglobulinemia is known to be associated with infections, most commonly hepatitis and HIV. This case demonstrates that uncommon infectious associations, such as Rocky Mountain spotted fever, exist, and cryoglobulinemia should remain on the differential despite negative testing for common viral infections.

444 TAKAYASU ARTERITIS PRESENTING AS SEVERE SECONDARY HYPERTENSION

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10.1136/jim-2016-000393.447

Case Report Takayasu arteritis is a rare but established cause of secondary hypertension which presents with indolent clinical manifestations often leading to a delay in care. A 42 year old woman presented to clinic for optimization of uncontrolled hypertension. The patient reported left arm claudication and blood pressure issues beginning in her teens. Since then, her hypertension progressively worsened despite being placed on four antihypertensives. Exam was significant for left arm weakness, a faintly palpable left radial pulse, and asymmetric blood pressures. A computed tomography (CT) angiogram was obtained due to suspicion of large vessel arteritis. This study demonstrated total occlusion of the left subclavian artery with reconstitution of the distal left brachial artery secondary to prominent collaterals from the thyrocervical trunk. Positron emission tomography CT demonstrated minimal active processes however multiple areas of atherosclerotic calcifications in the thoracic and abdominal aorta were seen indicating longstanding disease. A diagnosis of Takayasu arteritis was made and the patient was placed on prednisone and tocilizumab. Following six months of therapy the patient's blood pressures normalized. This case underscores the importance of pertinent exam findings with respect to alternative diagnosis in younger patients with chronic uncontrolled hypertension.



Abstract 444 Figure 1 Left arrow: Total occlusion of the left subclavian artery. Right arrow: Collateral vessel from the thyrocervical trunk.

445 HEMOPHAGOCYtic LYMPHOCYtic HISTIOCYTOSIS IN AN ADULT SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT: A RARE BUT POTENTIALLY FATAL COMPLICATION

D Fielder, W Crews, TM Crout, V. Majithia. *UMMC, Jackson MS.*

10.1136/jim-2016-000393.448

Introduction Hemophagocytic lymphocytic histiocytosis (HLH) is a rare and often lethal disorder of excessive immune activation characterized by fever, systemic inflammation, multi-organ damage, cytopenias in two or more cell lines, hyperferritinemia, hypertriglyceridemia, and coagulation disorders. It is more common in children but may occur in all ages. It may arise as a primary syndrome or secondary to autoimmune diseases, malignancy, or infections (reactive HLH). HLH is challenging to diagnose due to its rarity and nonspecific presentation.

Case Description A 21-year-old African American female with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) presented to the emergency department with a chief complaint of persistent fever up to 104° F. The initial working diagnosis was lupus flare versus sepsis, and broad spectrum antibiotics were begun. A complete blood count revealed leukopenia. Complements were normal and ferritin level was 447. Throughout the hospitalization the patient's clinical course worsened, with the development of multi-organ failure and pancytopenia. Blood cultures remained negative. She did not respond to plasma exchange, which was started for suspicion of catastrophic APS. HLH was suspected when repeat ferritin was >25,000 on day 7 of hospitalization. Diagnosis was confirmed by hemophagocytosis seen on bone marrow biopsy. The patient was started on Etoposide and Dexamethasone per the HLH94 treatment protocol. Unfortunately, she passed away on day 11 of hospitalization.

Discussion HLH is rarely seen in adult SLE patients with only a few (<10) cases described in literature. The diagnosis of HLH was elusive in this case due to rarity, nonspecific presentation, complicated medical history, and negative initial workup. Though HLH is exceedingly rare in adult SLE patients, it should be considered in SLE patients with fever, multi-organ involvement, and cytopenias. If suspected, serum tests—ferritin, NK cell activity, and sIL-2 receptor levels—along with a bone marrow biopsy should be collected and treatment rapidly initiated as the mortality is extremely high. This case highlights that HLH can occur in adult patients with SLE and may be extremely difficult to diagnose.

446 MALIGNANCY PREVALENCE AMONG PATIENTS WITH AUTOIMMUNE OVERLAP SYNDROMES

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10.1136/jim-2016-000393.449

Purpose of Study Autoimmune disorders, such as systemic lupus erythematosus (SLE), scleroderma (SSc), rheumatoid arthritis (RA), and Sjogrens syndrome (SjS), are associated with higher risk of certain malignancies. However, little is

known about the prevalence and types of malignancies among patients with autoimmune overlap syndromes (OS), defined as the co-occurrence of two or more autoimmune disorders in one patient. Our study tests the hypothesis that OS patients will have an increased risk of malignancy compared to non-OS patients due to the combined immune system dysfunction and the effect of different patterns of immunosuppressant use.

Methods Used This study was performed using data from a longitudinal registry of patients with SLE and scleroderma at MUSC. Data was reviewed including the patient demographics, medical history, historical and current medications, disease damage, and presence of malignancy. T-tests and regression analyses were used to compare these parameters between OS and non-OS patients with SLE and/or SSc.

Summary of Results Out of 755 patients in the study, OS patients (n=232) were 93.1% female compared to non-OS patients (n=523) who were 85.9% female (p<0.05). 54.7% of OS patients and 59.1% of non-OS patients were black (p=NS). The most common autoimmune diseases found in OS patients with SLE and/or SSc were: SjS, RA, and myositis. While followed in the registry, 6.0% of OS patients died compared to 5.0% non-OS patients (p=NS). OS patients had an older age of diagnosis with SLE compared to non-OS patients (p<0.05). 12.3% of OS patients had a malignancy compared to 7.5% of non-OS patients (p<0.05).

Conclusions OS patients had an increased prevalence of malignancy compared to non-OS patients. OS patients were more likely to be women and older at time of SLE diagnosis. Further studies should be pursued to validate these results and see if stricter cancer surveillance is beneficial in OS patients.

447 A COMMON VARIABLE MISCONCEPTION

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10.1136/jim-2016-000393.450

Case Report A 19yo WF diagnosed with Common Variable Immunodeficiency (CVID), asthma, and allergic rhinitis was sent for referral for second opinion for treatment of her CVID. She was currently receiving monthly IVIG infusion (Gammunex) through a left subclavian che-moport. At initial visit she reported fevers, pleuritic chest pain, shortness of breath, and dyspnea on exertion that did not always improve with albuterol. Immunoglobulins (IgG, IgA, IgM) were checked at that visit and all were noted to be within normal range. Workup was performed to evaluate for the constellation of symptoms not thought to be purely due to asthma. TTE revealed mild tricuspid regurgitation and an echogenic structure associated with her mitral valve. TEE was then performed which also showed the structure near the tip of her che-moport catheter tip and thought to likely be a possible thrombus or vegetation. She was treated for possible endocarditis with antibiotics but serial blood culture remained negative. She was taken to OR for removal of her che-moport. The culture from the catheter tip revealed no growth making thrombus more likely. Two days following removal of port, she developed

headaches, blurry vision in right eye and was noted to have anisocoria with right pupil (6 mm) larger than left (4 mm). Repeat TEE revealed no evidence of remnant of vegetation or thrombus. Evaluation by neuro-ophthalmology included CT Head, MRI brain and spine, and lumbar puncture. Differential included pseudotumor, multiple sclerosis, neuromyelitis optica, optic neuritis, and embolic phenomenon from catheter removal.

Discussion This clinical case reveals several important learning concepts. First, it is important to differentiate CVID from Hypogammaglobulinemia as IVIG is often required in the former while rarely in the latter. Second, this case demonstrates the importance of avoiding indwelling lines and catheters in patients with CVID or hypogammaglobulinemia if and when possible. The third and final concept is to illustrate the complex workup of these patients and how other autoimmune processes can often be associated, up to one quarter of patients.²

448 **PERIPHERAL SELECTION FOR TYROSINE AND AGAINST THREONINE IN ABSENCE OF CENTRAL PREBCR CHECKPOINT SELECTION**

M Khass, T Blackburn, P Burrows, HW Schroeder. *UAB, Birmingham, AL.*

10.1136/jim-2016-000393.451

Purpose of Study We sought to identify selection pressures on the amino acid content of the center of the immunoglobulin antigen binding site in the IgM repertoire created in the absence of bone marrow selection by the surrogate light chain (SLC), which is composed of $\lambda 5$ and VpreB. Lack of any of the preBCR components causes incomplete block in B cell development marked by passage of cells with untested receptor activity that can occupy peripheral compartments by time.

Methods Used We cloned, sequenced and analyzed μ heavy chain transcripts from immature, transitional, follicular, mature, and marginal zone B cells from mice genetically deficient for $\lambda 5$ and compared the amino acid composition of the third Ig heavy chain complementary determining region (CDR-H3) to wild type. We focused on CDR-H3 position 101 which is critical for antigen binding. We also evaluated B cell apoptosis by flow cytometry and serum dsDNA binding titers by ELISA.

Summary of Results In WT mice, SLC selection promotes the presence of tyrosine at position 101. In the absence of $\lambda 5$, immature B cells express threonine, valine and leucine more frequently. With development, however, there is a progressive increase in the presence of tyrosine, with a complementary loss of threonine, valine and leucine. The mechanism of selection appears to be apoptosis, which is greatly increased in the developing B cells in the $\lambda 5$ deficient mice. In spite of the partial correction of the repertoire, the presence of charged CDR-H3s remains high, and the mice express dsDNA binding IgM.

Conclusions The SLC serves as an invariant antigen to select the amino acid composition of μ heavy chain. In the absence of $\lambda 5$, and thus without SLC selection, the

unselected repertoire demonstrates an altered pattern of amino acid usage at specific positions at the center of the antigen binding site. Peripheral selection can ameliorate, but not fully correct the repertoire. SLC selection acts to prevent autoreactivity

**Cardiovascular I
Concurrent Session
2:00 PM
Sunday, February 12, 2017**

449 **A RATIO OF CLINICAL PARAMETERS PREDICTS LONG TERM SURVIVAL IN PATIENTS FOLLOWING CORONARY ANGIOPLASTY**

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10.1136/jim-2016-000393.452

Purpose of Study Older patients and those with reduced renal function are frequently omitted from randomized clinical trials of treatment for coronary artery disease because of increased mortality. A clinical finding that predicts long term mortality may be helpful. The purpose of this study was to correlate the ratio of creatinine clearance to age (crcl/age) in patients followed for longer than 10 years after treatment of disease of the left anterior descending (LAD) coronary artery.

Methods Used 130 patients with a mean age of 62.91 ± 10.09 years (range 41–85) with coronary angiography in 2003–2004 with LAD disease received coronary angiography and revascularization as indicated by angiographic parameters or measurement of fractional flow reserve. The patients were then treated with guideline directed medical therapy, including devices (pacemaker, implantable defibrillator) and treatment for renal disease by standard practice with dialysis if required, and followed with a computerized medical record system. The predictive value of the ratio of creatinine clearance/age (crcl/age) in estimating all-cause mortality was determined by Cox proportional hazards regression and tabulation of all cause mortality.

Summary of Results (1) Cox proportional hazards regression showed that the lowest hazard ratio for long term all cause mortality was estimated by the ratio of creatinine clearance to age. The hazard ratio was 0.29 ($p < 0.001$) for an average followup of 3146.03 days (range 3–5001). (2) Patients with a crcl/age ratio of ≥ 1.16 had a long term mortality of 33% (20 of 60), and patients with a crcl/age ratio less than 1.16 had a significantly increased mortality of 60% (42 of 70), $p < 0.01$.

Conclusions (1) This study shows that a ratio of creatinine clearance /age is able to assist in the estimation of long outcome in a group of patients with LAD disease. (2) This predictor may be helpful in the clinical evaluation of groups of patients that may be excluded from randomized clinical trials. (3) Additional studies will help to determine the application of these measurements.

450 HEART FAILURE WITH OR WITHOUT PRESERVED EJECTION FRACTION AND ATRIAL FIBRILLATION

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10.1136/jim-2016-000393.453

Purpose of Study Atrial fibrillation (AF) is a common arrhythmia frequently linked to the presence of ventricular dysfunction and presence of heart failure (HF). Herein, we sought to determine the presence of AF in patients having HF with reduced ejection fraction (HFrEF) vs. those with preserved (HFpEF).

Methods Used We performed a retrospective chart review of 120 patients who presented to the emergency room at an urban medical center with a diagnosis of AF on standard 12-lead ECG over a two-year period, 2014–2016. Two-dimensional echocardiography was performed on all patients as part of their workup. HFrEF was defined as an EF <50%, while HFpEF with diastolic heart failure was defined as an abnormal tissue Doppler measurement with an EF ≥50%.

Summary of Results Of the 120 patients with atrial fibrillation, 84 patients (70%) had a clinical diagnosis of HF of which 7 (8.3%) had HFrEF; 30 (35.7%) had HFpEF; and 16 (19.1%) had combined HFrEF and HFpEF. Atrial fibrillation was significantly higher ($p < 0.05$) in patients with HFpEF.

Conclusions In this patient cohort followed at an urban medical center, the incidence of AF by standard ECG was significantly higher among patients with HFpEF than those with HFrEF. This would suggest that the presence of diastolic dysfunction offers greater resistance to left atrial emptying raising the propensity to AF and perhaps via greater atrial distention.

451 INCIDENCE OF HIGH-GRADE ATRIO-VENTRICULAR BLOCK WITH ADENOSINE AND REGADENOSON SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY STUDIES: A META-ANALYSIS

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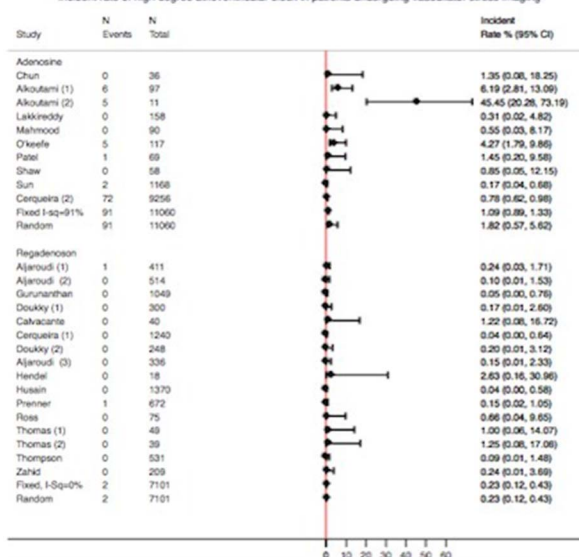
10.1136/jim-2016-000393.454

Purpose of Study Adenosine (ADE) and regadenoson (REG) are widely used in single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI). They have both been linked with cases of high grade atrio-ventricular block (AVB). We studied the incidence of high grade AVB (defined as type II Mobitz and third degree AVB) due to ADE and REG at doses given in MPI.

Methods Used A comprehensive search of SCOPUS was carried out from inception to March 2016. Only studies of at least 5 patients and reporting high grade AVB were included in the final analysis.

Summary of Results 10 studies used ADE (N=11060 patients) reporting a total of 91 cases of high grade AVB.

Incident rate of high degree atrioventricular block in patients undergoing vasodilator stress imaging



Abstract 451 Figure 1

The pooled random effect rate of high grade AVB was 1.8% (95% CI 0.57–5.62). 16 studies used REG (N=7101) reporting 2 cases of high grade AVB. I^2 statistic for heterogeneity for the REG group was 0% indicating a homogenous data set. The random effect rate of high-grade AVB in the REG group was 0.2%. When comparing the two groups using test for heterogeneity, the P value was 0.002 indicating a statistically significant difference.

Conclusions The overall incidence of high grade AVB is lower with REG than with ADE. High grade AVB is possible with REG but uncommon. REG-related high grade AVB may be higher in real life since it may be given to patients at higher risk.

452 LOW ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS PREDICTS A DECLINE IN QUALITY OF LIFE AMONG OLDER ADULTS

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10.1136/jim-2016-000393.455

Purpose of Study Low adherence to antihypertensive medication is associated with cardiovascular events and increased healthcare costs. Less is known about the effect of low adherence on quality of life (QOL) over time. We tested whether low adherence to antihypertensive medications predicts a decline in QOL using data from the Cohort Study of Medication Adherence among Older Adults (CoSMO).

Methods Used A telephone survey was administered to hypertensive older adults three times at yearly intervals. Low adherence was defined as a score >0 on the Krousel-Wood-4 scale (K-Wood-4). QOL was measured using a single item from the RAND Medical Outcomes Study 36-item tool: In general, would you say your health

is Excellent, Very good, Good, Fair, or Poor? Low QOL was defined as a 'Fair' or 'Poor' rating. The analysis was restricted to those without low QOL at first follow-up (n=1282). Multivariable logistic regression was used to obtain odds ratios (OR) and 95% confidence intervals (CI) for a decline in QOL from first to second follow-up, after adjusting for sociodemographic and clinical factors.

Summary of Results The sample was 58.8% female and 25.7% black with a mean age of 75.9. Among those without low QOL at first follow-up, the incidence of low QOL at second follow-up was 11.9%. After adjusting for sociodemographic and clinical factors, low adherence at first follow-up was associated with a decline in QOL over one year (OR=1.73, 95% CI 1.20, 2.51). Depressive symptoms (OR=2.22, 95% CI 1.31, 3.77), comorbidities (OR=1.69, 95% CI 1.16, 2.46), and 6 or more visits to a healthcare provider in the past year (OR=1.60, 95% CI 1.09, 2.36) were also associated with a decline in QOL.

Conclusions Low adherence to antihypertensive medication predicts a decline in QOL over one year among older adults with hypertension. Efforts to address low adherence may improve QOL for older adults.

453 INCIDENCE OF ECHOCARDIOGRAPHICALLY SEEN VEGETATIONS IN PATIENTS REFERRED FOR ECHOCARDIOGRAPHY TO RULE OUT INFECTIVE ENDOCARDITIS

NS Doctor, E Joye, P Leis, N. Coplan. *Lenoxhill Hospital, New York, NY.*

10.1136/jim-2016-000393.456

Purpose of Study Quality control study

Methods Used This is a single center retrospective analysis of 210 consecutive in-patient studies of 168 patients referred for echocardiography with indications of bacteremia, fever, or ruled out infective endocarditis which were reviewed retrospectively from May, 2014 through May, 2015.

Summary of Results In 168 patients a total of 210 studies were analyzed retrospectively: 134 (63.8%) patients underwent TTE, 76 (36.2%) patients underwent TEE. The mean age was 65 years, average creatinine 2.45, hemoglobin 11.2 and average LVEF 54.6%. 18 patients (10.7%) had PPM, 15 patients (8.9%) had previous history of IE, 12 patients (7.1%) had history of IVDU, and 12 (7.1%) patients had history of CVA. 139/168 (82.7%) patients received antibiotics at the time of evaluation.

95/168 (56.6%) patients had positive blood cultures: 28/168 (16.6%) patients with staph aureus, 20 (11.9%) patients with streptococcus species, 9 (5.3%) patients with MRSA, 5 (2.9%) patients with enterococcus (not including VRE), 1 patient with VRE, and 5 (2.9%) patients with candida. 23/168 patients (13.7%) had ESRD on HD.

Echocardiogram showed signs of vegetations on 36/210 (17.1%) studies. Vegetations were found by TEE in 20 patients and by TTE in 16 patients. 7 patients had both TTE and TEE positive for vegetations.

24 /168 patients had history of prosthetic valve (14.2%): 6/168 (3.6%) had mechanical valve and 16/168 (9.5%) had bioprosthetic valve. Out of the 24 patients vegetations found on valve: TV (2, 1.2%), MV (15, 8.9%), AV (14,

8.3%). Mod to severe associated valve regurgitation found on 15 patients (8.9%). In overall study, 21 (12.5%) patients underwent surgery.

Conclusions This study showed that 36/210 (17.1%) studies referred for echocardiography to rule out infective endocarditis showed signs of vegetation.

454 PRESENCE OF ATRIAL FIBRILLATION IN COMPARISON TO SERUM POTASSIUM LEVELS

EA Christian, DM Flatt, YI Harper, BM Ramos, MR Heckle, BZ Heard, JB Jasper, LA John, KT Weber. *University of Tennessee Health Science Center, Memphis, TN.*

10.1136/jim-2016-000393.457

Purpose of Study It has been well documented that mutations associated with atrial fibrillation have been linked to genes that encode sodium and potassium channel sub-units. It is postulated that fibrillation of the atrial tissue would be facilitated by hypokalemia. In this study, we hypothesize a correlation between patients with atrial fibrillation and hypokalemia when compared to patients in normal sinus rhythm.

Methods Used A retrospective review of 2,980 medical charts at a metropolitan hospital between January 2014 and June 2016. Serum potassium levels were obtained in all patients upon admission and in whom 214 had documented atrial fibrillation on standard 12-lead ECG.

Summary of Results Of the patients with documented atrial fibrillation, 53.3% were hypokalemic (serum potassium <4.0 mEq/L) compared to 49.6% with normal sinus rhythm (p=0.3). The average potassium level of patients in normal sinus rhythm was 4.03 mEq/L compared to 3.91 mEq/L for patients with atrial fibrillation (p=0.01) to suggest patients with atrial fibrillation were more likely to be hypokalemic.

Conclusions Thus it can be inferred that there is an association between atrial fibrillation and hypokalemia. These findings help to further confirm the importance of potassium repletion when attempting to control atrial fibrillation and to maintain normal sinus rhythm after cardioversion for this atrial arrhythmia.

455 THE ASSOCIATION BETWEEN CHILDHOOD OBESITY AND ADULTHOOD CAROTID INTIMA-MEDIA THICKNESS IS MODIFIED BY SERUM ADIPONECTIN LEVELS

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10.1136/jim-2016-000393.458

Purpose of Study Childhood obesity, measured by body mass index (BMI), is predictive of adult subclinical atherosclerosis as measured by carotid intima-media thickness (CIMT). However, accumulating evidence indicates that the consequences of childhood obesity are heterogeneous. We hypothesized that the association between childhood

BMI and adult CIMT is modified by levels of adiponectin, an adipocytokine that connects body fatness with cardiovascular risk.

Methods Used The sample included 1,056 adults (71% white and 29% black, 57% female) aged 23.8–43.5 years who were previously examined as children in the Bogalusa Heart Study cohort, with an average follow-up period of 26.5 years. Childhood BMI, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and systolic blood pressure at the first childhood examination were standardized to age-, race-, and sex-specific z-scores. General linear models were used for data analyses.

Summary of Results Significant childhood risk factors for adult CIMT included BMI ($P=0.047$), LDL cholesterol ($P<0.001$), and systolic blood pressure ($P=0.030$) after adjustment for age, race, sex, cigarette smoking, and adiponectin levels (which were inversely associated with CIMT, $P=0.002$). Further, adult adiponectin levels significantly modified the association between childhood BMI and adult CIMT (P for interaction= 0.042) such that a significant association ($P=0.003$) between childhood BMI and adult CIMT was only observed in those with low adiponectin levels (below the median).

Conclusions These results suggest that serum adiponectin levels modify the association between childhood obesity and adult atherosclerosis, which has implications for risk stratification and targeted intervention for obese children with low levels of adiponectin.

456 HEART RATE RESPONSE TO REGADENOSON IN PATIENTS WITH ATRIAL FIBRILLATION

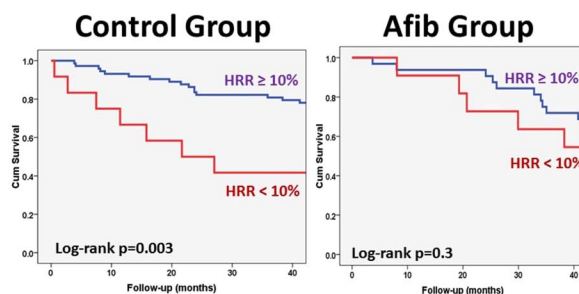
A Uzendu, A Farag, H Doppalapudi, AE Iskandrian, FG Hage. *University of Alabama Birmingham, Birmingham, AL.*

10.1136/jim-2016-000393.459

Purpose of Study Myocardial perfusion imaging (MPI) using regadenoson as a stress agent provides powerful prognostic data. We have previously demonstrated that for patients in sinus rhythm a blunted heart rate response (HRR) to regadenoson is an independent predictor of poor outcome, adds incremental value to MPI, and improves risk stratification. Whether the same holds true for patients in atrial fibrillation has not been studied.

Methods Used Of 1,400 patients (700 consecutive normal and 700 consecutive abnormal regadenoson MPIs) we identified 43 that were in atrial fibrillation at time of MPI. We matched each patient to 2 controls in sinus rhythm based on age, gender, diabetes and end-stage renal disease status, and perfusion defect size on MPI. The HRR was calculated as the percent change in ventricular rate from baseline. The primary outcome was all-cause death.

Summary of Results In the cohort with atrial fibrillation, heart rate increased from 82 ± 15 to 100 ± 18 bpm while in the control cohort it increased from 71 ± 15 to 89 ± 17 bpm. The HRR in the 2 cohorts (23 ± 20 vs. $27\pm 17\%$, $p=0.3$) was not statistically different. During a mean follow-up of 43 ± 17 months 35% died (44% atrial fibrillation, 30% control, $p=0.1$). In a Cox proportional model for mortality, a blunted HRR ($<10\%$) was



Abstract 456 Figure 1

associated with increased risk of death in the control group (hazard ratio 3.4 95%CI 1.4–8.2, $p=0.005$) but not in the atrial fibrillation group (1.7, 95%CI 0.7–4.7, $p=0.3$, figure).

Conclusions The ventricular rate increases significantly after regadenoson administration in patients with atrial fibrillation. However, a blunted HRR to regadenoson provides prognostic information only in patients with sinus rhythm.

457 THE INTRINSIC DELAY IN REPOLARIZATION AND QTc PROLONGATION IN FEMALES WITH ATRIAL ARRHYTHMIAS

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10.1136/jim-2016-000393.460

Purpose of Study The QTc interval, commonly measured on the standard 12-lead electrocardiogram, is an important prognostic and risk indicator of a proarrhythmic state. The mean QTc interval in women is greater than men and is also prolonged in the setting of atrial arrhythmias. Herein we hypothesized that the intrinsic delay in myocyte repolarization, as demonstrated by the QTc interval in females compared to males, will account for a less dramatic QTc prolongation in the presence of atrial arrhythmias.

Methods Used A retrospective study of 120 patients (63.9 yrs; 70.8% male) with AF demonstrated on EKG at an urban medical center from October 2015 to December 2016 was performed. These data were combined with a previous database from the same medical center that included 3202 patients from January 1, 2014 to June 30, 2015. The patient's sex, duration of the QTc (ms) interval, and the presence or absence of atrial arrhythmias were noted.

Summary of Results There was a statistically significant difference ($p<0.01$) in the QTc interval between males (464 ± 0.97 ms) and females (469 ± 0.96 ms) and in patients with AF (476 ± 5.4 ms) compared to those in normal sinus rhythm (NSR, 464 ± 0.97 ms). In men, there is a significant ($p<0.01$) difference in the QTc interval in patients with NSR (464 ± 0.97 ms) compared to patients with AF (476 ± 5.4 ms). However, no difference ($p<0.41$) was observed in the QTc interval in women with AF (473 ± 7.7 ms) compared to those in NSR (469 ± 0.96 ms).

Conclusions We confirm prolonged QTc interval in women, as compared to men, and in patients with AF, irrespective of sex, compared to NSR. In addition, the duration of QTc interval prolongation in the presence of atrial arrhythmias in women is less marked than in men.

458 PREVELANCE OF NON-STEROIDAL ANTI-INFLAMATORY DRUGS USE IN ORTHOPEDIC PATIENTS AND IMPACT OF BLACK BOX WARNING ON PRESCRIBER BEHAVIOR

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10.1136/jim-2016-000393.461

Purpose of Study The FDA issued a black box warning in 2005 stating that NSAIDs in patients with coronary artery disease, heart failure, and those with risk factors for cardiovascular disease (CVD), can increase risk of heart attack and stroke. Despite this, the use of NSAIDs in this population has remained widespread. To curtail the use of NSAIDs in these patients, the FDA re issued and strengthened its black box warnings in July 2015 regarding NSAID use in patients with cardiovascular disease. This study evaluated whether physicians are observing this black box warning, and whether there was any difference in prescribing rates of NSAIDs in patient with CVD vs. those without CVD.

Methods Used We conducted a chart review and included all patients admitted to the orthopedics service in the two months prior to the reissuing of the FDA warning (May-June 2015) and the two months after the warning was reissued (August-September 2015). Charts were reviewed for documented comorbidities including cardiovascular disease and history of stroke. Patients prescribed NSAIDs were analyzed according to whether they had CVD or not to reveal if there were any differences in prescribing rates of NSAIDs in patients with and without CVD.

Data was analyzed using a chi square analysis.

Summary of Results See table below for summary of results.

Conclusions There was no significant difference between NSAID prescription rates in those with CVD and those

without. There was also not a significant change in prescription practices after the FDA black box warning was reissued (P value 0.42). This study suggests that there is little consideration of the black box warning for the use of NSAIDs in patients with CVD. Further education regarding the appropriateness of NSAID prescriptions is warranted.

459 MYOCARDIAL PERFUSION IMAGING IN KIDNEY TRANSPLANT CANDIDATES AND MORTALITY AFTER TRANSPLANTATION

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10.1136/jim-2016-000393.462

Purpose of Study Cardiovascular disease is the main cause of death in patients with end-stage renal disease who undergo renal transplantation. The American Heart Association and American College of Cardiology propose that noninvasive stress testing may be considered in kidney transplant candidates to screen for cardiac disease as part of their pre-transplant evaluation. However, they acknowledge the lack of data for such an approach (Class IIb recommendation, Level of Evidence C).

Methods Used We retrospectively studied 1189 transplant recipients (50±13 yrs, 44% women, 34% diabetes, 95% hypertension, 14% current tobacco use, 40% living donors) who underwent renal transplantation at UAB from 2008 to 2012. Stress test using myocardial perfusion imaging (MPI) was performed in transplant candidates considered at elevated cardiovascular disease risk. The primary outcome was all-cause mortality.

Summary of Results MPI was performed in 819 transplant candidates (69%) and was abnormal in 182 of these (22%, abnormal myocardial perfusion in 11%, abnormal ejection fraction 14%). Of those with abnormal MPI 31 (17% or 3% of the entire cohort) underwent coronary revascularization (PCI in 21 and CABG in 13). During a follow-up of 56±24 months 138 (12%) died. Compared to patients who did not undergo screening MPI (1.7%), the annualized mortality rate was not statistically different in those with normal MPI (2.6%), and in those with abnormal MPI who underwent coronary revascularization (1.9%, p=0.2). In contrast, transplant candidates with abnormal MPI who did not undergo revascularization had a higher annualized mortality rate (4.0% vs. 1.7%, p=0.003).

Conclusions More than 1 in 5 candidates who undergo screening MPI prior to renal transplantation have cardiac abnormalities. Transplant candidates with abnormal MPI who are revascularized prior to transplantation have a similar rate of death after transplantation to those who have normal MPI and those who do not undergo screening since they are considered at low risk. Therefore, these candidates should not be denied transplantation. Prospective randomized studies are needed to establish whether coronary revascularization provides benefits in asymptomatic patients prior to renal transplantation.

Abstract 458 Table 1

	CVD	No CVD	P value
TOTAL			
# of patients	97	876	
NSAIDS prescription rate	60%	56%	0.62
PRIOR TO WARNING			
# of patients	45	442	
NSAID prescription rate	64%	59%	0.63
AFTER WARNING			
# of Patients	52	434	
NSAID prescription rate	58%	53%	0.78

460 A RARE DISORDER OF FAMILIAL TACHYARRHYTHMIAS

A Patel, BS Patel. *Bay Area Heart Center, Webster, TX.*

10.1136/jim-2016-000393.463

Purpose of Study To report a rare report of familial tachyarrhythmias.

Methods Used Retrospective analysis of records of four family members at Bay Area Heart Center, Texas.

Summary of Results A family of four - a father, a mother and two daughters - has been followed in south Texas for over 25 years for symptoms of palpitations with no accompanying dizziness or syncope with negative treadmill tests, normal echocardiograms and no electrocardiographic features of

Wolf Parkinson White syndrome. Father and two daughters has narrow complex tachyarrhythmia while mother has slow wide complex sustained tachyarrhythmia. All four are well controlled on low doses of metoprolol.

Conclusions A review of literature revealed that such familial form of tachyarrhythmia is extremely rare.

Clinical Epidemiology and Preventive Medicine

Concurrent Session

2:00 PM

Sunday, February 12, 2017

461 KNOWLEDGE, ATTITUDE, SELF-EFFICACY AND CRC SCREENING IN RURAL COMMUNITY CLINICS

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10.1136/jim-2016-000393.464

Purpose of Study To assess patient knowledge, beliefs, and self-efficacy about CRC screening and compare the effectiveness of two health literacy informed telephone follow-up strategies to improve initial and annual repeat screening with Fecal Immunochemical Test (FIT) in rural community clinics.

Methods Used A two-arm, randomized controlled trial is being implemented in four community clinics. Clinics reported CRC baseline screening rates of 1% to 3%. Eligible patients, age 50–75, are recruited at the clinic prior to a scheduled appointment. A research assistant (RA) conducts a baseline structured interview measuring CRC screening knowledge, beliefs, and self-efficacy. The RA then recommends screening and gives brief literacy and culturally appropriate education using a pamphlet (4th grade level), the FIT kit with pre-addressed envelope, simplified instructions (3rd grade level) and a demonstration of how to use it, At four weeks patients who have not returned their kit receive either 1) a personal follow-up call (PC) from a central prevention coordinator using motivational interviewing skills and reminding them to complete and mail FIT kits; or 2) an automated follow-up call (AC) using plain language and motivational messages encourages patients to complete and mail the FIT. Outcomes include FIT completion after intervention, and again at 12 and 24

months. 600 patients will be enrolled.

Summary of Results To date 591 patients not up-to-date with screening have been enrolled; 64% African American, 56% women; 40% inadequate literacy. Although 90% reported having heard of CRC, only 64% knew a test to check for CRC. 70% reported a provider had recommended CRC screening in the past and 91% reported they would want to know if they have CRC. Self-efficacy was high with over 90% indicating they would return the kit to the lab. 71% of patients in the first year of each arm have completed a FIT kit; 10% had a positive result. To date in year 2, 94 patients have been mailed their 2nd annual FIT kit. Completion rates are 50% in the PC arm vs. 34% in the AC arm.

Conclusions Implementing literacy and culturally appropriate CRC education and screening strategies using the FIT and phone reminders has the potential to increase CRC screening rural community clinics and address public health disparities.

462 SEX-RACE DIFFERENCES IN CORRELATES OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE AMONG HYPERTENSIVE OLDER ADULTS

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10.1136/jim-2016-000393.465

Purpose of Study Complementary and alternative medicine (CAM) use has been associated with low medication adherence among black but not white patients. Sex-race specific determinants of CAM use may provide insight into racial differences regarding CAM use and low adherence. We examined correlates of CAM use among older adults with hypertension (HTN) by sex-race groups.

Methods Used Cross-sectional analysis using data from 2180 older adults (58.5% female, 30.7% black; mean age of 75 years) with HTN in the Cohort Study of Medication Adherence in Older Adults (CoSMO). CAM use was defined as the use of health foods, herbal supplements, or relaxation techniques in the year prior to the baseline interview using a validated survey. Separate multivariable regression analyses examined the association between CAM use and potential determinants of CAM use (i.e., patient demographics, behavioral, clinical and self-management factors), overall and stratified by sex-race.

Summary of Results CAM use was reported by 25.1% of white women (WW), 30.3% of black women (BW), 24.2% of white men (WM), and 30.8% of black men (BM). After adjusting for covariates, race was not associated with CAM use. In sex-race specific multivariable models, factors associated with CAM use in WW include younger age (odds ratio (OR) 1.48; p-value<0.05), ≥2 lifestyle modifications (LM) (OR 2.62; p-value<0.001), high HTN knowledge (OR 1.57; p-value<0.05), and taking ≥3 classes of anti-HTN medications (OR 1.50; p-value<0.05). Reducing medications due to cost (OR 4.39; p-value<0.001), ≥2 LM (OR 3.42; p-value<0.05) and side effects (OR 2.61; p-

value<0.05) were associated with CAM use among BW. Among WM, high coping (OR 1.50; p-value<0.05), ≥ 2 LM (OR 2.10, p<0.01), and high stress (OR 1.80; p-value<0.01) were factors associated with CAM use. In BM, not being married (OR 2.85; p-value<0.05) and having at least a high school education (OR 3.24; p-value<0.01) were factors identified.

Conclusions Factors associated with CAM use among older hypertensive adults differ by sex-race.

463 SYSTEMATIC REVIEW OF CLINICAL PRACTICE GUIDELINES FOR USE OF ASPIRIN IN PRIMARY CARDIOVASCULAR DISEASE PREVENTION

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10.1136/jim-2016-000393.466

Purpose of Study The aim of this review is to conduct a systematic assessment of guidelines from national and international sources that contain recommendations for aspirin use in the prevention of primary cardiovascular disease (CVD) to better inform clinical practices.

Methods Used We searched MEDLINE, National Guideline Clearinghouse, and several international specialty society websites. Terms included *aspirin AND cardiovascular disease AND primary prevention*, alone and in conjunction with *guideline*. We also searched the previous terms combined with *diabetes*. The Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument will be used to review each of the selected guidelines. The AGREE II tool is comprised of 23 items organized into 6 domains: Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, and Editorial Independence. Each of the items will be rated from 1 (strongly disagree) to 7 (strongly agree) based on the degree to which the guideline addressed the criteria.

Summary of Results We identified n=28 guidelines that provided recommendations for aspirin use in the primary prevention of CVD in adults with and without diabetes. From US sources 16 guidelines were identified and international sources provided 12 guidelines. The majority of guidelines recommended the use of aspirin in primary prevention of CVD.

Conclusions Use of the AGREE II framework for evaluation of guidelines will assist clinical practitioners in assessing the quality of available guidelines for aspirin in primary prevention of CVD.

464 EVALUATION AND PREVALENCE OF HYPOTHYROIDISM AND ANEMIA IN HEALTH PROFESSIONAL STUDENTS WITH SYMPTOMS OF FATIGUE

MS Evangelista, L Love, C Parker, HD Smith. McGovern Medical School at UT Health, Houston, TX.

10.1136/jim-2016-000393.467

Purpose of Study Health professional students are subjected to long work and school hours, a rigorous curriculum and personal expectation of good performance. In our student health clinic, fatigue is a common complaint. In many of these clinic encounters, students seek evaluation for an underlying medical condition such as anemia and hypothyroidism. The purpose of this study is to determine if a laboratory examination evaluating for a thyroid and/or anemia disorder is warranted in health professional students with symptoms of fatigue.

Methods Used A retrospective chart review was performed looking at the incidence of thyroid or anemia disorder in this population coming in with a complaint of fatigue. We reviewed charts from March 2010 to December 2013. We used inclusion and exclusion criteria to determine the sample population. Anemia was defined by the World Health Organization (WHO) criteria; hemoglobin <12 grams/deciliter (g/dl) for non-pregnant women and hemoglobin <13 g/dl for men. Classification of anemia severity was also based on the WHO criteria. The reference range used for interpretation of TSH was based on the LabCorp established reference interval of 0.450–4.50 microinternational units/mililiter (μ IU/mL) (conventional units).

Summary of Results A total of 106 patients met our inclusion criteria for an anemia evaluation and 111 for a thyroid disorder evaluation. Abnormal hemoglobin values consistent with anemia were found in 12% of patients, while 4% had abnormal thyroid tests. Interestingly, all of the subjects with abnormal lab values (both anemia and thyroid tests) were females.

Conclusions This study highlights that the prevalence of hypothyroidism and anemia in health professional students is low and similar to what is seen in the general population. It also highlights the importance of looking at other reasons for fatigue including self-awareness of psychosocial stressors, evaluating sleep quality, coping skills, personal and financial stressors.

465 GENDER AND AGE-RELATED DIFFERENCES IN DOG BITE INJURIES, UNITED STATES, 2001–2014

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10.1136/jim-2016-000393.468

Purpose of Study Dog bite injuries are common in the US, and previous data have suggested differences in frequency based on age and gender. This study evaluated non-fatal dog bite injuries in US children to test the hypothesis that gender differences in dog bite injury are more pronounced in older children.

Methods Used We queried CDC's online injury database, WISQARS™ (Web-based Injury Statistics Query and Reporting System), evaluating non-fatal dog bite injuries from 2001–2014, separated by age (0–4, 5–9, 10–14, 15–19) and gender (male/female). Injuries are reported as national estimates based on data from U.S. Consumer Product Safety Commission's (CPSC) National Electronic Injury Surveillance System (NEISS). The primary outcome

was estimate of non-fatal dog bite injuries per 100,000 population. We utilized 95% confidence intervals (CI) to determine whether the rate differences met statistical significance.

Summary of Results From 2001–2014, non-fatal dog bite injuries declined from an estimated 182,138 to 135,854 from 2001–2014, but this difference did not reach statistical significance (overlapping CIs for the estimates). When comparing gender differences across all years of data pooled, males were significantly more likely to experience a dog bite injury (1,180,475; 95% CI 1,023,346–1,337,603) than were females (877,833; 95% CI 764,056–991,609), corresponding to a Relative Risk (RR) of 1.26 vs females. The differences by gender were predominantly driven by males in the 5–9 and 10–14 age groups, both of which had significantly higher estimated dog bite injuries than did females in the same age groups. For example, among 10–14 year olds, males experienced an estimated 316,453 dog bite injuries (95% CI 272,939–359,968) compared to 194,896 (95% CI 168,223–221,569) among females in that age range, RR 1.54.

Conclusions Non-fatal dog bite injuries in the US declined overall from 2001–2014, but the differences have not reached statistical significance. Males are significantly more likely to experience dog bites compared to females, and the difference in dog bite injury between the genders are driven by differences among children ages 5–14 years old. Despite the 27% decline in dog bite injury since 2001, ongoing efforts are needed to further reduce this injury type.

466 A RARE CASE OF FAMILIAL AUTOSOMAL DOMINANT MALIGNANT HYPERTHERMIA

BS Patel, AB Patel. *Bay Area Heart Center, Webster, TX.*

10.1136/jim-2016-000393.469

Purpose of Study Purpose of the study is to report a rare case of familial autosomal dominant malignant hyperthermia.

Methods Used Retrospective analysis of a patients case report with familial autosomal dominant malignant hyperthermia.

Summary of Results EK is a 70 year old morbidly obese Caucasian female with essential tremor of head and neck who also reported history of hypertension and angina pectoris. Upon detailed examination, patient revealed six of her close family members had died from muscle biopsy proven malignant hyperthermia during anesthesia for operative procedures. A preoperative anesthesia consultation was obtained for malignant hyperthermia prior to undergoing coronary arteriogram, coronary angioplasty and subsequent coronary bypass surgery. EK did well with close supervision of temperature by a team of anesthesiologists during these procedures.

Conclusions A review of literature revealed that such muscle biopsy proven case of familial autosomal dominant malignant hyperthermia is extremely rare.

467 CHARACTERIZATION OF YOUNG CHILDREN PRESENTING TO THE EMERGENCY DEPARTMENT FOR MENTAL HEALTH COMPLAINTS

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10.1136/jim-2016-000393.470

Purpose of Study Emergency departments across North America are seeing an increased incidence of pediatric mental health complaints. Previous research has focused on adolescent mental health, with little characterization of patients less than 10 years of age. The primary objective of this study was to characterize children less than 10 years of age who presented to a pediatric emergency department for mental health complaints.

Methods Used One researcher reviewed medical records of children less than 10 years old who presented to Children's of Alabama emergency department between January 2016 and April 2016 with a mental-health-related chief complaint. We then categorized patients based on demographic information, characteristics of the emergency department visit, and past medical and social history. Descriptive analyses were run using SAS® version 9.4.

Summary of Results 120 patients ages 10 years and under were seen between January and April 2016. This age group makes up 20% of all children seen in the ED for mental-health-related complaints. In this group of patients, 71% were male (n=85) and ages ranged from 3–10 years with a mean age of 7.7. Patients were 59% Caucasian (n=70), 40% African-American (n=48), and 1% other ethnicity (n=1). Patient's insurance coverage was 75% Medicaid (n=89), 18% private insurance (n=22), and 7% uninsured (n=8). 46% of patients were admitted (n=55). Univariate analyses showed increased odds of admission for children with 3 or more prior psychiatric diagnoses (OR=3.97, $p<.01$), a family history of psychiatric illness (OR=3.16, $p<.01$), and a history of Department of Human Resources (DHR) involvement (OR=2.69, $p<.01$).

Conclusions The pediatric emergency department sees a significant amount of children under age 10 for mental-health-related complaints. Nearly half of these children were admitted for psychiatric care. Several factors were found to predict admission, which reflect psychosocial influences.

468 EXAMINING PEDIATRIC RESIDENT VOTING PRACTICES

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10.1136/jim-2016-000393.471

Purpose of Study It is important to remember that as pediatricians, part of our responsibility is to be an advocate for our patients. Voting in local and national elections is an important part of advocacy and a way to impact policy that can benefit children. This study was conducted to examine

pediatric resident voting practices, their ability to vote, and to assess the significance of voting to residents. To our knowledge, no publications on this topic have been published previously.

Methods Used We asked residents at University of Alabama at Birmingham Department of Pediatrics to fill out an 11 question survey regarding voting interest and ability to vote. We had 54 surveys returned, which is 64% of pediatric residents at UAB. Results were compiled into an excel document and then analyzed.

Summary of Results Participants in the study were 63% female. We found that the majority, at 83%, of respondents are already registered to vote and that 89% plan to vote in the November presidential election. Of the participants, 15% had never voted before. 37% of respondents have little to no interest in politics, although 90% of these people still planned to vote. Most residents had at least some interest in politics at 63%, voting at 87% and advocacy at 94% of participants. There were some barriers to voting identified including not having adequate time off to vote and lack of interest.

Conclusions We found that the majority of residents are interested in politics, advocacy, and voting and plan to vote in the November election. Although barriers to voting were identified, we speculate that the importance of voting, particularly in a national election is recognized by residents since 89% plan to vote in the presidential election. This survey information is helpful to examine resident voting practices and factors that may be a barrier to voting. Further research is needed to determine how barriers to voting can be addressed and how to increase interest in voting and politics among residents.

**Gastroenterology
Concurrent Session
2:00 PM
Sunday, February 12, 2017**

469 CASE SERIES- TREATING CHILDREN WITH HEPATITIS C 1A WHO ARE TREATMENT-EXPERIENCED AND CIRRHOTIC WITH LEDIPASVIR-SOFOSBUVIR UNDER COMPASSIONATE USE

KM Reed, J Gamblin, J O'Connor, S Palle. *OU Childrens, Oklahoma City, OK.*
10.1136/jim-2016-000393.472

Purpose of Study Despite significant advances in landscape of treatment for adults with Hepatitis C virus (HCV) infections, there is limited data concerning those same therapies in children. For pediatric patients, PEG-IFN- α and Ribavirin (PEG-IFN/RBV) still used as first-line. Multicenter studies have shown that in children with genotype 1 HCV infections, only a 53% sustained virological response (SVR) using this therapy. We present three cases of vertically acquired HCV-genotype 1a infections and their response to therapy with ledipasvir-sofosbuvir (LDV/SOF), after previously failed therapy with PEG-IFN/RBV, within a single center under compassionate use. The aim is to increase awareness of outcomes of children treated with LDV/SOF as we await results from pediatric HCV drug trials.

Methods Used Three patients with HCV-Type 1a genotype who had failed previous PEG-IFN/RBV treatment, continued to have progressive liver disease and received therapy with LDV/SOF were studied. Demographic, Clinical, laboratory, and treatment characteristics were analyzed.

Summary of Results All patients completed their treatment course without significant side effects. All three had a rapid virological response. One patient has had a sustained virological response (SVR12) and the other two will be tested at 12 weeks post-treatment (as shown in the table below)

Conclusions Current first-line FDA approved therapy for children with PEG-IFN/RBV has a long course, significant side effects, and poor response rates for those especially with HCV genotype 1a infection. In this case series we show successful re-treatment of pediatric HCV 1a infected children using LDV/SOF. Each patient tolerated their treatment course and had viral clearance by treatment week 4 and all subsequent testing has remained negative.

470 PREDICTING QUALITY OF LIFE OF YOUTH SCHEDULED FOR AN ESOPHAGOGASTRODUODENOSCOPY

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10.1136/jim-2016-000393.473

Purpose of Study This study aimed to understand the current health related quality of life (HRQoL) of youth undergoing an esophagogastroduodenoscopy (EGD).

Abstract 469 Table 1

	Case 1				Case 2				Case 3			
	Day 0	Tx Wk 4	Tx Wk 12	SVR 12	Day 0	Tx Wk 4	Tx Wk 12	SVR 12	Day 0	Tx Wk 4	Tx Wk 12	SVR 12
AST	140	72	130	50	663	169	111		91	25		
ALT	161	82	163	67	770	293	140		98	21		
T Bili	2.9	1.4	1.2	1.4	1.6	2	1		0.5	0.8		
D Bili	1.9	0.8	0.6	0.6	0.9	1	0.5		0.2	0.3		
Albumin	3.6	3.8	3.5	4.2	3.9	3.7	3.7		4.1	4.4		
INR	1.26			1.2	1.1	1.2	1.2			1.1		
AFP	338.5		22.2	5.1	5.2	5.6			12.6	6		
HCV RNA PCR	1,075,518	detected	<12	none	403,000	none	none	pending	1,650,000	none	pending	

Research indicates that children with chronic illnesses often experience decreased HRQoL. The specific predictors of HRQoL in this pediatric gastroenterology (GI) population has not been explored.

Methods Used Parents of 68 youth (ages 2–17, mean age 10.38 years, SD 3.79) undergoing an EGD at Children's of Alabama were recruited. Pediatric diagnoses included Eosinophilic Esophagitis (36.20%), Eosinophilic Esophagitis (60.90%), Gastroesophageal Reflux Disease (18.80%) and other (e.g., cyclic vomiting syndrome, gastritis, Crohn's Disease; 20.30%). Caregivers completed the PedsQL General Quality of Life Inventory, PROMIS measures of anxiety and depression, and indicated their child's reported pain severity over the past week.

Summary of Results Using caregiver-proxy report, results indicate that quality of life of youth undergoing EGD can be predicted by both pain severity ($b=-.30$, $t=-2.93$, $p<.01$), and degree of depressive symptomology ($b=-.36$, $t=-2.65$, $p=.01$), after controlling for age, race, and gender ($F(6,58)=7.264$, $p<.01$). Experience of anxiety was not predictive of HRQoL.

Conclusions Understanding the amount of pain a patient is in and the level of their psychological distress can be used to predict a patient's HRQoL. Improved screening and targeted treatment for pain and depression in pediatric GI patients could serve to improve the HRQoL of these youth.

471 THE PROFILE OF BLOODSTREAM INFECTIONS IN INFANTS WITH INTESTINAL FAILURE: A 2 YEAR EXPERIENCE IN A TERTIARY NEONATAL INTENSIVE CARE UNIT

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10.1136/jim-2016-000393.474

Purpose of Study Infants with intestinal failure (IF) are common in the present day NICUs. Infants with IF have a higher rate of bloodstream infections (BSI). The purpose of this study was to describe the profile of BSI in infants with IF in a single tertiary neonatal intensive care unit and to use the knowledge gained to improve outcomes.

Methods Used 51 infants who were diagnosed to have IF at Texas Children's Hospital during the period, January 2012 to December 2014 were included in this study. IF was defined as dependence upon parenteral nutrition (PN) for ≥ 6 weeks duration. BSI was defined by a blood culture positive for either bacteria or fungi, treated with antibiotics or antifungals for ≥ 5 days. Data studied included details about demographics, the diagnoses, PN, diet, surgeries, venous accesses, and BSI.

Summary of Results 51 infants with an M:F ratio of 1.5:1 had a median gestational age at birth of 34 ± 5 weeks, and birth weight of 1.8 ± 0.9 Kg. The commonest conditions contributing to IF were necrotizing enterocolitis (22%), spontaneous ileal perforation (22%), and gastroschisis (20%). The median duration of in-hospital PN requirement was 83 ± 41 days. The median length of hospital stay was 117 ± 73 days. 35 (68%) infants achieved complete enteral

autonomy before discharge, 10 (20%) infants were discharged home on PN and 6 (12%) infants died before discharge. 23 (45%) infants had at least one BSI, and 14 (27%) infants had more than one episode of BSI. Gram-positive, gram-negative and fungi accounted for 54%, 26% and 18% of BSIs respectively. CONS and Methicillin-Resistant Staphylococcus Aureus (MRSA) were the commonest gram positive BSIs, while *Serratia Marcescens* was the commonest gram-negative BSI.

Conclusions In this interim analysis, the morbidity associated with IF including the duration of stay, duration of PN, proportion of infants achieving enteral autonomy, the incidence of BSI and the mortality rate are consistent with prior reports in the literature. Currently, we are continuing our analyses, to study the association of other risk factors. This comprehensive data and the knowledge gained of BSI in infants with IF will help us understand the risk factors, prognosticate, and device strategies to improve outcomes in this high-risk group.

472 AN ALTERNATIVE APPROACH IN THE CARE OF HEPATITIS B PATIENTS

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Purpose of Study The prevalence of Hepatitis B in VA patients is higher than the general population. Patients are generally treated following referral from Primary Care Providers. This study identified Hepatitis B patients by a retrospective review of the Laboratory data base. The objectives were to review patient notification, patient education to prevent transmission, and care of patients with Hepatitis B.

Methods Used A retrospective search of positive Hepatitis B surface antigen positive laboratory results was performed from December, 2010 and June, 2016 at the Memphis VAMC. The Computerized Patient Record System (CPRS) medical data of all patients with a positive Hepatitis B surface antigen were reviewed.

Summary of Results 50 patients were identified. 47 male, 3 female; age 39 to 89, mean age 62; 35 African-Americans, 13 Caucasians, 2 Asians. 42/50 patients had documentation that the patient was notified of the diagnosis of Hepatitis B. 33/50 patients had documentation of education to prevent transmission. 37/50 patients were tested for Hepatitis B DNA. 36/50 patients were screened for Hepatitis A immunity. 50/50 patients were screened for Hepatitis C. 45/50 patients were screened for HIV. 33/50 patients were screened for Hepatitis D. 41/50 patients were referred to Gastroenterology. 19/50 patients were treated with antiviral therapy.

Conclusions Systematic retrospective review of laboratory and clinical data revealed significant lapses in patient notification, prevention of transmission and referral of patients with Hepatitis B. These preliminary data suggest that Specialty care should be initiated by the laboratory result rather than by referral from Primary Care.

473 CELLULAR BIOENERGETICS: PERSONALIZING TREATMENT IN ALCOHOLIC LIVER DISEASE

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10.1136/jim-2016-000393.476

Purpose of Study Alcoholic hepatitis (AH) is associated with 40–50% mortality at 1 month. Liver biopsy is often needed especially for uncertain clinical diagnosis. Corticosteroids (CS) provide 50% survival benefit with their response evaluable only at 1 week. Defects in bioenergetics or mitochondrial oxygen consumption rate (OCR) in peripheral cells are shown in diseases associated with systemic inflammation like diabetes and sepsis. Similar data are unavailable for alcoholic liver disease (ALD). We tested the hypothesis that AH patients with severe bioenergetics defects will progress to liver failure and be non-responsive to CS (NRS).

Methods Used After informed consent, 20 mL blood was collected from ALD patients (with or without AH) and healthy controls. Monocytes and neutrophils were isolated within 30 min using CD14 and CD15 antibodies respectively. Cellular bioenergetics and OCR (pmol/min./mcg protein) were obtained using XF96 analyzer (Seahorse Biosciences).

Summary of Results Of 86 ALD patients (39 with AH), 78 without concomitant HCV and 40 healthy controls were analyzed. ALD with AH (n=37) compared to 41 without AH were younger (44±11 vs. 53±9 yrs.) with higher white blood cell count (16±10 vs. 6±9) and MELD score (30±10 vs. 16±10), P<0.0001 for all. Compared to 35 healthy controls, OCR differed among 63 ALD patients for basal (3.1±1.6 vs. 2.5±0.8, P=0.002), proton leak (0.6±0.4 vs. 0.5±0.2, P=0.03), non-mitochondrial (1.5±0.6 vs. 1.4±0.4, P=0.03), and oxidative burst in monocytes (8.5±5.2 vs. 6.3±3.7, P<0.05) and neutrophils (44±13 vs. 53±14, P=0.01). OCR among ALD with AH (n=28) compared to 35 without AH differed for basal (2.5±1.3 vs. 3.5±1.8, P=0.02), proton leak (0.4±0.3 vs. 0.7±0.5, P=0.02), and neutrophilic oxidative burst (44±13 vs. 51±12, P<0.05). After controlling for age, WBC, and MELD score, basal and ATP linked OCR predicted diagnosis of AH with OR (95% CI) of 0.5 (0.3–0.9, P=0.04) and 0.4 (0.2–0.9, P=0.04) respectively. Neutrophilic burst at baseline was different among responders (n=7) to steroids compared to 9 NRS (47±13 vs. 35±7, P=0.002).

Conclusions Baseline cellular bioenergetics seems a promising biomarker for personalized medicine in ALD patients for a) diagnosis of AH and b) predicting response to CS and outcome on follow up. Data in larger multicenter population are needed before accepting use of this novel biomarker in clinical practice.

474 ANALYSIS OF EOSINOPHILIC ESOPHAGITIS REGISTRY DATA FROM THE UNIVERSITY OF ALABAMA AT BIRMINGHAM AERODIGESTIVE PROGRAM

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10.1136/jim-2016-000393.477

Purpose of Study Eosinophilic esophagitis (EoE) is increasingly recognized as a contributor to cough and dysphagia in children. We compared our single center population to the current literature. We aim to analyze the EoE phenotype at Children's of Alabama.

Methods Used We evaluated our IRB approved EoE patient registry (2003–2016) to characterize initial patient presentation. T-tests and Fischer's exact tests compared groups with significance assigned at p<0.05.

Summary of Results We examined data from 180 patients. Mean age at diagnosis was 8.1±0.4 (mean±SEM) years, with atopy present in 79%. Males accounted for 77% of cases. Intraluminal eosinophils at diagnosis numbered 38.7±3.1 in the proximal and 57.9±2.9 in the distal esophagus. Sclerosis was present in 59%. Although most patients were Caucasian (74%), the percentage of African-Americans (24.9%) mirrored the state population (29.2%). Significant atopic differences were found between Caucasians and other racial groups. Specifically, the non-Caucasian population (96% African-American) had significantly more asthma (57% vs 37%, p<0.02), eczema (49% vs 27%, p=0.01), and rhinitis (64% vs 39%, p<0.005) with a decreased male predominance (60% vs 83%, p<0.005). Food allergies, intraluminal eosinophils, and sclerosis were similar between groups.

Conclusions Our general EoE population is consistent with previous reports. However, subgroup analysis identifies a distinct atopic phenotype in African-Americans at our center with a less-skewed male bias. These data suggest racial (and perhaps regional) variation in clinical presentation that has not previously been reported. Ongoing gene modifier studies will identify whether these observations have an inherited or environmental stimulus.

475 GASTROPARESIS-LIKE SYNDROME: THE SIMILARITIES AND DIFFERENCES AS COMPARED TO GASTROPARESIS AND THE PATHOLOGIC FINDINGS IN THE SMOOTH MUSCLE OF THE ANTRUM AND PYLORUS

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10.1136/jim-2016-000393.478

Purpose of Study Gastroparesis (GP)-like syndrome exhibits similar symptoms to gastroparesis (GP), but it lacks delayed gastric emptying (GE). The aim of our study was to compare GP to GP-like syndrome and the similarities and differences in antral and pyloric smooth muscle histopathological features. It is unclear if GP-like syndrome is encompassed as part of the GP spectrum.

Methods Used 34 GP and 15 GP-like syndrome patients had full-thickness pyloric and antral biopsies and underwent surgery for placement of a gastric electrical stimulator and subsequent pyloroplasty. The tissues were stained with H&E, C-Kit and trichrome based on prior control data. Depletion of interstitial cells of Cajal (ICC) was at a count of less than 10 per high power field in the antrum and/or pylorus. A 4-hour standardized scintigraphy was utilized to measure GE; retention of >10% at 4 hours was considered

delayed GE. Total symptom scale (TSS) for GP was recorded at baseline.

Summary of Results Eleven (32.4%) GP and 6(40.0%) GP-like syndrome patients had antral ICC-loss ($P>0.05$). 21 GP and 4 GP-like syndrome patients had pyloric biopsies taken. Pyloric ICC-loss was identified in 16 (72.7%) GP, but none in the GP-like syndrome patients ($p=0.01$). Pyloric ICC loss demonstrated an increased severity of GP symptoms. All 13 diabetic-GP patients were found to have eosinophilic inclusion bodies in the smooth muscle of the antrum and/or pylorus. Fibrosis was observed in 68.8% of the pyloric tissue in GP patients and one GP-like patient had fibrosis in the pylorus. Generally, those with antral fibrosis also exhibited fibrosis in the pylorus. GE at 4 hours was considerably delayed in diabetic-GP as compared to idiopathic-GP ($p < 0.05$). Inclusion bodies were exclusively observed in diabetic GP patients.

Conclusions The rate of antral smooth muscle ICC loss is similar in GP and GP-like syndrome, while pyloric fibrosis is more frequent in GP. Pyloric fibrosis can be a marker of 'pyloric dysfunction' and may potentially describe delayed GE during gastroparesis.

476 SOLID MEAL GASTRIC EMPTYING SCINTIGRAPHY IN PATIENTS WITH FUNCTIONAL DYSPESIA: ARE SYMPTOMS INDUCED BY THE MEAL DIAGNOSTIC?

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Purpose of Study Functional dyspepsia (FD) presents with nausea, early satiety, postprandial fullness and upper abdominal pain in the absence of organic gastrointestinal (GI) abnormalities. The other GI disorder which mimics the clinical features of FD is gastroparesis (GP). There is ongoing debate whether to measure gastric emptying (GE) in FD patients. As therapeutic options are not always similar, we believe that GE has value in categorizing FD. This study was designed to address whether the severity of symptoms differentiates GP from GP-like individuals who are identified as FD, but have normal GE.

Methods Used Patients with FD who were referred to our GI motility clinic from 2015 to 2016 were studied. GE was measured utilizing 4-hr standardized scintigraphy; a retention of $>10\%$ at 4-hr was considered delayed. The radiolabeled meal consisted of 2 egg beaters, toast, and water, 260 calorie content, 2% fat, and ingested within 10 minutes. Patients' symptoms were scored from a 1 (minimal) to 4 (severe) point scale, both before and during the test meal.

Summary of Results 21 GP patients (51.4 ± 17.9 years old; 16 females) and 14 GP-like patients (49.4 ± 11.2 years old; 11 females) were identified. In GP and GP-like groups, 52% and 29% of patients had nausea throughout the test, respectively, not a statistically significant difference. Overall symptoms scores were comparable in both groups.

Conclusions 1) In FD patients, symptoms induced during a 4-hr GE meal did not differentiate GP and GP-like

syndromes; 2) GE scintigraphy can differentiate GP and GP like-syndrome providing a strategy for treatment in FD patients.

477 DEFICIENCY OF CATECHOL-O-METHYLTRANSFERASE: CATECHOLAMINERGIC STIMULUS ENHANCES INTESTINAL MOTILITY

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10.1136/jim-2016-000393.480

Purpose of Study Catechol-O-methyltransferase (COMT) is a degrading enzyme of catecholamine including dopamine, epinephrine and norepinephrine (NE). Gastrointestinal dysfunction is often found in patients with inherent COMT deficiency who are treated with a COMT inhibitor. It has remained unclear the mechanism of GI dysfunction induced by COMT deficiency. The present investigation studies catecholaminergic functional changes in intestinal motility.

Methods Used In this study, organ bath system was employed to detect catecholaminergic effects in ileal and colonic motility in COMT knockout (KO) and wild type (WT) mice.

Summary of Results The results showed that application of dopamine ($10 \mu\text{M}$), quinpirole ($10 \mu\text{M}$, a D2 receptor agonist), A68930 ($5 \mu\text{M}$, a D1 receptor agonist), and apomorphine ($10 \mu\text{M}$) significantly increased ileal phasic and tonic contractions and colonic tonic contractions in all genotype mice, COMT (KO, male=8; female=10) and (WT, male 10; female=12). A68930 can inhibit electrical field stimulation (EFS) evoked tonic contractions. The stimulus effects of these dopaminergic agonists were inhibited or blocked by tetrodotoxin (TTX, $1 \mu\text{M}$). Dopamine only induced bowel relaxation in presence of TTX. The dopaminergic stimulus effects were significantly stronger in COMT KO than COMT WT mice. Dihydroergocristine, a non-selective antagonist for 5-HT receptor, can partially suppress the tonic contraction elicited by dopaminergic agonists. Application of NE and formoterol, a β_2 -adrenoceptor agonist, caused a relaxing response and completely blocked EFS-evoked contractions in all intestinal preparations ($n=64$). L741626, a D2 receptor antagonist, suppressed dopaminergic contractile responses, but it induced colonic tonic contractions in the presence of TTX.

Conclusions The results suggest that intestinal dopamine receptors mediate bowel neurogenic excitatory contractile function, but adrenoceptors mediated bowel inhibitory relaxing functions including neurogenic and myogenic effects. L741626 can directly evoke myogenic intestinal contraction. The results suggest that deficiency of COMT leads to hyperactivity of catecholaminergic system, in which dopaminergic excitatory actions may change intestinal motor behavior and lead to diarrhea. Future studies are needed to further elucidate the detailed mechanisms.

478 PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND TODDLERS ACCORDING TO THE ROME IV CRITERIA

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Purpose of Study The new pediatric Rome IV criteria have just been published, including changes to the diagnostic criteria for Functional Gastrointestinal Disorders (FGID) but it is not known how these new criteria affect prevalence rates. The aim of the current study was to assess the prevalence of Functional GI Disorders (FGIDs) in infants and toddlers aged 0–3 years old according to the Rome IV diagnostic criteria as reported by parents in a representative community sample.

Methods Used Mothers (n=296) of children aged 0–3 years old in the US were recruited to complete online surveys about their child's GI symptoms, quality of life, and other health conditions.

Summary of Results Based on the Rome IV criteria, 24.7% of infants and toddlers qualified for an FGID. Among infants less than 12 months old, 37.9% qualified, and 21.4% toddlers ages 1–3 qualified for an FGID. Infant regurgitation was the most common disorder among infants and functional constipation was the most common among toddlers. Toddlers with FGIDs had a lower quality of life than toddlers without FGIDs (M=79.41 vs. M=88.61, p<.001). No differences were found in gender or race in frequency or type of FGID.

Conclusions This is the first study to report prevalence of infant toddler FGID based on the new Rome IV criteria. The overall prevalence of FGIDs was similar to rates reported with Rome III criteria. There appear to be change in prevalence rates of functional constipation, infant dyschezia, and functional diarrhea. These data are of importance to treatment and research of FGIDs.

Hematology and Oncology
Concurrent Session
2:00 PM
Sunday, February 12, 2017

479 LYMPH NODE STROMAL CELLS ENHANCE PANCREATIC CARCINOMA METASTASIS IN AN ORTHOTOPIC XENOGRAFT MODEL

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Purpose of Study Pancreatic Carcinoma (PaCa) is an insidious disease with the shortest survival of any solid tumor. Complete remission is rare. A better understanding the mechanism of metastasis is needed to improve outcomes. It is known that lymph node (LN) involvement is

crucial for PaCa spread to distant organs or metastasis. Thus there is a strong need to develop mouse models for preclinical study. There are human PaCa mouse models where tumor cells/specimens are implanted subcutaneously, but they rarely cause metastasis and poorly recapitulate PaCa tumor microenvironment, such as LN stromal microenvironment, which likely plays critical role in tumor behavior. Here, we established an orthotopic xenograft mouse model to study the role of LN stromal cells (LNSCs) in PaCa growth and tumor metastasis *in vivo* and *in vitro*.

Methods Used For *in vitro* assay, pancreatic cell lines PANC-1 and Hs766T were cultured with/without LNSC line, HK-conditioned media for 48 hrs and measured by MTT assay for proliferation, while human fibroblast cell HFF-conditioned media served as a control. For *in vivo* assay, luciferase-tagged-PANC-1 and -Hs766T cells were injected intra-pancreatically into NOD/SCID mice with/without HK cells. Tumor growth and metastasis were measured weekly by bioluminescent imaging (BLI). At endpoint, the primary tumors were weighed, lung and liver metastasis were evaluated via BLI, H&E and immunohistochemical staining.

Summary of Results HK cell-conditioned media significantly increased the proliferation of PANC-1 and Hs766T cells in comparison to HFF cell-conditioned media or without treatment. In orthotopic xenograft model, addition of LNSCs significantly facilitated the tumor growth in primary cancer cell injection site and liver metastasis. Tumors generated from PANC-1 and Hs766T cells recapitulated the histological architecture, biomarkers, and other histopathologic features characterized in PaCa patient tumors.

Conclusions We developed a novel orthotopic PaCa model that closely recapitulates human disease. Our data suggested that LNSCs play a key role in PaCa growth and metastasis. This model provides a platform to investigate mechanism of tumor metastasis and screen novel treatments for PaCa patients.

480 THE EFFECTS OF RAB13 DERIVED FROM LYMPH NODE STROMAL CELL EXTRACELLULAR VESICLES ON THE PATHOGENESIS OF HUMAN COLORECTAL CANCER

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10.1136/jim-2016-000393.483

Purpose of Study Colorectal cancer (CRC) is the third leading cause of cancer death in the US. Its prognosis greatly depends on the formation of distant metastasis which drops 5-year survival rates to less than 15%. Therefore, a better understanding of advanced disease is essential for the development of new therapeutics.

Our previous data has shown that lymph node stromal cells (LNSCs) provide supportive roles for CRC growth *in vitro* and tumor progression and metastasis *in vivo*. Preliminary work suggests this is accomplished using extracellular vesicles (EVs) as mediators of cell-cell communication. To understand the role of LNSC-derived EVs in the

progression of CRC we analyzed EV-derived RNAs and identified the GTPase RAB13 as a potential mediator of disease.

Methods Used EVs were isolated from LNSCs by ultracentrifugation and their RNA contents analyzed using next-generation sequencing. RNAs were ranked by enrichment levels in EVs compared to LNSCs. HK, a LNSC line, was transfected with siRNAs to RAB13 and co-injection with CRC cells using our established orthotopic human CRC model. Results were compared to RAB13 non-silenced controls. Transfected HK cell supernatant was also collected and added to CRC cells in vitro. RAB13 silenced vs non-silenced controls were used for cell proliferation assays, as well as transwell and scratch migrations assays.

Summary of Results The small GTPase RAB13 was highly enriched within LNSC-derived EVs, and was shown to be successfully silenced by siRNA using qPCR. RAB13 silenced HK cells co-injected into the mouse rectum with CRC cells showed a significant decrease in tumor formation and metastasis compared to non-transfected HK cells. Preliminary data is also beginning to suggest that RAB13 may also act as a facilitator of cell proliferation and migration in vitro.

Conclusions RAB13 is highly enriched in LNSC-derived EVs and preliminary data suggests it has a significant effect on CRC progression and metastasis. Further studies assessing drugs to RAB13 are necessary to uncover its use as a novel therapeutic target.

481 COMPARING SURFACE EXPRESSION OF IMMUNE INHIBITORY MODULATORS IN STRESS INDUCED DRUG TOLERANT MELANOMA CELLS AND PATIENTS WITH REFRACTORY METASTATIC MELANOMA

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10.1136/jim-2016-000393.484

Purpose of Study In melanoma, tumor cells exhibit an early stress induced drug tolerant state upon hypoxia or drug exposure, causing treatment resistance. This state is characterized by the expression of CD271, a marker involved in CD8⁺ or cytotoxic T lymphocyte (CTL) suppression, and the downregulation of T cell recognized melanoma antigens, MelanA and tyrosinase. However, whether the expression of immune inhibitory modulators, such as PD-1 and PD-L1, plays a role in treatment resistance remains unknown. This study aims to investigate whether the stressed state impacts CTL killing, and whether the expression of immune inhibitory markers could predict therapy resistance in metastatic melanoma patients.

Methods Used Human melanoma cell lines were stressed with hypoxia or docetaxel chemotherapy, and CD271 expression was assessed by flow cytometry. To investigate CTL lysis, murine melanoma cells were stressed with hypoxia or docetaxel, cultured with tumor-specific CTLs, and assessed for lysis by flow cytometry. To investigate immune inhibitor expression in refractory metastatic

patient tumors, 128 tumor blocks from 85 patients with Stage IIIc/IV disease were selected, and a tumor tissue microarray was constructed for immunohistochemistry staining of these markers.

Summary of Results Expression of CD271 on human melanoma cells was upregulated under hypoxia or docetaxel treatment. CTL lysis of stressed murine melanoma cells was reduced by 40%. Patient demographics indicate >50% of Stage IIIc/IV patients undergoing targeted, immunotherapy or both had recurrence. Expression of CD271, PD-1, and PD-L1 in these patients is currently underway.

Conclusions Stressed human melanoma cells upregulate inhibitory molecules, such as CD271, and stressed murine melanoma cells show increased resistance to CTL killing. Future experiments will investigate inhibitory marker expression in metastatic patients with recurrence despite targeted or immunotherapy, to then determine their predictive value and thus the most appropriate and effective therapy for each patient.

482 PROSPECTIVE ANALYSIS OF CHEMO-PREDICTIVE ASSAY TO TARGET CANCER STEM CELLS IN GLIOBLASTOMA

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Purpose of Study Prognosis of glioblastoma (GBM) treated with standard-of-care is <15 months. Cancer stem cells (CSCs) within GBM contribute to tumor propagation, maintenance, & treatment resistance. Ineffective chemotherapy causes unnecessary toxicity & selects resistant cancer clones.

We have developed a drug response assay (ChemoID) that identifies the most effective chemotherapy against CSCs & bulk of tumor cells. A prospective study evaluated the use of the ChemoID assay in GBM patients.

Methods Used Fresh tissue samples were collected for drug sensitivity testing from 41 GBM patients. Patients were all treated with standard-of-care TMZ plus radiation +/- maximal surgery. Treatment was classified by the assay: sensitive, intermediate, or resistant. Patients were prospectively monitored for tumor response, time to recurrence, progression-free survival (PFS), & overall survival (OS). Associations of assay response for the standard-of-care TMZ selected treatment with tumor response, time to recurrence, PFS, & OS were determined.

Summary of Results Median follow-up analysis was 8 months (3–49 months). ChemoID on CSCs had a sensitivity of 100% & specificity of 97% and on bulk of tumor a sensitivity of 100%, but specificity of only 89%.

Using a separate model of logistic regression for CSCs or Bulk, with a positive test threshold set at 40% cell kill for CSCs and 55% for Bulk, for every 5% increase in cell kill, there was a statistically significant 2-fold increase in Odds Ratio (OR) of patient response to TMZ (non-recurrence) at 12 months for the CSC test. Using a single multivariate model for CSCs & Bulk together, the CSCs test was statistically supported with a 2.36 OR of patient response vs. a non-significant OR of 1.46 for Bulk.

We analyzed improvement of patient categorization who were negative by CSC (<40% cell kill) but positive for Bulk (>55% cell kill) by using the CSCs results & correctly reclassified 11% of non-responders ($p=0.030$).

Overall, patients treated with assay-sensitive or -intermediate TMZ against CSCs had significantly improved tumor response & time to recurrence.

Conclusions This prospective study on ChemoID demonstrated that patients whose CSCs were sensitive (>40% cell kill) to TMZ, had a significant 2-fold increase OR to respond (non-recurrence) at 12 months.

483 ROLE OF NOTCH1 IN REGULATING THE METABOLISM OF TRIPLE NEGATIVE BREAST CANCER CELLS

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Purpose of Study The Notch pathway regulates cell proliferation, cell fate, differentiation, and apoptosis. The Notch pathway is also involved in different aspects of tumorigenesis. Notch1 is overexpressed in a subset of triple negative breast cancers (TNBC). Recent research has been aimed at finding unique biomarkers that can be used to target TNBC. Notch1 overexpression correlates with poor relapse-free survival rates in TNBC. Interest in cancer cell metabolism has dramatically increased in recent years, as metabolic reprogramming has emerged as a key biological feature and therapeutic target in many cancers. Though it is clear that Notch is important in TNBCs, not much is known about its role in the regulation of their metabolism. One of the most important regulators of metabolism is the AKT pathway, which controls glucose utilization and mitochondrial respiration.

Methods Used Since data from our lab and others have revealed a cross-talk between Notch activity and the AKT pathway, we have investigated the impact of these two pathways on mitochondrial respiration and glycolysis in the TNBC cell line MDA-MB-231, which is representative of a TNBC subset characterized by high Notch1 expression. AKT activity was measured by determining the level of mTORC2-catalyzed phosphorylation at Ser 473. We used an Agilent Seahorse Analyzer to determine Notch's role in glycolysis and mitochondrial respiration of these cells.

Summary of Results JAG1 increases AKT activation in these cells in a Notch1-dependent manner. Using investigational drugs, we determined that JAG1-induced AKT phosphorylation requires mTORC2 and $IKK\alpha$, but not mTORC1. Using immunofluorescence, we found co-localization of Notch1 with mitochondria. When cells were stimulated with JAG1, the cellular oxygen consumption rate (OCR) and extracellular acidification rate (ECAR), which measure mitochondrial respiration and glycolysis respectively, both increased. Notch1 knockdown or pharmacologic inhibition of mTORC2 or $IKK\alpha$ inhibited cellular metabolism.

Conclusions Our studies suggest that Notch1 plays a crucial role in regulating the metabolism reprogramming of this TNBC cell line through a non-nuclear, mitochondrial pathway. Since metabolic reprogramming has been recently investigated as a therapeutic intervention in TNBC,

inhibition of the Notch pathway may be a future area of focus for novel combination therapies.

484 A SURVEY OF PEDIATRIC ONCOLOGY PATIENTS COMPLEMENTARY AND ALTERNATIVE MEDICINE USE INPATIENT VS OUTPATIENT WITH COMPARISON OF PHYSICIAN DISCLOSURE RATE AND TYPE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE VARIATION IN BOTH SETTINGS

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Purpose of Study The purpose of this study is to assess complementary and alternative medicine (CAM) use-rates in both the inpatient and outpatient settings by pediatric oncology patients. The hypothesis is that pediatric oncology patients are using CAM, particularly ingestible CAM, in the inpatient setting without disclosing CAM use to their physician.

Methods Used Patients were identified by a chart review to confirm eligibility. Patients admitted to the hospital after January 1, 2013, who were less than 18 years of age at the time of admission, and with a diagnosis of cancer were deemed eligible. They were given an anonymous survey to complete at their oncology clinic visit.

Summary of Results 143 patients were surveyed out of 152 eligible patients. 68.5 % used CAM at home and 53.1% in the hospital. When any CAM therapy (from prayer to cannabinoid) was used at home, according to the parents physicians were aware 32.7% of the time and in the hospital 44.7% of the time. However, physicians/APRNs documented CAM use 10% of the time. The percentage of patients using ingestible CAM therapies was 41.3% at home and 19.6% inpatient. When CAM was ingested at home, according to the parents physicians were aware 35.6% of the time and in the hospital 53.6% of the time. However, physicians/APRNs documented ingested CAM use is 88.1% with home use and 14.3% with hospital use. Commonly ingested CAM included vitamins, supplements, guanabana peppermint, melatonin, specialized diets, and cannabis.

Conclusions Pediatric Oncology patients are using CAM therapies both at home and in the hospital without the documented knowledge of their physicians. This data demonstrates patients are also ingesting CAM products that may interfere with chemotherapy/medications or may cause side effects without physician knowledge while in the hospital.

485 EVALUATION OF EARLY EMPIRIC CEFTRIAXONE PROTOCOL FOR PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS PRESENTING WITH FEVER

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10.1136/jim-2016-000393.488

Purpose of Study In pediatric patients with fever and neutropenia, initiating antibiotic therapy within one hour

improves outcomes, yet there are no established protocols for empiric antibiotics. In 2013 our institution implemented an Early Empiric Ceftriaxone (EEC) protocol to reduce time to antibiotic administration in these patients, wherein ceftriaxone is given immediately after obtaining blood for culture and lab studies. In patients found to be neutropenic, ceftriaxone is discontinued and cefepime is initiated. To evaluate this protocol, we reviewed ceftriaxone sensitivity rates and patient outcomes before and after its implementation.

Methods Used Hematology-oncology patients with at least one positive blood culture between January 2011 and December 2013 were identified. Patient demographics, neutrophil count, antibiotic treatment, isolated organisms, antibiotic sensitivities, and patient adverse outcomes (including increased respiratory support, hypotension requiring fluids or inotropes, and ICU admission) were obtained by retrospective chart review. Fisher exact test was used to compare dichotomous variables between patient groups.

Summary of Results We identified 89 pediatric patients with a total of 272 bacterial isolates from blood cultures. Of organisms isolated from neutropenic patients (n=124), a total of 47 organisms were tested for sensitivity to ceftriaxone and 20 (45%) were resistant, 6/18 (33%) of gram positive cultures and 18/29 (62%) of gram negative cultures. Sixty-three percent of EEC patients had an adverse outcome versus 44% of non-EEC patients (p=0.277). Notably, 31% of EEC patients required ICU admission versus 11% of non-EEC patients (p=0.049).

Conclusions In this retrospective study, no statistically significant difference was seen in overall adverse outcome rate between EEC and non-EEC patients, though ICU admission rates were higher in EEC patients. Ceftriaxone resistance rates were high in tested isolates. Given these data, EEC may not be effective at improving outcomes in febrile pediatric hematology oncology patients.

486 SURVIVORSHIP ANALYSIS FOR PEDIATRIC WILMS' TUMOR: A CHILDREN'S HOSPITAL OF NEW ORLEANS EXPERIENCE

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Purpose of Study Wilms' Tumor is the most common renal malignancy seen in pediatrics, and accounts for 5% of all pediatric malignancies. It is staged I-V based on the extent of disease at diagnosis and whether or not the tumor was able to be completely resected up front. It is treated with a combination of surgical resection, systemic chemotherapy, and possible radiation. The National Wilms Tumor Study Group (NWTS) and Children's Oncology Group (COG) have been heading up clinical trials over the last several decades in an effort to improve survival and minimize treatment related morbidity. As a result of their efforts the overall survival of this disease has increased from <80% in the 1960s to 90% today. The Surveillance, Epidemiology, and End Results (SEER) organization has gathered data regarding the incidence, initial staging, treatment obtained, and overall survival outcomes from across

the country. Our project aims to compare the treatment outcomes for pediatric Wilms Tumor at Children's Hospital of New Orleans from 1995–2015 with the SEER data to determine if we are meeting the national standards of care.

Methods Used We performed an extensive chart review of pediatric patients diagnosed with Wilms Tumor at our institution from 1995–2015 looking at the following data points: age of diagnosis, sex of patient, stage at diagnosis, treatment received (surgery, radiation, chemotherapy), and their overall outcome. We then compared the treatment outcomes achieved at our institution with the current national Surveillance, Epidemiology, and End Results (SEER) data to determine if we are achieving the national standard of care here at Children's Hospital of New Orleans.

Summary of Results We have identified 56 pediatric patients who were diagnosed with Wilms Tumor and treated at our institution. Of these patients, 8 were stage I; 18 were stage II; 15 were stage III; 10 were stage IV; and 5 were stage V. After reviewing their clinical course 7 of our 56 patients (12.5%) experienced a relapse and 3 (5.3%) have died from disease.

Conclusions When we compare our data to the SEER data, our patients are experiencing superior outcomes than those of the national standard, 94.7% overall survival compared to 87.4% respectively.

487 PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: A 5-YEAR INSTITUTIONAL REVIEW

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Purpose of Study Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal hematopoietic stem cell disorder. This rare hematologic disorder primarily affects adults, accounting for only 10% of reported pediatric cases. Over the last 5 years, we have noticed an increase in children presenting with severe aplastic anemia (SAA) where PNH clones were identified as the underlying etiology. SAA is a bone marrow failure (BMF) syndrome characterized by pancytopenia and hypoplasia of the marrow.

Methods Used We conducted a comprehensive, retrospective chart review of patients presenting with SAA who were subsequently diagnosed with PNH clones at our institution from 2010–2015. Data collected through medical record review included demographic information, presenting symptoms, laboratory findings, diagnosis and treatment.

Summary of Results Six subjects were identified with SAA and PNH clonality: 2 females and 4 males; ages 10 to 17 years, with a median age of 11.5 years. There were 3 African Americans and 3 Caucasians. No trend was recognized when assessing for ethnicity, sex, age and geographic location. A PNH clone was identified upon presentation in 3/6 patients. Two patients progressed with an increasing percentage of PNH clones requiring transplant. The remaining patients have been maintained with immunosuppressive therapy. All of our patients are alive and transfusion independent.

Conclusions SAA, a BMF syndrome, is the initial presentation for PNH in our pediatric cohort as previously documented when compared to adults. Pediatric individuals with SAA should undergo diagnostic workup for PNH. When compared with published data, a higher number of patients in a 5 year period is identified (6 individuals versus 12 over an 18 year period at another pediatric institution). Even though our numbers are small this trend has triggered our interest about potential reasons for this. Among possible hypotheses to further analyze are environmental factors, technological advances, education and higher index of suspicion among the pediatric hematologists-oncologists at our institution. To further explore this hypothesis, we plan to invite other neighboring Gulf Coast pediatric institutions to participate in this study.

488 **PROGNOSTIC ROLE OF ANTITUMOR IMMUNITY WITHIN TUMOR MICROENVIRONMENT IN FOLLICULAR LYMPHOMA**

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Purpose of Study Follicular lymphoma (FL), one of the most common forms of non-Hodgkin lymphoma, is an incurable disease with a highly variable outcome. The majority of patients experience favorable response to therapy but 20% of patients progress rapidly, associated with poor outcomes. A clinical prognostic tool such as the FL International Prognostic Index (FLIPI) has not been useful in identifying this patient subset. Therefore, biomarkers to allow risk-stratified treatment and predict response to novel therapies are needed. While the prognostic role of the tumor microenvironment has been demonstrated, the optimal quantitative methods are to be elucidated. We aim to analyze the role of immune effectors and checkpoints within the tumor microenvironment in predicting the clinical outcome of FL patients, to provide a reliable prognostic marker for informed clinical decision making.

Methods Used Patients with FL from the Ochsner Hospital System (OHS) were collected for use as validation cohort of the immune score, in addition to the discovery cohort of 112 from the Princess Alexandria Hospital in Queensland, Australia. Patients diagnosed with FL from 1988 to 2008 with pathological specimen were included in the study and patients with grade IIIB, transformed FL, or HIV-positive were excluded. Clinical data was extracted from clinical records including Eastern Cooperative Oncology Group score, blood tests, imaging, pathology, stage, FLIPI score, treatment regimen, and outcomes. The pathological specimens were submitted to Prof. Gandhi's lab for the quantification of immune effector and checkpoint gene expression.

Summary of Results A total of 130 patients were identified. 98 cases were found to have complete chart reviews and pathology specimens. We identified 27 patients with localized disease (stage I-II) and 71 patients with advanced disease (stage III-IV). FFPE tissue was retrieved and tissues were cut and submitted for DMGE.

Conclusions We have established a patient-derived tissue

database of FL patients diagnosed at the OHS. This cohort will be used as a validation cohort in the development of an 'immune score' in patients with advanced stage FL. We expect this score will be predictive of survival in patients with FL that is independent of conventional clinical prognostic models.

489 **HIGH-DOSE DEXAMETHASONE IN IMMUNE THROMBOCYTOPENIA**

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Purpose of Study Immune thrombocytopenia (IT) is defined by a platelet count less than $100 \times 10^9/L$ in the absence of other causes. Corticosteroids are first line treatment, while IVIg, rituximab, splenectomy, and thrombopoietin receptor agonists are considered for relapsed or refractory disease.¹ High-dose dexamethasone (HD-DXM) has yielded the best results as first line therapy.²

The autoimmune pathophysiology of IT involves immune dysfunction, with abnormal antigen presentation to T-cells leading to platelet lysis and impaired megakaryocytes.³ IT has been linked to increased levels of CD16+ monocytes, which promote T-helper cells and downregulate regulatory T-cells.^{4,5} Myeloid-derived suppressor cells (MDSCs) are also suppressed in IT, and HD-DXM has been found to work at the transcription level to enhance MDSC activity.⁶

While the dose of HD-DXM is established (40 mg \times 4 days), the response is not sustained after one cycle (Table 1). Therefore, the optimal number and interval time between cycles, as well as addition of delayed consolidation therapy, are yet to be defined.

Methods Used Literature was reviewed. Multiple trials with different number of HD-DXM cycles and interval time between cycles are compared in Table 1.^{2,7-9}

Summary of Results See Table 1. Wei et al showed the first head to head comparison of HD-DXM and prednisone, with superior initial RR (82.1% vs 67.4%, $P=0.044$), complete RR (50.5% vs 26.8%, $P=0.001$), median time to response (3 days vs 6 days, $P<0.001$), and fewer side effects for HD-DXM.² Although sustained RR was unchanged (40.0% vs 41.2%, $P=0.884$), only 1-2 cycles of HD-DXM were administered. A statistically significant

Abstract 489 Table 1 Response Rates with HD-DXM

Study	#cycles* of HD-DXM	Initial RR† (%)	Sustained‡ RR (%)
Andersen	6 cycles Q 28 days	100	100
Cheng	1 cycle	84.8	42.4
Mazzucconi	6 cycles Q 28 days	89.2	67.6
V	4 cycles Q 14 days	85.6	74.4
Wei	1 cycle, if no response, 2nd cycle	82.1	40.0

*cycle=40 mg daily \times 4 days (160 mg)

†Response=improved platelet count by at least $30 \times 10^9/L$

‡Sustained=> 6 months

improvement in sustained RR is seen between the second and third cycles (75.8% vs 89%, $P=0.018$).⁸

Conclusions These findings suggests that a minimum of 3 cycles HD-DXM are needed. Adding a delayed consolidation phase with additional cycles of HD-DXM also warrants further investigation.

Infectious Diseases I Concurrent Session 2:00 PM Sunday, February 12, 2017

490 MORTALITY RISK AFTER HERPES ZOSTER INFECTION IN END-STAGE RENAL DISEASE PATIENTS

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Purpose of Study End-stage renal disease (ESRD) patients are at increased risk of developing herpes zoster (HZ) compared to the general population; however, the mortality risk in ESRD patients who develop the disease is unknown. We investigated the mortality risk within 1 year following a diagnosis of HZ in ESRD patients using the United States Renal Data System (USRDS).

Methods Used All incident dialysis cases from the USRDS for calendar years 2006–2009 were queried for a diagnosis of HZ and clinical covariates using ICD-9 and CPT-4 codes from Medicare inpatient hospital claims. The Charlson Comorbidity Index (CCI) was used to assess the number and severity of clinical covariates. Cox Proportional Hazards modeling was used to determine the adjusted hazard ratio (aHR) for death within 1 year between those with and without HZ, adjusting for clinical covariates.

Summary of Results For the 4-year study period, 221,546 ESRD patients were available for analysis. HZ was identified in 2,784 (1.3%). A 5% random sample of non-HZ patients was used for comparative analysis ($n=10,984$) giving a total analysis sample size of 13,768 (53.4% male, 63 ± 14.8 years old). Compared to those without HZ, those with HZ were more likely to score higher on the CCI, to have other clinical diagnoses apart from the CCI, and to be female, white, and older. Adjusting for other risk factors, those with HZ were 2.09 (95% confidence interval=1.93–2.27) times more likely to die within 1 year than those without HZ. The only demographic factor that showed an increased risk of death within 1 year was a one-year increase in age (aHR=1.03). The top 3 comorbid conditions significantly associated with mortality included malnutrition (aHR=1.47), bacteremia/septicemia (aHR=1.28), and increasing CCI (aHR=1.14).

Conclusions HZ is associated with an increased risk of death in ESRD patients. Older age and the severity of clinical covariates significantly increase mortality. HZ vaccination in the ESRD population may favorably impact mortality and warrants further study.

491 USE OF CEPHALOSPORINS FOR UNCOMPLICATED PEDIATRIC COMMUNITY-ACQUIRED PNEUMONIA

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Purpose of Study National guidelines for pediatric community-acquired pneumonia (CAP) published in 2011 recommend therapy with a penicillin for uncomplicated CAP, reserving cephalosporins and anti-staphylococcal drugs for the most ill patients. Our hospital created internal guidelines with these recommendations but high cephalosporin use continues. The purpose of this study was to review pneumonia cases to determine characteristics of patients treated with broad-spectrum antibiotics to guide interventions to improve antibiotic use.

Methods Used We reviewed patients discharged with a diagnosis of all-cause pneumonia from December, 2014 to August, 2015. Demographics, prior hospitalizations, comorbid conditions, antibiotics, chest radiograph findings, microbiology and complications were collected. High risk patients were defined as having: healthcare associated pneumonia (HCAP, admission in last 90 days), a condition predisposing to pneumonia (recurrent aspiration, cerebral palsy, tracheostomy) or complicated pneumonia (one or more of multi-lobe consolidation, moderate to large pleural effusion, lung abscess/cavity or vasopressor use).

Summary of Results There were 255 patients discharged with a diagnosis of pneumonia. Patients were predominantly male (52.5%) and black (48.6%). Median age was 2.7 (interquartile range (IQR) 3 to 9) years and median length of stay was 4 (IQR 1 to 7) days. There were 101 high-risk patients (84 (33%) with HCAP and/or a condition predisposing to pneumonia and 17 (7%) patients with complicated pneumonia). Of those with a bacterial etiology, 2 had *S. pneumoniae* (one blood, one pleural fluid), 3 had *Staphylococcus aureus* (1 blood, 2 pleural fluid), 3 had atypical pneumonia pathogens. Of the 159 subjects without high risk conditions, only 48 (24%) received ampicillin alone. Most (84, 52%) received ceftriaxone (25 (30%) of whom also received vancomycin or clindamycin) or an extended spectrum beta-lactam (e.g. piperacillin-tazobactam).

Conclusions Ampicillin is underutilized for uncomplicated pneumonia. Ceftriaxone with or without vancomycin or clindamycin was the most commonly used drug for pneumonia even among low-risk patients. Continued educational interventions are needed to reduce inappropriate use of ceftriaxone for uncomplicated CAP.

492 EPITOPE MAPPING OF MULTIVALENT M PROTEIN-BASED GROUP A STREPTOCOCCAL VACCINES

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10.1136/jim-2016-000393.495

Purpose of Study The M protein of group A streptococci is a leading vaccine candidate. Protection against GAS

infections has classically been considered ‘type-specific’, indicating that immunity to one M type would not afford protection against heterologous types. However, a recent sequence-based analysis of M proteins resulted in a new *emm* cluster typing system that classified 175 *emm* types into 48 *emm* clusters containing structurally and functionally related M proteins. The overall hypothesis is that immunity to GAS is largely cluster-specific, as opposed to type-specific, and that immunity to one M type may afford protection against multiple M types within the same cluster. To test this hypothesis, we used a novel computational structure-based design approach to select five M peptides from one M cluster (E4) that were predicted to elicit antibodies against all 17 members of GAS in the cluster. Synthetic (sE4) and recombinant hybrid (rE4) pentavalent vaccine antisera reacted with all 17 E4 M peptides and opsonized the majority of GAS in the E4 cluster. The current study was designed to precisely map the peptide epitopes responsible for eliciting cross-protective antibodies.

Methods Used Rabbit antisera against the sE4 and rE4 vaccines were used in ELISA to map the immunodominant epitopes of each vaccine. A panel of thirty-five 15mer synthetic peptides that overlapped by 10aa were used as solid-phase antigens and soluble inhibitors.

Summary of Results Immunodominant epitopes in the rE4 and sE4 vaccines were similar, indicating that antigenicity is determined by epitope structure and sequence, and less so by the vaccine assembly method. Cross-reactivity assays indicated that on average two distinct epitopes provided most of the cross-protection observed against each E4 M type. In some cases, cross-reactivity did not correspond with sequence homology, suggesting the importance of epitope structure in cross-reactivity.

Conclusions These results will be useful in determining key physicochemical and structural characteristics of broadly cross-reactive M epitopes. These data also suggest the possibility of designing precise, epitope-based GAS vaccines that are compact, yet broadly efficacious in most regions of the world.

493 C-REACTIVE PROTEIN PREDICTS SUBCLINICAL CARDIOVASCULAR DISEASE PROGRESSION IN HIV- BUT NOT HIV+ WOMEN

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Purpose of Study HIV infection is associated with an increased risk of cardiovascular disease (CVD), but identifying patients who would benefit from targeted CVD risk modification is challenging. CRP improves CVD prediction in the general population but its use with HIV is less clear. We assessed the association of CRP with subclinical CVD progression among women enrolled in the Women’s Interagency HIV Study (WIHS).

Methods Used Retrospective analysis of the WIHS

cardiovascular substudy, in which carotid artery (CA) ultrasound was performed at baseline (BL) and at follow-up visits from 2004–2013 to assess CA plaques and CA intima-media thickness (CIMT). BL plasma CRP was measured. We used multivariable logistic and linear regression models stratified by HIV status to determine the association of BL CRP with CA plaque and CIMT progression, adjusting for CVD risk factors.

Summary of Results 783 women [572 HIV⁺, 211 HIV⁻, 62% Black, 29% Hispanic, median age 41 (IQR 35–47) yrs] were followed for a median 6.6 (IQR 6.4–7.0) yrs. For HIV⁺ women, median CD4 was 452 (IQR 288–658) cells/mm³; 46% had HIV RNA <80 cop/mL at BL. BL median (IQR) 10-yr Framingham risk was 1% in both groups (p=0.43). BL median (IQR) CRP was 2.2 (0.8–5.3) mg/L in HIV⁺ and 3.2 (0.9–7.7) mg/L in HIV⁻ women (p=0.005). Unadjusted CA plaque progression occurred in 12% vs. 8% of HIV⁺ and HIV⁻ women, respectively. Mean (SD) CIMT change was 25 (47) μm in HIV⁺ and 26 (62) μm in HIV⁻ women. The adjusted odds of CA plaque progression in HIV⁺ women were 0.99 (95%CI 0.77–1.28) per unit higher CRP (p=0.94) and 3.74 (95%CI 1.34–10.24) in HIV⁻ women (p=0.01). The adjusted mean difference in CIMT change per unit higher CRP among HIV⁺ women was 3.0 μm (95%CI -1.5–7.5, p=0.20) and 5.4 μm (95%CI 0.2–10.7, p=0.04) in HIV⁻ women.

Conclusions CRP was associated with progression of CA plaques and CIMT in HIV⁻, but not HIV⁺, women despite similar BL CVD risk, suggesting that the pathogenesis of, and therefore the biomarkers associated with subclinical CVD may be different in the setting of HIV infection. Additional studies of CVD pathogenesis in the HIV population are warranted.

494 CHOLINE-BINDING-PROTEIN-A AS A TARGET FOR A UNIVERSAL STREPTOCOCCUS PNEUMONIAE VACCINE

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10.1136/jim-2016-000393.497

Purpose of Study The widespread use of *S. pneumoniae* protein-conjugated vaccine PCV7 in 2000 and PCV13 in 2010 decreased invasive pneumococcal disease (IPD) due to vaccine serotypes, but resulted in an increase of replacement serotypes. Identifying a protein consistent between serotypes that potentially can serve as a universal vaccine would prevent IPD and limit replacement serotypes. We investigated choline-binding protein A (CbpA), a cell wall protein of *S. pneumoniae*, as such a vaccine.

Methods Used We tested 199 isolates recovered from patients with IPD admitted to three affiliated hospitals from 1983 to 2014. Isolates were serotyped by Quellung and their penicillin susceptibility assayed. Genomic DNA from harvested colonies was extracted and amplified by PCR for detection of the *cbpA* gene region using previously published primers. All products were run on gel electrophoresis and sequenced. EMBL-EBI Clustal Omega and Percent Identity Matrix were used for analysis.

Summary of Results Of 186 isolates, 94% contained *cbpA*

gene by PCR and agarose gel electrophoresis and we sequenced 124 to date. We selected serotypes of PCV7 because five of these serotypes develop resistance. We cross-checked 53 strains of the seven serotypes in PCV7 and identified 95% or greater homogeneity among six serotypes - 6B, 9V, 14, 18C, 19F and 23F. Serotype 18C exhibited homogeneity with five, 19F with three, and 6B, 9V and 14 each with two serotypes. We sequenced 39 strains of four additional serotypes in PCV13 -1, 3, 7F and 19A - and identified homogeneity only with serotype 19A and three serotypes in PCV7-6B, 18C and 19F. Three resistant serotypes in PCV7-9V, 14 and 19F - and one in PCV13-19A - exhibited homogeneity with sensitive and intermediate PCV7 serotypes.

Conclusions The high level of homogeneity of the cell wall protein CbpA among serotypes of PCV7 suggested that CbpA may be a potential component of a universal *S. pneumoniae* vaccine provided that the protein elicits antibody production. A universal vaccine would likely reduce or eliminate the occurrence of replacement serotypes that cause most of the new IPD. The next step is to determine whether CbpA is immunogenic and induces protective antibody.

495 STREPTOCOCCAL SECRETED ESTERASE AS A GROUP A STREPTOCOCCAL VACCINE COMPONENT

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Purpose of Study M protein-based group A streptococcal (GAS) vaccines elicit bactericidal antibodies against vaccine *emm* types and non-vaccine *emm* types. However, gaps remain in the potential global coverage of infections which has prompted the search for additional antigens that are shared by many or all GAS. One such antigen is streptococcal secreted esterase (SSE), which has previously been shown to be protective in animal models of infection. SSE is a virulence determinant of GAS that inactivates platelet activating factor (PAF), a potent mediator of neutrophil chemotaxis. This study was undertaken to identify peptides of SSE containing linear epitopes that could serve as GAS vaccine components that elicit neutralizing antibodies.

Methods Used Recombinant SSE was purified from extracts of *E. coli*. Human sera were screened for SSE antibodies by ELISA and SSE-specific antibodies were purified by affinity chromatography. Antibody-mediated inhibition of SSE activity was detected using a modified version of a Cayman Acetylhydrolase kit. Four peptides potentially containing linear epitopes of SSE were synthesized based on their locations in the predicted 3-D structure of SSE. Reversal of antibody inhibition of SSE activity was assessed by pre-incubating purified SSE antibodies with inactive holoenzyme or synthetic peptides prior to adding to the colorimetric assay.

Summary of Results Serum from three volunteers had significant levels of SSE antibodies, as determined by ELISA. Of the three affinity-purified antibody samples, one showed significant inhibition of rSSE activity. Each of the four synthetic peptides showed modest reversal of antibody-

mediated inhibition of SSE activity. However, when tested in combination, significant reversal was observed.

Conclusions Human sera contain SSE antibodies but not all antibodies inhibit the esterase activity of the enzyme. Our results suggest that some neutralizing epitopes may be linear, which will be confirmed by testing a panel of overlapping 15mer peptides copying the entire sequence of SSE. Identification of short peptides that elicit neutralizing antibodies against SSE may prove to be important vaccine components that will broaden the potential coverage and efficacy of current GAS vaccines.

496 HIV RISK BEHAVIORS AMONG IMMIGRANT LATINO YOUTH: A PUBLIC HEALTH PRIORITY

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10.1136/jim-2016-000393.499

Purpose of Study HIV/AIDS disproportionately affects Latino youth in the US. Structural inequalities render immigrants more vulnerable to HIV. We compared rates of HIV sexual risk behaviors (HRB) among Latinos who immigrated at age 12 or younger (children migrants, CM) and those who did after age 12 (young adults migrants, YAM) and explored the association between acculturation strategies and HRB.

Methods Used We collected demographic, migration, acculturation strategies and sexual behaviors history (condom use, transactional sex, sex while intoxicated and sex with multiple partners) in a convenience sample of HIV (-) Latinos ages 18-29 in Atlanta. Acculturation was measured based on the *Bidimensional Acculturation Scale*. Socio-demographic and migration characteristics were summarized by descriptive statistics. Univariate and multivariable logistic regression models were applied to explore the effects of acculturation and age at migration on occurrence of HRB.

Summary of Results We enrolled 132 subjects [60% male, mean age 23 years (SD: 3.4)], 96% of them were Mexican. Ninety four percent of CM had a high school education or higher compared to 62% of YAM ($p < 0.001$). Fifty five percent of CM lived with their parents, compared to 15% of YAM ($p < 0.001$). Moreover, 79% of YAM had an undocumented immigration status, compared to 41% of CM ($p < 0.001$). YAM engaged in HRB significantly more than CM (73% vs. 53%, $p = 0.02$) and these differences were driven primarily by poor condom use (56% vs. 31%, $p = 0.009$) and having sex with a commercial sex worker (13% vs 0% $p = 0.001$). CM utilized assimilation and integration strategies (both $p < 0.05$), while YAM adopted primarily the separation strategy ($p < 0.001$); which was more frequently seen in participants who engage in HRB. Multivariate analysis showed that odds of HRB were two and three times more likely in males and when living with someone other than parents, respectively (both $p < 0.05$). Undocumented immigration status and using separation strategies had borderline significance for HRB (both $p < 0.1$).

Conclusions YAM engage in HRB more than CM, notably males and those living outside the parental household. Scaling up PrEP, improving condom use amongst recently immigrated undocumented Latino male youth and curtail-ing their social isolation are critical in decreasing HIV risk.

497 NECK INFECTIONS AT A MID-SOUTH CHILDREN'S HOSPITAL

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10.1136/jim-2016-000393.500

Purpose of Study Acute lymphadenitis (LAD) and deep neck abscess (NA) are common infections in children. Signs and symptoms vary as deeper infections may have more swallowing and respiratory problems. Patients are often treated with broad spectrum antibiotics but coverage for gram negative pathogens may be unnecessary. The purpose of this study was to describe the clinical findings and microbiology of neck infections to determine the most appropriate antibiotic therapy.

Methods Used Patients with LAD and NA (retropharyngeal, parapharyngeal) admitted from January, 2009 to December, 2014 at Le Bonheur Children's Hospital in Memphis, TN were reviewed. We collected demographic information, presenting signs and symptoms, such as fever, sore throat, neck pain, and drooling. Diagnostic imaging, surgical procedures and microbiology results and antibiotics were recorded.

Summary of Results There were 376 patients with a discharge diagnosis of LAD or NA; 324 LAD or NA identified on CT scan. The median age was 3.0 years (range 0–18 years), 58% were male, 70% were black, 39% had LAD only and 61% had NA with or without LAD. Patients with LAD were more likely to have visible neck swelling (82% vs 66%, $p=0.001$) and less likely to have odynophagia (2% vs 8%, $p=0.02$) or sore throat (12% vs 28%, $p=0.001$). Clindamycin (97%) and ceftriaxone (83%) were the most commonly used antibiotics with 82% receiving both (70% LAD, 88% NA, $p<0.001$); 14% received vancomycin and ceftriaxone. 238 patients had surgical drainage of infection and cultures were done in 18% of LAD and 32% of NA. Cultures (blood and abscess) grew Group A *Streptococcus* in 16 cases, methicillin susceptible *Staphylococcus aureus* in 17, methicillin resistant *Staphylococcus aureus* in 37 and 9 other pathogens. Five of the other pathogens that would not be treated by clindamycin: 1 *Citrobacter* (LAD), 1 *Klebsiella* (NA), 1 *Hemophilus* and 2 non-tuberculous mycobacteria.

Conclusions In this group of children with neck infections, NA was most common. There were no clinical findings that sufficiently discriminated between LAD and NA. Most positive cultures grew gram positive organisms. Clindamycin (or vancomycin in regions with high resistance to clindamycin in *S. aureus*) can be used to empirically

treat non-life threatening, community-acquired, neck infections.

498 IMPLEMENTATION OF HIV PRE-EXPOSURE PROPHYLAXIS IN THE HEALTH DEPARTMENT SETTING IN ATLANTA, GA

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10.1136/jim-2016-000393.501

Purpose of Study African Americans and men who have sex with men (MSM) are disproportionately affected by HIV, and factors such as poverty and lack of access to health care contribute to these disparities. HIV incidence in Atlanta, GA is high, and access to HIV pre-exposure prophylaxis (PrEP) could limit its use. Therefore, we implemented an open-access PrEP clinic at a county health department.

Methods Used Demographic and HIV risk behavior data were collected via chart review from all patients seen in the Fulton County Health Department PrEP Clinic from its inception in October 2015 through September 2016 and summarized with descriptive statistics. Patients were deemed eligible for PrEP therapy using a standardized questionnaire based on CDC guidelines. Patients engaged in quarterly follow-up appointments were defined as retained in clinic; patients with a lapse in follow-up appointments ≥ 5 months were defined as not retained. Factors associated with retention in PrEP clinic were assessed with logistic regression.

Summary of Results Since its inception, 292 patients were evaluated for PrEP in the clinic: 244/288 (85%) male, 172/249(69%) black, 127/290(44%) aged 18–28 years, 185/239(77%) MSM, and 79/140(56%) uninsured. To date, 76/203(37%) patients were retained in PrEP clinic. In unadjusted analyses, non-black race (3.8; 95% CI 2.01, 7.23) was significantly associated with retention. Age, gender, education, income, sexual orientation, and insurance status were not significantly associated with retention. Phone contact was attempted for 93 patients who were not retained in PrEP clinic; of the 43 who were reached, 15 (35%) were no longer interested in taking PrEP, 13(30%) had difficulty scheduling an appointment, and 4(12%) did not start PrEP due to side effect concerns.

Conclusions Implementation of PrEP in the county health department setting is feasible. MSM comprise the largest risk population in our clinic; however, additional efforts will be needed to identify women at risk for HIV. Furthermore, we have identified significant challenges with retention in PrEP clinic that deserve attention, particularly for black patients. Further research will be needed to design and target PrEP retention interventions for key populations at risk of HIV infection in Atlanta.

Neurology and Neurobiology Concurrent Session 2:00 PM Sunday, February 12, 2017

499 THE CONTRIBUTION OF PRO-INFLAMMATORY CYTOKINES TO MECHANISMS OF NEURODEGENERATION IN MULTIPLE SCLEROSIS

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10.1136/jim-2016-000393.502

Purpose of Study We previously reported that antibodies to the RNA binding protein heterogeneous nuclear ribonuclear protein A1 (hnRNP A1) contribute to neurodegeneration in multiple sclerosis (MS). The purpose of this study is to explore the role of individual and combinations of pro-inflammatory Th17 cytokines on molecular events important to the pathogenesis of MS, including mislocalization of hnRNP A1 and the formation of stress granules (SGs). Importantly, both mislocalization (from neuronal nucleus to cytoplasm) of hnRNP A1 and SG formation have been shown to contribute to the pathogenesis of neurodegenerative diseases.

Methods Used SK-N-SH cells (a neuronal cell line) were exposed to individual and combinations of Th17 cytokines (IL-17A, IL-23, IL-1 β , TGF- β , and IL-6) in vitro and examined for SG formation, mislocalization of hnRNP A1 and colocalization of hnRNP A1 with a SG marker, Poly (A)-binding protein (PABP).

Summary of Results Untreated SK-N-SH cells showed nuclear localization of hnRNP A1 and no SG formation. After treatment with all of the Th17 effector cytokines (IL-17A, IL-23, IL-1 β) together, there was both hnRNP A1 mislocalization to the cytoplasm and PABP positive SG formation. Under these conditions, hnRNP A1 colocalized with the SGs. When individual effector cytokines were tested, only exposure to IL-1 β resulted in colocalization of hnRNP A1 within SGs. SK-N-SH cells treated with a combination of Th17 inducer cytokines (TGF- β , IL-6) showed some hnRNP A1 mislocalization, but hnRNP A1 did not colocalize within the SGs formed. However, in cells exposed to TGF- β alone, there was SG formation, hnRNP A1 mislocalization and colocalization with the SGs. After treatment with IL-6 alone, hnRNP A1 mislocalized to the cytoplasm and SGs formed, but hnRNP A1 did not colocalize within the SGs.

Conclusions Taken together, these data suggest a potential role of pro-inflammatory Th17 cytokines in the pathogenesis of MS utilizing hnRNP A1 mislocalization and SG formation as mechanisms of neurodegeneration.

500 BEHAVIORAL & MOLECULAR EFFECTS OF ANTENATAL SSRI EXPOSURE

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10.1136/jim-2016-000393.503

Purpose of Study Maternal mood disorders complicate 15% of pregnancies & are often treated with SSRI antidepressants such as fluoxetine (FLX). Clinical studies have reported associations of maternal antenatal SSRI use with behavioral disturbances in early childhood & autism spectrum disorders (ASD). We seek to understand the behavioral & molecular effects of antenatal FLX in ePet-EYFP (Enhanced Yellow Fluorescent Protein) transgenic mice whose serotonin (5HT) neurons are genetically tagged with EYFP. We hypothesize that antenatal FLX exposure will lead to behavioral pathogenesis by disrupting the regulatory programs that govern 5HT neuron development.

Methods Used Pregnant ePet-EYFP mice were treated with FLX 15 mg/kg/d i.p. or saline from E9-E17. We tested offspring (N=40) longitudinally at 4, 10, & 18 months for emotional behavior with the elevated plus maze (EPM), marble burying (MB), open field, acoustic startle response (ASR), & the light-dark box, as well as cognitive behavior with novel object recognition & fear conditioning. We flow-sorted EYFP+ 5HT neurons from E18 embryos (N=3 replicates) for RNA-seq & used Cufflinks v2.2.1 for gene expression quantification & differential expression analysis. Behavioral analysis was done with multilevel hierarchical analysis and modeling (Figure 1).

Summary of Results In ePet-EYFP transgenic mice, antenatal exposure to FLX resulted in behavioral pathogenesis with anxiety-like behaviors in: males at 4-months-old by EPM; females at 10-months-old by MB; & females at 10- & 18-months-old by ASR. We saw no behavioral pathogenesis by cognitive testing. RNA-seq identified 546 genes (out of 22,549 genes) whose expression changed at least 1.5X fold at <5% FDR between FLX & control groups. Two of the downregulated genes were from the serotonergic-type gene battery: post-synaptic serotonin receptors 5HT1f & 5HT4. Seven of the downregulated genes are associated with ASD: WAC & MEF2C (Figure 2) & the Rho family of GTPases (specifically VAV3, ARHGAP15, ARHGAP10, ARHGAP25, DEPDC1B; Figure 3).

Conclusions In ePet-EYFP transgenic mice, antenatal exposure to FLX resulted in behavioral pathogenesis with anxiety-like behaviors at 4-, 10-, & 18-months; decreased gene expression in the serotonergic-specific gene set for 5-HT1f & 5-HT4; & decreased expression for two genes (WAC & MEF2C) and one gene network (Rho family of GTPases) associated with ASD.

501 EARLY LIFE GENERAL ANESTHESIA INDUCED BY ISOFLURANE PLUS NITROUS OXIDE IMPAIRS LATER COGNITIVE TEST PERFORMANCE IN MONKEYS

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10.1136/jim-2016-000393.504

Purpose of Study In both rodents and primates general anesthesia (GA) during early brain development produces neurotoxicity that can lead to subsequent impairment in cognitive function. This is concerning given the number of young children that undergo GA for surgical and other

procedures. This study examined the effects of neonatal GA induced by isoflurane plus nitrous oxide on the later ability of monkeys to perform several operant tasks that measure cognition and complex brain function.

Methods Used Eight monkeys were anesthetized with 1.5% isoflurane and 70% NO₂ in oxygen for 8 hours at PND 5 and six monkeys served as controls. At 7 months subjects began training to perform food-reinforced operant tasks designed to assess aspects of learning [incremental repeated acquisition (IRA)], motivation [progressive ratio (PR)], color discrimination [conditioned position responding (CPR)] and short-term memory [delayed matching-to-sample task (DMTS)].

Summary of Results Monkeys exposed to Iso/NO₂ progressed through early training levels for each task at approximately the same rate as control monkeys. However, once the final parameters for the IRA and PR tasks were implemented, exposed monkeys began to significantly lag behind their unexposed peers in their level of performance. In contrast, the performance of exposed monkeys on the CPR and DMTS tasks was no different from that of controls based on accuracy on the CPR task and on the rate of acquisition of longer delays on the DMTS task.

Conclusions These data indicate that a single bout of Iso/NO₂-induced general anesthesia can result in significant, long lasting impairments in learning and motivation which persists for many months and, in some cases, appear to be permanent. Since accuracy on this same IRA task has been found to correlate significantly with IQ in children, it is reasonable to assume that similar exposures in children would also lead to deficits in IQ. Therefore, it is important to develop strategies to mitigate the adverse effects of the use of these agents during development. (Supported by NCTR Protocol E7285)

502 A PTSD-INDUCTION PARADIGM FOR MICE

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10.1136/jim-2016-000393.505

Purpose of Study Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric disorder which affects approximately 5 percent of children in the US. Symptoms, including hyperarousal, hypervigilance, and abnormal sleep cycles, manifest following exposure to a traumatic event, which often includes sexual and physical violence, and neglect. While the cause of the disorder seems clear, the etiology of the disease is highly heterogenous. Further research is needed to fully understand the underlying biological mechanisms of this disease.

Methods Used Animals are exposed to a traumatic stimulus in the form of an unavoidable electric foot shock. PTSD-affected animals are diagnosed through a series of behavioral tests for various symptoms of PTSD: light/dark transfer and marble burying tests for increased risk assessment, auditory startle response and pre-pulse inhibition for hyperarousal, and 48-hour home cage locomotion for sleep cycle disruptions. Animals undergo a restrained stress test for assessing corticosterone response. Animals are scored on their performance in these behavioral tests; animals with sufficiently high scores are designated 'PTSD

vulnerable,' while animals with sufficiently low scores are designated 'PTSD resilient.'

Summary of Results We exposed 48 wild type male mice to the PTSD-induction paradigm, and identified 10 PTSD-affected and 10 PTSD-resilient animals. We performed statistical analysis to ensure that the paradigm was reliably and consistently applied and that the behavioral symptomatology between the affected and resilient animals were statistically different. We will perform ELISA for corticosterone to determine the stress-induced corticosterone response for the two groups, will assess large-scale brain area activation patterns in fixed brains, and analyze blood for biomarkers and predictors for PTSD vulnerability and severity.

Conclusions Currently, investigations into PTSD rely heavily on epidemiologic and post mortem data on affected individuals. A reliable and reproducible paradigm for the induction of PTSD in mice allows for reater investigative power, including structural, molecular, biochemical, and behavioral investigations on living affected organisms, and transgenic animals. We feel that establishing a reliable paradigm for PTSD induction in mice positions our lab to make valuable advances in research into this debilitating disorder.

503 MECHANISM OF TRANSFORMING GROWTH FACTOR BETA GROWTH-SUPPORTIVE EFFECT ON DELAYED NERVE REPAIR

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10.1136/jim-2016-000393.506

Purpose of Study Previous rat models have demonstrated that suboptimal functional recovery after injury to large nerve trunks is mostly due to chronic Schwann cell denervation and neuronal axotomy. This study examined TGF-β/Smad signaling pathway involved in modulating the mitogenic effects of TGF-β1 and forskolin on Schwann cell reactivation and axonal regeneration

Methods Used Adult female rats were used for chronic tibial nerve injury and delayed repair. After 2 months, end-to-end repair was done and treated with TGF-β1 (1 ng/mL), TGF-β1 plus forskolin (0.5 μM, T/F), or saline. After 6 weeks, the site of injury-repair and distal nerve stump were harvested. Tissues were homogenized and processed for total RNA and protein extraction. Total RNA was prepared for real-time RT-PCR analysis using Taqman probe to Smad2, Smad3, Smad4, and Smad7. Western blot was carried out for Smad2, 3, 4, 7, and myelin protein zero (MPZ) and analyzed by chemiluminescence staining and image using ChemiDoc MP imager.

Summary of Results Compared to saline, gene and protein levels for Smad2 and Smad3 did not change at the site of repair treated with either TGF-β1 or T/F. However, in the distal stump, expression of Smad2 and Smad3 increased 4-fold. The expressions of Smad4 and Smad7 did not change at the site of repair. In the distal stump, Smad4 increased 4-fold and Smad7 increased 10-fold after T/F and 4-fold and 8-fold after TGF-β1. However, protein levels

for Smad4 increased at both the site and distal stump after TGF- β 1 (site-44 fold; distal-5-fold) and T/F (site-40 fold, distal-23-fold). The protein levels for Smad7 did not change at site but increased 5- and 6-fold after TGF- β 1 and T/F in the distal stump. Protein levels for MPZ increased 3-fold at the site. In the distal stump, MPZ increased 17-fold after TGF- β 1 treatment and 59-fold after T/F treatment.

Conclusions The mitogenic effects of TGF- β 1 and forskolin on axonal regeneration and Schwann cell reactivation involve participation of the common Smad4 and the inhibitory Smad7 signaling components suggesting alternative pathways are induced in maintaining Schwann cells in a reactivated state necessary for axonal regeneration

504 NEUROCOGNITIVE DEVELOPMENT IN INTRA UTERINE GROWTH RESTRICTED NEWBORN RATS

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10.1136/jim-2016-000393.507

Purpose of Study Intra uterine growth restriction (IUGR) follows prematurity as the number two cause of perinatal morbidity & mortality worldwide. IUGR is associated with oxidative stress (OS), which can cause delay in neurocognitive developmental (NCD) outcome. There is limited research on the effect of OS exposure during pregnancy & NCD outcomes. This study focuses on the effect of OS on motor & behavioral skills of low birth weight (LBW) rat pups with IUGR due to placental insufficiency induced by reduction in uterine perfusion

Methods Used A rodent model of placental insufficiency was induced by reduced uterine perfusion (RUP) surgery in pregnant rats at 14 days of gestation that lead to IUGR & delivery of LBW offspring. Control & LBW offspring were examined at postnatal days (P) 7, 13, & 20 using grip strength test (GST), open field test (OFT) & novel object recognition test (NORT)

Summary of Results GST: Offspring from dams exposed to RUP showed significant \downarrow in grip strength at P7 compared to offspring from control dams. (1.39 ± 0.16 vs. 0.40 ± 0.12 , $P < 0.05$ Control vs Restricted). Additionally, trends of \downarrow at P13 and increments at P20, were identified when compared to offspring from control dams. Figure(F)1

OFT: Offspring from dams exposed to RUP showed significantly \downarrow activity at P20 when compared to offspring from control dams. (24.2 ± 3 vs. 14.3 ± 2 , $P < 0.05$ Control vs Restricted). Also, trends of \downarrow activity at P7 and \uparrow activity at P13 were detected when compared to offspring from control dams (F2)

NORT: Offspring from dams exposed to RUP showed a trend of \downarrow interest in novel objects when compared to offspring from control dams (F3)

Body Weight: Offspring from RUP dams showed significant \downarrow in body weight at P20 vs offspring from control dams (71.82 ± 4 vs. 60.16 ± 2 , $P < 0.05$ Control vs Restricted) (F4)

Conclusions Offspring from dams exposed to RUP

showed differences in body weight, grip strength, open field activity, & interest in novel object when compared to offspring from control dams. These findings suggest that early exposure to RUP could alter motor & behavioral skills later in life. Our future studies will compare oxidative stress markers in the brain of control and IUGR rat's offspring. Further studies will explore antioxidant compounds & their neuroprotective effects on IUGR rat pups.

505 MACHINE LEARNING PREDICTIVE MODELING FOR MECHANICAL THROMBECTOMY

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10.1136/jim-2016-000393.508

Purpose of Study Logistic regression was used to assess mechanical thrombectomy patient outcomes in major trials, but machine learning has not been appropriately assessed for predicting patient outcomes including modified rankin scale (mRS) or class 2 hemorrhage including symptomatic intracranial hemorrhage (sICH). This abstract will compare machine learning predictive models to traditional multivariate logistic regression for outcomes including prediction of class 2 parenchymal hematoma and hemorrhagic infarction. Functional outcomes including mRS will also be compared.

Methods Used 600 consecutive patients evaluated with CT perfusion for stroke were retrospectively analyzed. Patients were included if thrombectomy was attempted and excluded if the pre-intervention dataset was incompletely documented, 85 patients were included in the study. Previous RCT and retrospective analysis guided items selected for data collection. Using data available prior to intervention, machine learning models including artificial neural network (ANN), support vector machine (SVM), decision tree, naive bayes, and also traditional multivariate logistic regression were created with bootstrap sampling to predict hemorrhage, and symptomatic intracranial hemorrhage. T-test with Sidak multiple testing correction was used for to compare models overall accuracy and area under the receiver operator curve (AUC) generated from model application to unseen testing data.

Summary of Results SVM (accuracy 67.01% \pm 7.73 AUC .739 \pm .089) and naive bayes (accuracy 72.75 \pm 7.49% AUC .726 \pm .088) models significantly outperformed logistic regression, (accuracy 62.34 \pm 8.01%, AUC .536 \pm .085) with $p < .001$ for both overall accuracy and AUC at hemorrhage classification. In predicting class 2 hemorrhage (including SAH and sICH) all machine learning models significantly outperformed logistic regression, with $p < .001$ for accuracy and AUC. Analysis for mRS showed SVM (AUC .903 \pm 0.55) and Naive bayes (AUC 0.936 \pm .070) to be superior with $p < .001$.

Conclusions: Machine learning methods outperform logistic regression at the prediction tasks including functional outcome and prediction of complications based on pre-intervention data and could improve outcomes by aiding the neurointerventionalist with patient selection.

506 PATIENT REPORTED OUTCOMES IN STROKE CLINICAL TRIALS

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10.1136/jim-2016-000393.509

Purpose of Study Stroke is the 5th-leading cause of death in the US and the major cause of disability. Many patients who have suffered from strokes are left with neurological deficits that may vary considerably from patient to patient. Solicitation of patient reported outcomes is therefore imperative.

Methods Used We examined a list compiled in 2013 by Magin et al. of representative stroke-related, randomized clinical trials published in 10 high-impact journals between 2002 and 2012 to assess whether PROs were collected and which constructs were reported. We categorized PRO measures as stroke-specific (e.g. Stroke Impact Scale), health profile and utility scales (e.g. Beck Depression Scale), or general (e.g. pain visual analog scale). Two reviewers independently abstracted PRO measures from each article and disagreements were resolved by consensus. Fisher's exact test was used for statistical analyses.

Summary of Results Of the 99 articles that met study inclusion criteria, 20% concerned prevention, 22% acute treatment, and 58% rehabilitation. A plurality of trials were European (43%) followed by studies based in the US (25%), Asian countries (10%), and Australia (10%). Altogether, 37% of studies used a PRO of any kind. Stroke-specific PROs were collected in 17% of studies, health profile and utility scales were used in 17%, and general PROs were used in 23%. There were no significant differences in PRO use with regards to year of publication or study location. Health profile and utility scales ($p=0.01$) and unclassified PROs ($p<0.001$) were most-commonly reported in rehabilitation trials. Stroke-specific PROs were most commonly published in the journals *Brain* and *Journal of Stroke and Cerebrovascular Diseases* ($p=0.001$).

Conclusions Overall, our review and analysis detected a low prevalence and a large degree of heterogeneity of PRO measures reported in stroke-related clinical trials. Future stroke research must routinely incorporate PROs into the study design to help patients, caregivers, and providers make informed decisions about stroke prevention, treatment, and rehabilitation options that yield outcomes of greatest importance to them.

507 ADRENOMYELONEUROPATHY PRESENTING AS CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY MIMIC

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10.1136/jim-2016-000393.510

Introduction Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a neurological disorder

characterized by progressive weakness, hyporeflexia and impaired sensory function in the arms and legs, caused by damage to the myelin sheath of peripheral nerves. Adrenomyeloneuropathy (AMN) is milder adult form of Adrenoleukodystrophy (ALD). It affects spinal cord and peripheral nerves, and less often brain. Presenting symptoms may include adrenal insufficiency, incontinence, gait instability, sensory changes, hyperactive reflexes and spasticity. We present a case with AMN presenting as a CIDP mimic. The primary purpose of our study was to determine if cases of AMN presenting as a CIDP mimic have been reported, and to review the varying clinical presentations and findings.

Case We have a 23-year-old Male who has had a 2 year history of progressive weakness without spasticity, decreased sensations and reflexes. EMG/NCS were suggestive of demyelinating polyneuropathy. The presumed diagnosis was CIDP. Despite treatment with IVIG and immunosuppressant therapy he continued to deteriorate. Over the next year new myelopathic exam findings also emerged, and he subsequently developed adrenal insufficiency as well. A brain MRI showed abnormal enhancement extending bilaterally from the inferior thalamus, cerebral peduncle, anterior pontine and medulla which was non-specific but concern for a process other than CIDP. Given his young age and a history of a prior sibling's death at a young age for an unknown 'muscular dystrophy', the diagnosis of an ALD spectrum disorder was considered. Serum VLCFA were drawn and noted to be elevated, confirming AMN in the setting of his clinical findings. No other cases of AMN diagnosed as CIDP were found.

Conclusion AMN is a rare inherited disease and has many varying clinical presentations. This case demonstrates that AMN can present as CIDP, which has not been previously documented in literature. Our case demonstrates that early states of AMN can present as CIDP and it is not until later stages where a myelopathic picture arises. In adolescent males presenting with progressive weakness, hyporeflexia, or chronic neuropathy, AMN should be considered.

508 PAROXETINE LOWERING THE THRESHOLD FOR CRACK DANCING

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10.1136/jim-2016-000393.511

Case Report Choreoathetosis is a well documented phenomenon which literally means irregular migrating contractions with writhing. Differentials for this phenomenon consist of: cocaine use, anti-psychotic medications, Parkinsons Disease, Huntingtons Disease, and Cerebellar Tumors. We present a first time occurrence of choreoathetosis also known as the 'crack dance' in a patient one month after beginning Paroxetine for Major Depression. Choreoathetosis in cocaine use is secondary to excess dopamine at the synaptic cleft. We propose that having started Paroxetine reduced the cocaine threshold for development of choreoathetosis, as the patient had no such previous symptoms with his cocaine use in the past.

We present a 32-year-old-male with a past medical history of hypertension, major depressive disorder, and chronic cocaine abuse who presented with uncontrolled limb and facial movements. He initially noticed abnormal movements of his mouth, which then progressed into full body spasms. He had no other complaints and was alert and oriented. Patient was placed on Paroxetine by his PCP one month before these abnormal movements began for Major Depression. His vitals were within normal limits on presentation. A urine toxicology screen was positive for cocaine. He received diphenhydramine and benztropine without relief. The choreoathetosis lasted for 2 days and resolved with fluids and benzodiazepines.

Cocaine inhibits dopamine transporter receptors thereby blocking its reuptake which results in an increase in dopamine availability at the synaptic cleft. Selective Serotonin Reuptake Inhibitors (SSRIs) such as Paroxetine inhibit serotonin reuptake resulting in an increase of serotonin at the Synaptic Cleft. Serotonin also has an affinity for dopamine receptors. In our patient his recent use of Paroxetine most likely synergistically increased dopamine activity thereby lowering the threshold for the development of choreoathetosis. One case report showed a similar presentation in a 37 year old male after taking 3 consecutive doses of 'bath salts' intravenously. The active compounds in bath salts are 3,4-methylene-dioxypyrovalerone or 4-methylmethcathinone, which inhibit norepinephrine and dopamine reuptake. We propose that the recent use of Paroxetine lowered the threshold to develop choreoathetosis in the setting of cocaine use.

509 EXTRA-CRANIAL CAROTID EMBOLCTOMY AND ENDARTERECTOMY IN ACUTE ISCHEMIC STROKE

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10.1136/jim-2016-000393.512

Purpose of Study Cardio-embolic stroke account for 14–30% of ischemic strokes, approximately half of which are from non-valvular atrial fibrillation. Common carotid thrombosis is an atypical location for cardiogenic emboli. Embolectomy & carotid endarterectomy are not often performed acutely due to concern of Hyper-perfusion syndrome. Primary purpose of the study is to review literature to determine the incidence & utility of surgical intervention in acute ischemic stroke with extra-cranial carotid involvement.

Methods Used Articles on PubMed were reviewed utilizing the phrases 'embolectomy', 'carotid endarterectomy' & 'acute ischemic stroke'. Articles were analyzed to determine if surgical intervention was performed extra-cranially for an acute (< 2 days) thrombosis. Cases with stenting & intra-cranial intervention were excluded.

Summary of Results 15 articles were retrieved and 2 cases reviewed. Acute embolectomy & surgical carotid intervention for treatment of acute stroke is uncommon. Both reviewed cases presented with acute ischemic stroke with extra-cranial carotid involvement & underwent urgent surgical intervention. Within 1 week of surgery both patients demonstrated >60% improvement in NIHSS score. On

follow up both patients showed favorable prognosis with mRS of 2 or less. No significant complications were noted from surgical intervention or hyper-perfusion related injury. Our case involved an 85-year-old male with PMHx of HTN & Atrial fibrillation (not on anticoagulation) presenting with left sided motor deficits & right gaze preference. He was given an NIHSS score of 8 & received IV-tPA. CTA neck revealed thrombus of the distal right common carotid artery extending into the internal carotid artery resulting in >70% stenosis. The next day patient underwent carotid embolectomy & endarterectomy. On day 7 he was discharged to an acute rehabilitation facility.

Conclusions Acute stroke due to high-grade stenosis of cerebral and/or carotid vasculature is characterized by severe progression & poor outcome. Maintaining reperfusion of affected intra-cranial vessels depends on the condition of the carotid artery that feeds into it. Our case & review reinforces that urgent surgical approach in acute ischemic stroke with high-grade carotid stenosis might be a reasonable rescue therapy with a favorable prognosis in carefully selected patients.

Nutrition Concurrent Session 2:00 PM Sunday, February 12, 2017

510 ROLE OF NUTRITION IN POSTNATAL GROWTH OF EXTREMELY PREMATURE INFANTS- A SINGLE CENTER EXPERIENCE

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10.1136/jim-2016-000393.513

Purpose of Study Appropriate growth in extremely premature infants is achieved through adequate nutrition, and has been linked to improved neurodevelopmental outcomes. However, meeting nutrition goals in this population is challenging due to clinical instability and immature organ systems. The purpose of this single-center retrospective chart analysis was to compare weight Z-scores from birth and discharge of preterm infants, and determine the relation of macronutrients provided during their hospital stay.

Methods Used Daily enteral and parental intakes were collected on 50 preterm infants, born under 1500 grams and less than 32 weeks gestation, from one Level IV neonatal intensive care unit. Average birth weight and gestational age were 1035 grams and 27.8 weeks respectively; average length of stay was 70 days. Excluded were infants with birth defects including cardiac, gastrointestinal and genetic abnormalities. Those treated for medical NEC were analyzed initially and then separated. Calories and protein provided daily were compared to ideal goals, and to stepwise realistic goals. Deficits were calculated again, using enteral equivalents to adjust nutrition provided intravenously. Infants were weighed daily, and Z-score data was collected weekly. Acceptable discharge Z-scores were considered greater than -1.

Summary of Results When compared to a lower threshold of realistic nutrition goals, infants accrued a positive balance. However, deficits existed in both calories and protein when compared to ideal goals. Only 4% of all infants achieved a positive change in weight Z-score, from birth to discharge. 58% of infants were discharged with an unacceptable Z-score of less than -1 , and nutrient deficits were slightly greater in these infants.

Conclusions Nutritional deficits begin to accumulate on day one, and require aggressive nutrition to overcome. Although realistic goals were met, infants did not meet the ideal goals, resulting in a deficit that was not regained and which correlated to lower discharge Z-scores. This raises an interesting question that estimated goals need to be reexamined, and could be closer to the ideal goals. Further research is warranted to determine the most accurate nutrient goals to produce acceptable weight gain in preterm infants.

511 EFFECT OF HIGH PROTEIN INTAKE ON PRETERM INFANT GROWTH AND BODY COMPOSITION

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10.1136/jim-2016-000393.514

Purpose of Study Standard growth goals for premature infants are based on the age-equivalent reference fetus. Premature infants often fall short of meeting these goals by the time of hospital discharge. While typical feeding regimens increase weight gain, fat accretion may be increased which could program the body for disease later in life. We wanted to determine if a high protein diet in premature infants could increase weight gain without affecting fat accretion, similar to that shown in older infants.

Methods Used This IRB-approved, prospective, controlled trial randomized infants born <32 weeks gestational age to receive either the Enhanced Diet (protein-energy ratio [PER] 4 grams/100 calories) or Standard Diet (PER 3 grams/100 calories) once an infant reached full enteral feeds. Depending on maternal diet choice, macronutrients from a 24-hour pooled sample of maternal human milk was analyzed weekly, provided by the donor milk bank, or provided by the formula company. Human milk was fortified and/or liquid protein was added to formula to achieve the desired PER. Growth and body composition measurements were obtained weekly using air displacement plethysmography. The study continued for four weeks or until discharge. Enhanced diet infants were compared to standard diet infants using t-tests for weight gain and repeated measures for fat accretion.

Summary of Results Weight gain was 15.8 g/kg/day (95% CI 13.9, 17.7) for the Enhanced Diet group (n=14) versus 14.1 g/kg/day (95% CI 12.8, 15.5) for the Standard Diet group (n=13), p=0.12. Fat accretion did not differ (p=0.29) between groups.

Conclusions These findings may support our hypothesis that a high protein diet in premature infants improves weight gain without increased fat accretion once we are able to achieve our target enrollment of 36.

512 DOES PROTEIN HELP REGAIN HEAD GROWTH IN MICROCEPHALIC INFANTS WITH BIRTH WEIGHTS OF ≤ 1 KG?

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10.1136/jim-2016-000393.515

Purpose of Study To study if the differences in head growth can be explained by nutritional differences in babies with birth weights (BW) of ≤ 1 kg (ELBW).

Methods Used A retrospective chart review was done for all ELBW preterm infants born 2013–15. Gestational age (GA), weight & head circumference (HC) centiles @ birth, and @ D/C, mean daily protein, calories, fluids/kg while on full enteral feeds, and morbidities such as BPD, NEC, IVH ROP were collected. Growth velocity (GV) was calculated using an exponential model. All babies received 4 g/kg/d of protein from birth while on TPN. Infants were excluded if they died before reaching 36 weeks of corrected GA or never reached full enteral feedings. Postnatal growth restriction (PNGR) was defined as weight or HC AGA @ birth becoming ≤ 10 th centile (SGA) at @ D/C or 40 weeks CGA. We compared **Group 1** (AGA for HC @ birth becoming SGA for HC @40 wks or D/C) with **Group 2** (SGA for HC @ birth becoming AGA for HC @ 40 wks or D/C).

Summary of Results 156 infants were analyzed. Mean BW was 784 \pm 140 grams and median GA -26 weeks. The majority were African American (84%) and female (54%). PNGR occurred for weight in 44% and in 19% for HC. 7.3% and 28% of SGA infants at birth became AGA for weight and head respectively @ D/C. There was no statistically significant difference in the mean protein and calorie intake between AGA& PNGR for weight. However, mean protein intake was significantly higher in Group 2 (3.88 \pm 0.28 g/kg) vs Group 1 (3.61 \pm 0.20 g/kg), p=0.005. Baseline characteristics of Group 1 and Group 2 were comparable (Table 1). Linear regression showed a significant correlation between protein intake and growth velocity controlling for total calories, GA, CLD and NEC.

Conclusions Higher enteral protein intake, but not calories was associated with higher GV, and regain of normal HC in more ELBW infants born with microcephaly. Some microcephaly at birth can be reversed with higher protein administration.

Abstract 512 Table 1

Parameters	Group1 (N=23) Mean +/-	Group2 (N=10) Mean +/-	P value
Calories Kcal/kg/d	123 \pm 6.02	126 \pm 8.8	.26
Fluids ml/kg/d	155 \pm 9.4	157 \pm 11.6	.48
BW-grams	776 \pm 126	734 \pm 153	.41
Duration on vent Median.IQR.days	15	14	.23
DOL Bw regained	12 \pm 9	6 \pm 3	.06
CLD	48%	60%	.70

513 IMMUNE MEDIATORS AND VITAMIN D STATUS IN THE DEVELOPMENT OF COMORBIDITIES OF PREGNANCY

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10.1136/jim-2016-000393.516

Purpose of Study Comorbidities of pregnancy (COP) lead to adverse neonatal outcomes. Improper maternal immune system regulation may be a contributing factor to the development of COP. Vitamin D is a known immune modulator of the innate and adaptive immune system. Prior studies confirm a decreased risk of COP with sufficient vitamin D [25(OH)D] levels >40 ng/mL. The objective was to examine the relationship between maternal immune mediators and vitamin D levels in relationship to the development of COP.

Methods Used Hematologic samples were obtained each trimester from subjects enrolled in a RCT supplementing either 400 IU or 4400 IU of vitamin D per day during pregnancy. Maternal 25(OH)D levels were assayed. Plasma cytokines and other immune regulatory product concentrations were measured by ELISA. COP were defined as preterm labor/birth <37 weeks gestation, preeclampsia and chorioamnionitis. Associations of both 25(OH)D and immune mediator concentrations with COP were evaluated with Wilcoxon rank-sum tests or Spearman correlation, as appropriate.

Summary of Results Of 270 participants, 21 subjects developed preterm labor/birth, 10 preeclampsia and 4 chorioamnionitis. No significant correlations were found between maternal 25(OH)D levels and the development of COP. Subjects with preterm labor/birth had decreased TGF- β concentrations throughout pregnancy, significant in the 1st ($p < 0.01$) and 2nd trimesters ($p < 0.02$), increased TNF- α concentrations, significant in all trimesters ($p < 0.05$), and decreased IL-6 concentrations in the 2nd and 3rd trimesters ($p < 0.05$), compared to subjects without COP.

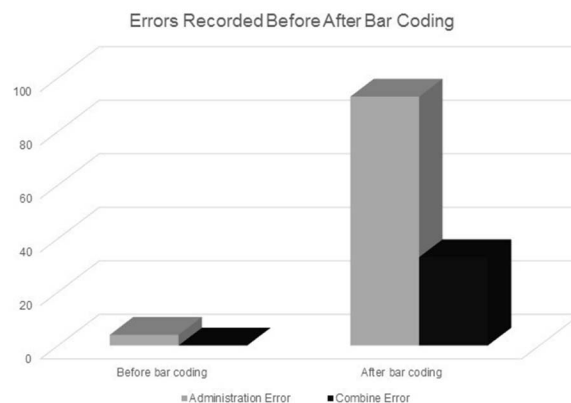
Conclusions Mothers who developed preterm labor/birth were found to have alterations in their immune mediators, including decreased TGF- β and IL-6, in addition to increased TNF- α . This data suggests that these early immune mediator changes are possible predictors for preterm labor/birth. Low prevalence of COP in the study group did not allow for adequate power to detect a relationship between 25(OH)D levels and COP, but further analyses are underway to delineate this intricate relationship.

514 BREAST MILK BAR CODE SCANNING INCREASES DETECTION OF ERRORS

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10.1136/jim-2016-000393.517

Purpose of Study The rigors of human milk handling include receiving, labeling, storing, thawing, mixing, confirming expiration, & administration of appropriate milk to recipient. This process demands strict vigilance at each step,



Abstract 514 Figure 1

& therefore increases the risk for human error. The purpose of this study was to evaluate whether the institution of the breast milk bar code (BMBC) scanning system prevents errors of breast milk administration.

Methods Used BMBC scanning was introduced at Augusta University NICU milk lab in 2015 and data was obtained from 09/01/15 to 09/30/16. This system provides printed labels with bar codes for breast milk & an individualized patient bar code on the infant's arm band. Bedside confirmation is therefore made for each patient. In the past, this confirmation was done at bedside by two person system. Parents are given patient labels and provide labeled breast milk for the milk lab staff to scan. Errors which could result in an infant receiving the wrong breast milk or formula were detected by the bar code scans. These errors were reported and compared with errors reported by the milk lab over a 3 year period prior to instituting the bar coding system.

Summary of Results During the study period, 126 errors were prevented after scanner detection. Of these, 106 were breastmilk & 20 were formula errors. 33 were combined errors (1 or more bottles of breastmilk combined into a new container). 93 were administration errors (nurses would have fed the infant the wrong milk/formula). For the 3 yrs prior to coding system, when there were two nurses confirming that the milk was appropriate for the patient, only 4 administration errors were reported. This drastic difference suggests an underestimated rate of errors in the era prior to bar code scanning.

Conclusions The addition of BMBC scanning has proven to be a major improvement in preventing misadministration of prescribed diet to infants.

515 RARE CASE OF PELLAGRA IN THE UNITED STATES

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10.1136/jim-2016-000393.518

Introduction Pellagra, a disease that marks the latest stages of severe cellular niacin deficiency, manifests in a wide array of clinical presentations. The disease is known by the classical presence of the 4D's: photosensitive



Abstract 515 Figure 1

Dermatitis, Dementia, Diarrhea, and Death. Diagnosis is usually made by the presence of characteristic skin manifestations and response to niacin therapy. Due to worldwide improvement in socio-economic standards, this disease is rarely seen, manifesting largely secondary to chronic alcohol abuse, carcinoid tumors, anorexia nervosa, gastric bypass surgery, isoniazid, and antiepileptic use.

Case Report A 60-year-old female with a past medical history of hypertension and chronic alcohol abuse presented with generalized weakness and confusion after being found at home in her own feces with multiple empty beer cans around her. Physical exam was remarkable for denuded skin on her breast with hyperpigmented periphery (Image 1), hyperpigmented and hyperkeratotic skin of the upper back and neck 'casal necklace' (Image 2), perifollicular hyperkeratosis of bilateral lower extremities 'goose skin' (Image 3). Further history showed that she had very loose stool for the past few months. Upper Endoscopy showed erythematous and eroded mucosa. She was started on niacin for treatment of pellagra. Confusion and diarrhea resolved within thirty-six hours of niacin administration.

Discussion Diagnosis of pellagra is usually made by the presence of characteristic skin manifestations, gastrointestinal symptoms and response to Niacin therapy. Untreated pellagra will gradually progress, eventually leading to death within five years due to multiorgan failure. However, if treated appropriately the prognosis is excellent.

516 EVALUATION OF ENVIRONMENTAL AND BEHAVIORAL PRACTICES OF OVERWEIGHT AND OBESE CHILDREN SIX AND UNDER IN THE EARLY LIFESTYLE INTERVENTION CLINIC USING THE FAMILY NUTRITION AND PHYSICAL ACTIVITY SCREENING TOOL

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10.1136/jim-2016-000393.519

Purpose of Study To determine the difference in family environment and behavioral practices of overweight or obese children age 2 to 6 years enrolling in the Early Lifestyle Intervention (ELI) Clinic, a multidisciplinary obesity program, versus two control groups in the general pediatric population.

Methods Used Parents filled out the Family Nutrition and Physical Activity (FNPA) screening tool. Higher scores correlate with healthier environments and behaviors, with a total maximum score of 80. FNPA scores for children enrolling in the ELI clinic (n=30) were compared to two control groups recruited from the general pediatric population: one consisting of overweight and obese (ow/o)

children (n=22) and one consisting of normal weight (nw) children (n=43). Data was evaluated using one-way ANOVAs.

Summary of Results The overall total score and subscales between the three groups showed no statistically significant difference. Three individual questions showed statistical significance. For monitoring chips, cookies and candies there was a difference between ELI Clinic (2.37 +/- .890) and nw patients (2.95 +/- .925) (p=.024). For family encouragement of physical activity there was a difference between ELI Clinic (3.03 +/- .928) and nw patients (3.63 +/- .618) (p=.004). For physical activity in free time there was a difference between ELI Clinic (2.73 +/- .907) and ow/o patients (3.36 +/- .848) (p=.027).

Conclusions Children enrolling in ELI Clinic are less encouraged to be physically active by their family and have less monitoring of their sweets intake when compared to nw children in the general pediatric clinic. The survey also found that ELI Clinic patients are less physically active during free time when compared to ow/o patients in the general pediatric clinic. As such, strong encouragement of healthy behavioral practices and family environments should be incorporated in the comprehensive approach to addressing childhood overweight and obesity in the future. Future studies will aim to further differentiate environment and behavioral practices between all three groups.

517 LOW SENSITIVITY OF OVERWEIGHT/OBESE DOCUMENTATION FOR PEDIATRIC OVERWEIGHT/OBESE PATIENTS IN ELECTRONIC HEALTH RECORDS

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10.1136/jim-2016-000393.520

Purpose of Study The sensitivity of overweight/obesity documentation in Electronic Health Records (EHR) is not known, although the sensitivity of proper documentation in written charts is poor. Since medical record documentation is associated with providers addressing obesity, this study tested the sensitivity of overweight/obesity documentation in EHR using Body Mass Index (BMI) classification as a gold standard.

Methods Used De-identified electronic record data was obtained from a multi-state learning collaborative. Eligible patients between 2–18 years old had at least one visit in 2014 and 2015 with their health care provider and had a calculable BMI in 2015. Overweight/Obesity documentation in EHR included overweight, obesity, abnormal weight gain, and dysmetabolic syndrome listed as an ICD-9/ICD-10 code, a test/consult order indication, or in the patient's problem list. Sensitivity of overweight/obesity documentation compared to patients' BMI percentile (overweight=BMI percentile \geq 85th and $<$ 95th, obese=BMI percentile \geq 95th) was calculated. Odds ratios of receiving proper documentation was also calculated.

Summary of Results There were 173,424 patients in this analysis. Overweight and obese prevalence was 23% and 21% respectively based on patients' BMI. Sensitivity of overweight/obesity documented in the EHR when BMI percentile was categorized as overweight/obese was 13%.

However, sensitivity of obesity documented in EHR when BMI percentile was categorized as obese was 29%. The odds of receiving an overweight/obese documentation if the patient was overweight/obese was 6.72 (95% CI 6.41–7.04, $P < .01$). The odds of receiving an obese documentation if the patient was obese was 14.57 (95% CI 14.0–15.16, $P < .01$). The sensitivity of an obesity diagnosis according to age was 18.4% (2–5 years old), 29.6% (6–12 years old), and 30.7% (13–18 years old). Thus, sensitivity of obesity documentation increased as patient's BMI percentile and age increased.

Conclusions The sensitivity of overweight/obesity documentation in EHR is low. Since providers' documentation is associated with addressing obesity, future research should focus on improving physicians' documentation/attention of pediatric obesity.

518 MENKES KINKY HAIR DISEASE: A RARE NEURODEGENERATIVE DISORDER THAT PEDIATRICIANS SHOULD NOT MISDIAGNOSE

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10.1136/jim-2016-000393.521

Case Report Menkes kinky hair disease (MKHD) is a very rare X-linked copper metabolism disorder that results from an ATP7A gene mutation, which is inherited as an X-linked recessive trait and, as expected, the vast majority of patients are males. Estimates of the incidence of MKHD range from 1 in 100,000 live births to 1 in 250,000. The mutation of ATP7A activity results in the transport protein mediating copper uptake from the intestine. Progressive neurodegeneration and connective tissue disturbances, together with refractory seizures and hair shaft abnormalities (most commonly pilli torti), are the main manifestation. Patients usually exhibit a severe clinical course resulting in death during early childhood. The severity of the symptoms and lifespan are variable. Treatment consists of parenteral administration of a copper-histidine complex, which is not consistently effective. Early diagnoses of this condition are critical for a response to copper therapy.

We demonstrated an eight-month-old Caucasian male presented with hypotonia, hypopigmented with unusual sparse and lusterless scalp hair that becomes tangled on the top of the head. Developmental regression was presented. Light microscopy of hair shaft showed pilli torti. MKHD was confirmed by low serum copper 5 mg/dL and low serum ceruloplasmin 18 ug/dL. A MRI of the brain showed diffused prominence of the sulci along the cerebral hemispheres, mild hypoplasia of the cerebellar vermis and prominence of the cerebellar sulci. Mildly increased frontal lobe white matter signal on the T2 can be seen with delayed myelination. Overall, these findings may correlate with the clinical history of Menkes disease. The ATP7A mutation revealed a deletion of a gene of ATP7A that affects the last four amino acids of exon 12. This mutation is severe and does not appear to be compatible with any copper transport similar to the other ATP7A mutations. He has been trying a treatment with copper chloride intravenous once a week. His physical examination has improved.

He is able to move his upper and lower extremities and hold his head.

519 THE INFLUENCE OF BMI FROM CHILDHOOD TO ADULTHOOD ON COGNITION AND PHYSICAL PERFORMANCE IN MIDDLE AGE

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10.1136/jim-2016-000393.522

Purpose of Study It is unclear whether BMI from childhood and young adulthood predicts cognition and physical performance in mid-life.

Methods Used Using data from Bogalusa Heart Study (n=880; mean (SD) age at baseline=10.6 years (2.8), BMI=18.1 (3.6), 64.1% female, 33.0% black), we examined the longitudinal association of BMI, measured at recurrent clinic visits, with cognition (the sum of standardized scores on 11 validated neuropsychological tests) and physical performance (the Short Physical Performance Battery [SPPB]).

Summary of Results A one-unit increase in BMI was associated with a decrease of 0.14 points ($p < 0.001$) on the SPPB and of 0.001 ($p = 0.02$) standard deviations in the global cognitive z-score in multivariable GEE models. The association disappeared in whites but remained for blacks when analyzed separately, suggesting a possible difference by race.

Conclusions Models investigating rate of change of BMI provided similar results, suggesting that interventions targeting BMI reduction or preventing obesity in childhood may improve cognition or physical function in middle age.

520 VITAMIN B12 DEFICIENCY PRESENTING AS SEVERE HEMOLYTIC ANEMIA

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10.1136/jim-2016-000393.523

Case Report A 61 y.o. male with no prior past medical history presented to our institution with a multitude of complaints, including fatigue, chest pain, abdominal pain and weight loss for 1 week. On presentation, he was hemodynamically stable and afebrile. Examination was significant for scleral icterus and jaundice. He also looked pale and cachectic. Blood tests showed significant anemia with a Hgb 4.1 g/dL, MCV 133 fL, with no suspected bleeding source. Guaiac and FOBT were negative. Testing also showed elevated indirect bilirubin, low haptoglobin <10 mg/dL, elevated LDH 2323 U/L, retic count 18%, WBC 6.3 thou/mm³, and low platelets 61 thou/mm³. Vitamin B12 was significantly low <30 pg/mL, with elevated homocysteine and methylmalonic acid levels. Folate level was normal. Iron panel was unremarkable and HIV negative. Coombs' test was negative. Intrinsic factor antibodies were positive. MTHFR (Methylene tetrahydrofolate reductase) gene mutation was also positive. He was

transfused a total of 4 units packed red blood cells during hospitalization. Vitamin B12 was started and continued indeterminately due to this new diagnosis of pernicious anemia. At the time of discharge, he had completed daily vitamin B12 injections for 1 week, and received his first weekly injection. Hemolytic panel and hemoglobin levels were improved upon discharge. He continues to take ferrous sulfate, folic acid and pyridoxine daily.

Vitamin B12 (cobalamin) is a key coenzyme for methionine synthase and L-methylmalonyl-coenzyme mutase. Hemolytic anemia from vitamin B12 deficiency occurs as a result of ineffective erythropoiesis. Homocysteine has also been known to increase the risk of hemolysis in cobalamin deficiency. There is a high frequency (30%) of cobalamin deficiency in patients with homozygous methylene tetrahydrofolate reductase (MTHFR) C677T mutation, a known cause of hyperhomocysteinemia. Physicians should be aware of these associations to recognize, prevent and manage the detrimental complications of vitamin B12 deficiency.

Perinatal Medicine I Concurrent Session 2:00 PM Sunday, February 12, 2017

521 ADRENOMEDULLIN SIGNALING IS NECESSARY TO PROTECT NEONATAL MICE AGAINST EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA

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10.1136/jim-2016-000393.524

Purpose of Study Interrupted pulmonary angiogenesis is a hallmark of bronchopulmonary dysplasia (BPD), which is the most common respiratory morbidity in human preterm infants. Adrenomedullin (AM) is a multifunctional peptide with potent angiogenic effects. We observed that AM-deficient human pulmonary microvascular endothelial cells have an increased susceptibility to hyperoxic injury. Yet, whether AM signaling is necessary to protect neonatal mice against experimental BPD is not well known. Therefore, we tested the hypothesis that AM-deficient neonatal mice will display increased susceptibility to hyperoxia-induced experimental BPD compared to AM-sufficient neonatal mice.

Methods Used One-day old AM-sufficient (AM^{+/+}) or -deficient (AM^{-/-}) mice were exposed to room air or hyperoxia (FiO₂ 70%) for up to 14 days, following which the mouse lungs were harvested to determine angiogenesis, alveolarization, and the expression of AM and its signaling receptors, calcitonin receptor-like receptor (CRLR) and receptor activity-modifying protein 2 (RAMP2).

Summary of Results Initially, we determined the effects of hyperoxia on the AM-signaling axis. In contrast to other studies, we observed that exposure of neonatal mice to 70% oxygen decreases the expression of AM. Also, hyperoxia exposure decreased the expression of CRLR and RAMP2, which indicates that hyperoxia disrupts AM

signaling in neonatal mice. Further, hyperoxia-induced alveolar and pulmonary vascular simplification, and pulmonary vascular remodeling was augmented in neonatal AM^{+/-} mice compared to AM^{+/+} mice. Mechanistically, these findings were associated with decreased endothelial nitric oxide synthase expression and extracellular signal-regulated kinases 1/2 activation.

Conclusions We conclude that AM signaling is necessary to mitigate hyperoxia-induced experimental BPD in neonate mice. Our results indicate that AM and CRLR-RAMP2 interface are potential therapeutic targets for the management of BPD in human preterm infants.

522 MICROBIOTA REGULATED AIRWAY EXOSOMAL MIR 876-3P PREDICTS SEVERE BRONCHOPULMONARY DYSPLASIA (BPD)

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10.1136/jim-2016-000393.525

Purpose of Study We have recently discovered the role of epigenetic factors and airway microbiome in BPD pathogenesis.

Methods Used 1. Exosomes extracted and characterized (quantity, size) using NanoSight from:

- Tracheal Aspirates (TA), BPD infants vs controls.
- Human bronchial epithelial cell (NHBE) supernatants, normoxia vs hyperoxia.

2. Prospective cohort study conducted with separate *discovery* (Birmingham, AL) and *validation* (Philadelphia, PA) cohorts of preterm infants. Total 805 different exosomal microRNAs analyzed in each of the 30 early TA samples, using Nanostring. Statistical modeling and pathway analysis conducted between *BPD Susceptible* vs *Resistant* groups.

3. The top predictive miR - 876-3p further studied by *in vitro* and *in vivo* hyperoxia models utilizing NHBE and C57BL6 mice respectively. Mimic miR 876-3p (gain of function) and Locked Nucleic Acid (LNA) miR 876-3p (loss of function) used for functional analysis.

4. For effects of microbiota on miR 876-3p, *in vitro* and *in vivo* hyperoxia experiments conducted with *Proteobacterial* lipopolysaccharide (LPS) inoculation in NHBE cells and postnatal intratracheal LPS administration in mice, respectively.

Summary of Results (All differences p<0.05, compared to respective controls)

1. TA from infants with BPD and hyperoxia exposed NHBE cell supernatants, had larger but fewer exosomes.

2. miR-876-3p expression was significantly decreased at birth in *BPD Susceptible* infants.

3. Exosomal miR-876-3p in BPD:

a) *In vitro*: miR 876-3p was decreased in hyperoxic NHBE cells. Top targets of miR876-3p - RBBP61 and MCL1 were correspondingly increased in hyperoxia. On functional analysis- mimic miR 876-3p increased miR 876-3p and reduced target genes expression. LNA miR 876-3p reduced miR 876-3p and increased target genes expression.

b) *In vivo*: Hyperoxia pups showed decreased miR 876-3p (P14).

4. Microbiota regulates miR-876-3p:

a) *In vitro*: LPS significantly reduced the expression of miR 876-3p in normoxic and hyperoxic cells, compared to hyperoxia or normoxia alone.

b) *in vivo*: Postnatal LPS reduced miR 876-3p in normoxia and hyperoxia pups compared to controls.

Conclusions Decreased airway exosomal miR 876-3p predicts severe BPD, and is regulated by microbiota.

523 EFFECT OF SURFACTANT PROTEIN A ON RETINAL CYTOKINES AND MICROGLIA IN SYSTEMIC INFLAMMATION

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10.1136/jim-2016-000393.526

Purpose of Study Activation of retinal microglia is associated with retinal neovascularization (NV) in the mouse model of oxygen induced retinopathy (OIR) and systemic inflammation (SI). Furthermore, surfactant protein A (SPA) expression is upregulated in the retinas of wild type (WT) mice after intravitreal injections of toll like receptor (TLR) 2 and 4 ligands. SPA expression is also increased in NV in WT mice. We hypothesize that retinal SPA is upregulated in SI and also modulates retinal cytokine and microglial expression.

Methods Used SI was induced in WT mice by intraperitoneal (IP) injection of lipopolysaccharide (LPS) at P₄. Retinal SPA protein was measured after 48 and 72 hours. IL1 β , TLR4, TNF α , VEGF and a microglial specific marker Iba-1 were quantified by real-time PCR at P₆ and P₁₀ in WT and SPA^{-/-} mice. Total number of microglia were compared between WT and SPA^{-/-} mice on flatmounts stained with antibody for Iba-1.

Summary of Results SPA protein was significantly increased in WT mice, 48 hours after LPS injection (899 \pm 93.53 pg/mg retinal protein) vs controls (374 \pm 62.93 pg/mg retinal protein) but there was no difference at 72 hours. At P₆, cytokines, Iba1, and VEGF were increased in WT vs SPA^{-/-}. However, at P₁₀ there was an increase in TNF α , TLR4, and Iba-1 in SPA^{-/-} vs WT. VEGF remained high in WT mice at P₁₀ but there was no difference in IL1 β . At P₆, the number of total microglia in central and peripheral retinal zones were significantly higher in WT vs SPA^{-/-}. At P₁₀ the number of microglia in the central zone of retina was higher in the SPA^{-/-} vs WT mice but there was no difference in the periphery.

Conclusions SPA is upregulated in the neonatal mouse retina in SI. Absence of SPA was associated with an initial decrease in retinal cytokines 2 days after induction of SI but the cytokines were higher at 6 days suggesting that SP-A has differing roles during the acute and late phase of SI. Absence of SP-A was associated with a decrease in microglia on retinal flatmounts 48 hour after SI suggesting that SP-A may play a role in chemotaxis of microglia. The decreased retinal VEGF expression in the SPA^{-/-} mice also suggests that SP-A may be

important in the progression of inflammation leading to vaso-obliteration and NV.

524 NEUTROPHIL EXTRACELLULAR TRAPS IN NECROTIZING ENTEROCOLITIS

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Purpose of Study Necrotizing enterocolitis (NEC) continues to be one of the major causes of morbidity and mortality in preterm infants. NEC is characterized by intestinal inflammation and leukocyte infiltration that can rapidly progress to perforation, systemic inflammatory response syndrome, and death. We previously showed that extensive neutrophils extracellular trap formation (NETs) occur in intestinal tissues from infants with NEC. NETs is a novel cell death process in which activated neutrophils expel their nuclear content in the form of web-like structures. Although, NETs has been shown to exhibit antimicrobial functions by trapping and killing pathogens, NET-associated factors, specifically histones, cause 'collateral damage' to the host. The role of NET formation in NEC is currently unknown. We hypothesize that NET inhibition would decrease mortality, pro-inflammatory cytokine releases and organ injury in NEC.

Methods Used NEC was induced in CD1 pups using the Dithiazone/Klebseilla (DK) method. To determine the role of NETs in NEC, Cl-amidine (a NET inhibitor), was given 15 minutes before oral *klebsiella* and 3 hours after. At the end of the experiment, surviving pups were euthanized; blood and small intestinal tissues were harvested. Histological NEC severity was determined by H&E by a blinded pathologist. Pro and anti-inflammatory cytokines (IL1 β , IL-10, TNF- α , IL6, IL12 p70, IFN- γ , GRO- α) in plasma were measured using 7-plex XMAP procartaplex[®] multiplex immunoassays. IHC staining was performed in intestinal tissue for cit-histones (marker of NETs).

Summary of Results NEC histological injury score was not statistically different between the groups (1.8+0.44 in NEC +Cl-amidine group vs 2.0+0.41 in NEC group, $P=0.71$). However, surprisingly pups in the NEC+Cl-amidine group had higher mortality (90.78% in NEC+Cl-amidine vs 51.7% in NEC, $P<0.0001$), and increased pro-inflammatory cytokine release compared to NEC alone.

Conclusions Inhibiting NET formation increases mortality and proinflammatory cytokine release in DK NEC model. We plan to compare bacterial counts in blood, peritoneum, and tissues between the groups in future experiments. If we demonstrate higher bacterial counts with NET inhibition, this would suggest that NET formation play an important innate immunity role in NEC.

525 **PRACTICE VARIABILITY IN TREATMENT OF HYPOTHYROIDISM AMONG PREMATURE INFANTS WITH ABNORMAL NEWBORN SCREENINGS: A SINGLE CENTER EXPERIENCE**

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10.1136/jim-2016-000393.528

Purpose of Study To understand practice variations in treatment of congenital hypothyroidism (CH) and thyroid disease of prematurity among preterm neonates (PTN) that occur following an abnormal newborn screen (NBS) result at a large academic center.

Methods Used We conducted a retrospective review of all PTN (<35 weeks gestational age) admitted to Children's Memorial Hermann Hospital's neonatal intensive care unit (NICU) in Houston, TX, and treated for hypothyroidism with levothyroxine between January 1, 2005 and December 31, 2014. Patients were excluded from analysis if treatment was started at an outside hospital or if NBS results were incomplete. Electronic medical records of qualifying patients were reviewed, and newborns screen results and thyroid function testing (TFT) results and related data were collected. We calculated the incidence of abnormal newborn testing among study subjects and identified the median thyroid-stimulating hormone (TSH) level prompting treatment initiation among study subjects. Data analysis was done using Microsoft Excel.

Summary of Results We identified 80 PTN who were treated with levothyroxine at the recommendation of a pediatric endocrinologist during the study period at our institution; 6 patients were excluded for incomplete/missing NBS records. Of the remaining 74, 99% (73/74) had abnormal NBS results. 76% (56/74) had abnormal results on the first NBS, 86% (64/74) had abnormal results on the second NBS. 5% (4/74) received treatment after the first NBS, 72% (53/74) after the second NBS, 23% (17/74) after three or more NBS. The median age to the first TFT was 60 days of life (IQR: 40–90 days). An average of 3 TFT studies (range: 1–8) were done before treatment initiation with levothyroxine. The median TSH level for treatment initiation was 11.95 U/mL (IQR: 8.54–19.01 U/mL).

Conclusions Screening and treatment of hypothyroidism among PTN is highly variable at our institution. Further evaluation is needed to identify reasons for the wide range in response to abnormal NBS in PTN, a population that is at high-risk for thyroid dysfunction due to immaturity and suppression of the hypothalamic-pituitary-thyroid axis. Collaboration with the Texas Department of State Health Services is ongoing to examine NBS results of all PTN admitted to our NICU.

526 **DIFFERENTIAL SEX-SPECIFIC EFFECTS OF OXYGEN TOXICITY IN HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS: EFFECTS ON ANGIOGENESIS**

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10.1136/jim-2016-000393.529

Purpose of Study Pulmonary angiogenesis is critical for alveolarization and arrest in vascular development adversely affects lung development. Postnatal exposure to high concentrations of oxygen (hyperoxia) contributes to this process eventually leading to the development of bronchopulmonary dysplasia (BPD). Despite the well-established sex-specific differences in the incidence of BPD and impaired lung function in males, the molecular mechanism(s) behind these are not completely understood. Human umbilical vein endothelial cells (HUVECs) are neonatal endothelial cells and provide a robust in vitro model for the study of endothelial cell physiology and function.

Methods Used Male and Female HUVECs were exposed to room air condition (37% O₂, 5% CO₂) or in hyperoxia condition (95% O₂, 5% CO₂) for upto 72 hrs. Cell viability, proliferation, H₂O₂ production (as a measure of oxidative stress) and angiogenesis were analyzed. Sex-specific differences in expression key mediators of angiogenesis (VEGFR2 and Tie2) and modulation of NF-kappa B pathway was measured.

Summary of Results In hyperoxic conditions in vitro, male HUVECs have decreased survival, greater oxidative stress and impairment in angiogenesis compared to similarly exposed female cells. There is differential expression of VEGFR2 and Tie-2 between male and female HUVECs with a greater decline in male HUVECs exposed to hyperoxia. There was greater activation of the NF-kappa B pathway in female HUVECs compared to male under hyperoxic conditions.

Conclusions The results indicate that sex differences exist between male and female HUVECs in vitro after hyperoxia exposure. Since endothelial dysfunction has a major role in the pathogenesis of BPD, these differences could explain in part the mechanisms behind sex-specific differences in the incidence of this disease among preterm neonates.

527 **OMEGAVEN VERSUS LIPID MINIMIZATION IN PREVENTION OF PARENTERAL NUTRITION ASSOCIATED LIVER DISEASE**

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10.1136/jim-2016-000393.530

Purpose of Study Parenteral nutrition associated liver disease (PNALD) manifests as direct hyperbilirubinemia, elevated liver enzymes and can progress to irreversible liver damage. PNALD prevention strategies include lipid minimization (LM) and the use of fish oil based lipids such as Omegaven. Omegaven at a dose of 1 g/kg/day has been shown to prevent PNALD when compared to soy-based lipids at >1 g/kg/day. It is unclear whether the benefit is due to a lower lipid dose or the constitution of Omegaven. No previous studies have compared the effect of soy-based lipids at LM dose (<1 g/kg/d) with Omegaven at ≈1 g/kg/d on PNALD progression.

Methods Used A retrospective chart review of patients who received the LM dose of soy-based lipids followed by Omegaven for at least 4 weeks each. Anthropometric characteristics, serum total and direct bilirubin, alanine transaminase (ALT) and aspartate transaminase (AST) were

Abstract 527 Table 1 Summary of results

	Change during 4 weeks of LM (mean, SD)	Change during 4 weeks of Omegaven (mean, SD)	p value
Total bilirubin (mg/dl)	0.47 (3.88)	-2.10 (1.31)	0.04
Direct Bilirubin (mg/dl)	0.39 (3.25)	-1.82 (1.14)	0.04
AST	27.9 (71.4)	-35.7 (52.7)	<0.01*
ALT	39.4 (46.6)	-21.7 (32.5)	<0.01*
Weight (kg)	0.35 (0.28)	0.73 (0.36)	<0.01*
Head Circumference (cm)	1.31 (1.19)	2.48 (1.33)	<0.01*

*Wilcoxon signed-rank test

analyzed for each of the 4 weeks of LM and Omegaven use. Data were compared between groups using paired sample T test or Wilcoxon signed-rank test.

Summary of Results 16 patients were changed from soy-based lipids at LM mean dose 0.66 g/kg/d (SD, 0.47) to Omegaven mean dose 0.92 g/kg/d (SD, 0.19) at median age 78 d (range 38–142). Bilirubin and liver enzymes levels increased with LM dose of soy based lipid and decreased with Omegaven (Table). Omegaven use was associated with increased rate of rise in weight and head size.

Conclusions Switching from LM to Omegaven was associated with an improvement in PNALD markers associated with increased rate of weight gain and head size over 4 weeks. Previous studies demonstrating an improvement in PNALD with fish-oil based lipids used plant-based lipids at higher doses. This study shows the superiority of Omegaven over LM doses of soy-based lipids. Our findings support the proposed mechanism that Omega-3 fatty acids present in fish oil based preparations slow and reverse PNALD progression.

528 MATERNAL FLUID SUPPLEMENTATION IN RATS DURING ABDOMINAL SURGERY PREVENTS FETAL RESORPTION

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10.1136/jim-2016-000393.531

Purpose of Study Performing surgery in pregnant women is a high risk procedure and can affect the pregnancy. We investigated whether fluid supplementation during surgery in rats could help prevent fetal resorption.

Methods Used This is an ancillary study linked to a project studying the effects of reduced uterine perfusion (RUP) during late pregnancy and developmental origins of diseases. We compared outcomes of pregnant rats who underwent RUP surgery treated and not treated with fluid supplementation during surgery. 100 pregnant rats were distributed into 4 groups (n=25 for each group): Sham Control, RUP Control, Sham+Saline, and RUP+Saline. At 14 days of gestation (G14) pregnant rats underwent abdominal surgery RUP, by placing silver clips around abdominal aorta and ovarian arteries. Fetuses were

exteriorized and counted. Fluid supplementation with 2 ml saline was administered intraperitoneally, before abdominal closure. Sham rats were exposed to abdominal surgery without RUP procedure. Pregnant rats delivered at term (G21), and offspring were assessed for viability and counted and compared to G14. Dead offspring at birth were considered stillbirth, and counted as well. Control group underwent RUP or Sham surgery without fluid supplementation. Statistical analysis was performed using GraphPad 6 software. Experimental groups were compared using analysis of variance (ANOVA) and T-test when appropriate.

Summary of Results The average number of pups at G14 did not show differences among groups. Fetal resorption rates in RUP Control group were greater compared to Sham Controls (60% vs 12% P<0.05); saline administration during surgery significantly (P<0.05) reduced these number in both groups (35% and 3% RUP vs Sham respectively). Additionally, survival rates after birth were greater in Sham and RUP groups treated with saline compared with controls (P<0.05).

Conclusions Results suggest that fluids supplementation during surgery in pregnant rats significantly prevented fetal reabsorption compared to control group. Additional studies are warranted to investigate the exact mechanism(s) involved. Fluid supplementation should be explored as an additional measure to prevent fetal complications from surgery.

529 ORAL ADMINISTRATION OF HYALURONIC ACID IN EXPERIMENTAL NECROTIZING ENTEROCOLITIS

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10.1136/jim-2016-000393.532

Purpose of Study Necrotizing enterocolitis (NEC) continues to be one of the most devastating diseases in preterm infants. Hyaluronic acid (HA), a glycosaminoglycan in human milk, promotes gastrointestinal epithelial proliferation in gut injury models and protects against intestinal bacterial infections. The role of HA in NEC is currently unknown. The main objective of our study is to investigate if oral administration of HA reduces mortality, maintains intestinal integrity, and attenuates pro-inflammatory cytokine release in experimental NEC

Methods Used NEC was induced in CD1 pups using the Dithiazone/Klebsiella method. Pups were divided into sham, NEC, and NEC+HA. HA ~35 kDa was given at 72, 48, 24, and 1 hr prior to NEC. At the end of the experiment pups were euthanized; blood and small intestinal tissues were harvested. NEC severity was determined by H&E. Intestinal permeability was determined by plasma FITC dextran. Pro and anti-inflammatory cytokine expression (IL1 β , IL-10, TNF-a, IL6, IL12 p70, IFN gamma, GRO-a) in intestine and plasma were measured using 7-plex XMAP procartaplex immunoassay.

Summary of Results Pups in the NEC+HA group had higher survival (76% vs 52%, P=0.02), lower NEC scores (1.2 vs 2.3, p <0.01), and lower pro-inflammatory

cytokines compared to the NEC group.(see Fig:1) Moreover, HA treated pups had lower plasma FITC dextran compared to the NEC group.

Conclusions Hyaluronic acid reduces the incidence and severity of experimental NEC. Further studies are needed to determine its protective mechanism in NEC

530 A PHYSIOLOGIC, EXTRAPULMONARY ROLE OF SURFACTANT PROTEIN-A TO REDUCE TLR4 IN THE NEONATAL GASTROINTESTINAL TRACT THROUGH A PROTEIN DEGRADATION PATHWAY

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10.1136/jim-2016-000393.533

Purpose of Study The integrity of the gastrointestinal tract (GI) is critical in preventing necrotizing enterocolitis (NEC). We know that SP-A reduces Toll like receptor 4 (TLR4) activities in alveolar macrophages, and that TLR4 is central in modulation of GI tract inflammation. We found that SP-A reduces TLR4 activity in the murine neonatal GI tract, and in its absence (SP-A null; SPA^{-/-}), TLR4 levels and inflammation were increased compared to wild type (WT) mice. Thus, we hypothesize that exposure of the neonatal GI tract to oral SP-A reduces TLR4 levels through proteolysis.

Methods Used For *in vivo* analysis, newborn SPA^{-/-} and WT mice were gavaged with purified human SP-A (5 µg in PBS) or PBS (control) twice (d3 and d6) and ileum harvested on day 7 to assess TLR4 levels (Western). For *in vitro* analysis, various human epithelial cells (colonic HT-29, alveolar A549 and kidney HEK293 cells) were exposed to purified SP-A (25 µg/ml) and harvested after 24 h. (Epithelial cells of non-GI origin are used to determine if the effect of SP-A is specific to the gut). When necessary, the proteasome inhibitor MG132 (10 µM) was added to HT-29 cells.

Summary of Results TLR4 levels in the ileum of WT mice did not show a significant difference between the SP-A and PBS groups. In the SPA^{-/-} group, oral SP-A resulted in a significant decrease (50%, p<0.04) in TLR4 expression compared to oral PBS. Exposure of colonic HT-29 cells to SP-A significantly decreased cellular TLR4 levels by 30%, but the addition of MG132 and SP-A prevented the inhibitory effect. In A549 and HEK293 cells SP-A exposure decreased TLR4 levels by 44% (p<0.001) and 36% (p<0.02), respectively.

Conclusions Oral SP-A significantly decrease ileal TLR4 levels clearly demonstrating a physiological effect of SP-A exposure on TLR4 expression in the neonatal GI tract. The mechanism involves the ubiquitin-proteasomal pathway since inhibition of this pathway blocked the activity of SP-A, and it could not reduce TLR4 levels. The ability of SP-A to modulate TLR4 is not restricted to epithelial cells of the GI tract, as exposure to cells lines of non-GI origin significantly reduces levels of TLR4. In totality, these results suggest an extra-pulmonary, immunomodulatory role for SP-A on TLR4 through the ubiquitin-proteasomal pathway.

531 EFFECTS OF CHRONIC HYPEROXIA ON GENE EXPRESSION AND MICROBIOME IN THE ILEUM OF NEONATAL MICE

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10.1136/jim-2016-000393.534

Purpose of Study To test the hypothesis that chronic hyperoxia alters gene expression and microbiome in the neonatal murine ileum.

Methods Used We utilized a hyperoxia protocol commonly used to model BPD in neonatal mice. Neonatal mice were exposed to either 85% oxygen (hyperoxia) or 21% oxygen (normoxia) from P3. Animals were euthanized on P15 and ileum and lung samples were collected for RNA and DNA analysis. Microarray gene expression profiling followed by Ingenuity pathway analysis was conducted for genes that changed ≥2 fold at q<0.05. The microbiome in terminal ileal samples was analyzed by 16 S ribotyping from isolated microbial DNA. Principal Component Analysis (PCA) was performed using SPSS to identify similarities and dissimilarities in colonization.

Summary of Results Top 5 genes upregulated by hyperoxia in ileum were Nox4(7.6x), Fncl5(6.2x), Actb(5.7x), Spp2(4.4x), S100a1(4x) and the top 5 downregulated genes were Saa1(-19x), Dnase1(-14x), Ubd(-8.8x), ZG16(-7.4x), Pglyrp1(-6.7x). Top affected pathways were Glutathione mediated detoxification, Eumelanin biosynthesis and sucrose degradation. Among the top downregulated genes (≥3 .5 fold) were Pglyrp1, Defcr20, Defcr21, Pla2g2a, Lyz1 which are members of innate antibacterial defense mechanisms. In the ileum, compared to lung, there was no overlap in the top 10 up or downregulated genes or in the top five affected canonical pathways. Microbiome analysis indicated hyperoxia increased Clostridia and Mollicutes (e.g. Mycoplasma, Ureaplasma) which have been implicated in NEC pathogenesis.

Conclusions Hyperoxia alters gene expression in the ileum, but the effects are very distinct from those in the lung. Key biological functions affected by hyperoxia in the ileum include antioxidant pathways and antibacterial defense mechanisms implicated in the pathogenesis of NEC.

Pulmonary and Critical Care

Concurrent Session

2:00 PM

Sunday, February 12, 2017

532 FEASIBILITY OF A SLEEP TELEMEDICINE PROGRAM FOR VETERANS

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10.1136/jim-2016-000393.535

Purpose of Study Obstructive sleep apnea (OSA) affects at least 2-4% of the general population and nearly 54% of active duty military personnel. Access to care at the Atlanta

VA Sleep Medicine Center is challenging; about 48% of North Georgia Veterans live in rural areas. Little research compares traditional, in-person (INP) to telemedicine-based (TELE) sleep care. This pilot study compared feasibility of a TELE sleep model to an INP model for the diagnosis and treatment of veterans with OSA.

Methods Used This prospective, parallel-group cohort included 140 patients. One group of patients (n=70) received in-person evaluation for OSA at the Atlanta VA Clinic, while the other group (n=70) received real-time TELE care at community-based clinics in Rome and Blairsville, GA. The study evaluated feasibility of TELE care in terms of Continuous Positive Airway Pressure (CPAP) adherence, patients' symptomatic improvement, and travel distance and cost.

Summary of Results At baseline, TELE and INP patients did not differ in terms of BMI, fatigue, or OSA severity. However, TELE participants were older, not as sleepy, and more predominantly Caucasian male compared to INP patients. The overall mean apnea-hypopnea index (AHI) was 24.6 ± 24.0 events/hr. After 3 months of treatment, TELE patients and INP patients showed similar improvements in AHI, ESS and FSS scores. Notably, TELE patients adhered significantly more to CPAP treatment after 3 months ($p=0.028$). The average cost and mileage saved were \$50.90 and 122.7 miles per patient round trip (Blairsville) and \$38.13 and 96.1 miles per patient round trip (Rome).

Conclusions Telemedicine sleep care was feasible for the Veterans at the Atlanta VA Clinic in terms of patients' symptomatic improvement, treatment adherence, and travel distance and cost savings.

533 THE BUFADIENOLIDES DETECT AND PREVENT/TREAT THE ACUTE RESPIRATORY DISTRESS SYNDROME

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10.1136/jim-2016-000393.536

Purpose of Study The acute respiratory distress syndrome (ARDS) is a life threatening disorder with a persistently high mortality rate of 40% to 52%. It does not have a well-defined pathogenesis, however certain predisposing conditions can cause a progression towards this disease. We have examined the role of marinobufagenin (MBG), a bufadienolide with a 6-membered lactone ring in the detection of ARDS. Resibufogenin (RBG), an antagonist of MBG was also evaluated for its potential therapeutic benefits in an animal model.

Methods Used The exposure of rats to 100% O₂ for 48 hours, produced a syndrome closely resembling human ARDS. In a separate group of rats, following a period of hyperoxia, RBG was administered intraperitoneally and serum MBG was measured. H&E stains and neutrophil recruitment of rat lungs from these experimental groups were also evaluated. In human ICU patients, urine samples were examined for MBG as were those from patients that had illnesses unrelated to ARDS.

Summary of Results The mean serum MBG value for control and hyperoxic rats was 25 pg/ml and 39 pg/ml respectively ($p<0.05$). RBG acted as an antagonist of MBG by lowering its level in hyperoxic rats to 22 pg/ml ($p<0.05$). H&E stains and immunohistochemistry analysis of neutrophil recruitment in hyperoxic rat lungs indicated low recruitment of alveoli, perivascular and interstitial inflammation. In contrast, hyperoxic rats treated with RBG showed an improved histological picture. MBG values in human ARDS subjects were significantly higher than control patients ($p<0.01$).

Conclusions The elevated level of MBG in ARDS patients and hyperoxic rats indicate its importance in the pathogenesis of this syndrome. Considering the antagonist and therapeutic role of RBG in hyperoxic rats, a clinical trial on the administration of RBG to ARDS patients with suitable controls is planned following efficacy and safety studies of RBG.

534 THE ROLE OF HISTONE DEACETYLASE 8 IN TGF- β 1-INDUCED FIBROBLAST-MYOFIBROBLAST DIFFERENTIATION

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Purpose of Study We have previously shown that histone deacetylase 8 (HDAC8) expression is increased in lungs of patients with idiopathic pulmonary fibrosis (IPF). HDAC8 belongs to a family of HDAC enzymes that deacetylate histones and regulate gene transcription. HDAC8 is also known to associate with α -smooth muscle actin (α -SMA), which is a marker for FMD (fibroblast-myofibroblast differentiation); a key phenomenon in the pathogenesis of IPF. This study investigates a role for HDAC8 in FMD.

Methods Used To assess whether HDAC8 inhibition represses FMD, normal human lung fibroblasts (NHLFs) were pretreated with HDAC8 siRNA or HDAC8 inhibitor (NCC-170 10 μ M) then co-treated with or without recombinant human TGF- β 1 (1 ng/ml) for 24/48 hours. Protein expression was assessed using immunoblots, and mRNA levels were assessed using qRT-PCR.

To assess whether HDAC8 regulates TGF- β 1-induced contraction, NHLFs were cultured in rat type-I collagen gel, with or without TGF- β 1 and HDAC8 inhibitor.

To assess whether HDAC8 regulates PPAR- γ gene expression by binding its regulatory regions, chromatin immunoprecipitation (ChIP)-PCR was performed using anti-HDAC8 antibody.

To assess the effect of HDAC8 on mRNA stability, TGF- β 1-treated NHLFs were further treated with actinomycin D (10 μ g/ml) for 8 hours.

Summary of Results In TGF- β 1-treated NHLFs, HDAC8 expression is not significantly increased. However, inhibition of HDAC8 represses TGF- β 1-induced α -SMA protein expression and fibroblast contractile activity. Furthermore, inhibition of HDAC8 also represses induction of CTGF and PAI-1 as well as reduction of PPAR- γ (a transcription factor known to negatively regulate expression of these genes) at both mRNA and protein level.

The ChIP-PCR experiments revealed that TGF- β 1 increases recruitment of HDAC8 to regulatory regions of PPAR- γ gene.

HDAC8 inhibition does not enhance PPAR- γ mRNA stability.

Conclusions Inhibition of HDAC8 represses TGF- β 1-induced α -SMA protein expression and fibroblast contractile activity. TGF- β 1 represses expression of PPAR- γ gene (and induces genes negatively regulated by PPAR- γ , such as CTGF and PAI-1), at least partially by recruiting HDAC8 to its regulatory regions.

535 ZINC AND S-ADENOSYLMETHIONINE MEDIATE LUNG INFLAMMATORY CYTOKINES IN OTHERWISE HEALTHY HIV-1-INFECTED INDIVIDUALS

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10.1136/jim-2016-000393.538

Purpose of Study Despite antiretroviral therapy, HIV-1-infected individuals are at increased risk for lung infections. We have previously shown that HIV replication within alveolar macrophages impairs phagocytic function, that HIV-1-infected individuals have zinc and glutathione deficiency leading to oxidative stress, and that *in vitro* supplementation of zinc and glutathione improves phagocytic function. We hypothesize that dietary zinc and antioxidant S-adenosylmethionine supplementation also enhances the inflammatory response in the lung to modulate the host response to pneumonia.

Methods Used In a prospective cohort study, HIV-1-infected subjects were given zinc 30 mg and S-adenosylmethionine 1600 mg daily. All subjects underwent bronchoalveolar lavage (BAL) and blood sampling pre-treatment and after 12 months on therapy. Interferon-gamma (IFN- γ), Interleukin-4 (IL-4), Interleukin-10 (IL-10), Granulocyte-macrophage colony-stimulating factor (GM-CSF) and Tumor Necrosis Factor-alpha (TNF- α) were measured by ELISA and normalized to urea. Matched-pair Wilcoxon test was used to compare pre- and post-treatment data and simple linear regression models were calculated to correlate plasma and BAL data.

Summary of Results We enrolled 33 HIV-1-infected subjects (median CD4 count=364 μ l with undetectable viral loads). Median age was 53 years and 58% were smokers. In the plasma, there was a significant increase between pre- and post-treatment median levels of IL-4 (0.24 vs. 6.16 pg/mg, $p=0.02$), IL-10 (6.42 vs. 24.3 pg/mg, $p=0.05$) and TNF- α (11.3 vs. 23.0 pg/mg, $p<0.01$). Also, there was a significant increase in median BAL TNF- α levels post-treatment (3.8 vs 12.9 pg/mg, $p<0.01$). There were no significant changes in BAL levels of IFN- γ , IL-4, IL-10, or GM-CSF. Only GM-CSF showed a correlation between plasma and BAL levels ($r=0.40$, $p=0.02$).

Conclusions In HIV-1-infected individuals on antiretroviral therapy, dietary supplementation with zinc and S-adenosylmethionine increased both systemic and pulmonary inflammatory mediators, which may enhance the innate immune response to lung infections.

536 LIPOPOLYSACCHARIDE INDUCES MMP-9 AND MMP-12 AND MODULATES ALVEOLAR EPITHELIAL CELLS ACTIVATION

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10.1136/jim-2016-000393.539

Purpose of Study Metalloproteinases (MMP), MMP-9 and MMP-12, play key roles in extracellular matrix (ECM) remodeling and inflammation-mediated lung diseases. In the present study, we investigated whether bacterial endotoxin, lipopolysaccharide (LPS), an inducer of pulmonary inflammation, induces the activation of alveolar epithelial cells through MMP-9 and MMP-12.

Methods Used A549 cells were subcultured in normal growth media for 24 h, followed by treatment with LPS (1 or 10 ng/ml) for 6 or 24 h. Alveolar epithelial transcellular permeability was measured using blue dextran extravasation. The expression level of TGF β , Col3A1, MMP-9, and MMP-12 were analyzed using real-time quantitative PCR (qPCR). NF- κ B activation was analyzed using immunofluorescence, and cell migration was analyzed using wound-scratch assay and Boyden chamber.

Summary of Results Alveolar epithelial transcellular permeability was significantly increased by LPS regardless of the dose. The 10 ng/ml LPS potently induced dextran blue extravasation, an increase by 30% vs the 1 ng/ml LPS, respectively. LPS significantly increased the expression of TGF β by 3.5-fold, Col3A1 by 5.5-fold, MMP-9 by 1.61-fold, and MMP-12 by 3.8-fold. LPS stimulated NF- κ B nuclear translocation. LPS stimulated cell migration toward wound healing and cell migration using Boyden chamber assay by 19 and 37%, respectively.

Conclusions These results suggest that LPS plays an important role in the activation of alveolar epithelial cells toward lung ECM remodeling by regulating TGF β and its target Col3A1 and modulation of MMP-9 and MMP-12 expression via NF- κ B nuclear translocation. These results suggest that alveolar epithelial cells may contribute to ECM remodeling and that MMP-9 and MMP-12 may serve as a potential therapeutic targets in LPS-induced lung injury and lung remodeling via inflammation.

537 NEUTROPHIL STIMULATION INCREASES CAPACITY TO DEGRADE THE MATRIKINE PROLINE-GLYCINE-PROLINE VIA EXOSOMES

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10.1136/jim-2016-000393.540

Purpose of Study Leukotriene A4 hydrolase (LTA4H) has two catalytic sites; one converts leukotriene A4 into leukotriene B4, a neutrophil chemotactic agent. Another degrades the collagen-breakdown product Proline-Glycine-Proline (PGP), implicated in pathogenesis of chronic obstructive pulmonary disease (COPD). PGP causes neutrophil chemotaxis. Consequently, PGP breakdown by LTA4H is anti-inflammatory.

LTA4H is secreted by neutrophil-derived exosomes. We hypothesized that stimulation of neutrophils would increase PGP degradative capacity of these exosomes.

Methods Used Neutrophils were purified from peripheral blood from healthy volunteers and placed on ice X5 minutes. 5×10^6 cells were incubated with 2 μ M formyl-Methionine-Leucine-Phenylalanine-OH (fMLP) or equivalent quantity of DMSO solvent in 1 mL of RPMI for 30 minutes at 37 C. Cells were pelleted (4 kG X7 minutes), followed by centrifugation at 10 k G X40 minutes. Supernatant was then ultracentrifuged at 100 k G X2 hours and pellet was resuspended in filtered PBS. Exosomes were counted by nanotracking analysis on the Nanosight NS300. After counting, exosomes were diluted to a concentration of 10^6 /mL and incubated with PGP in 100 μ L at 37 C with 5% CO₂ X1 hour. Exosome-only and PGP-only negative controls as well as LTA4H+PGP positive control were used. After incubation, solutions were diluted 1:100, frozen at -20 C, and analyzed by mass spectroscopy. PGP remaining was measured and LTA4H activity inferred.

Summary of Results Exosome counts were similar between stimulated and quiescent neutrophils. Exosomes derived from stimulated and quiescent neutrophils degraded PGP. PGP degradation increased with fMLP-stimulation (67% versus 22%, $p=0.019$). This was inhibited by coincubation with the LTA4H inhibitors bestatin or captopril.

Conclusions Neutrophil-derived exosomes degrade the matrikine PGP. Stimulation of neutrophils produces qualitatively distinct exosomes with increased activity of LTA4H, an enzyme with both pro- and anti-inflammatory properties. This is a novel mechanism of innate immune modulation.

538 RED CELL DISTRIBUTION WIDTH AS A BIOMARKER OF PULMONARY HYPERTENSION

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10.1136/jim-2016-000393.541

Purpose of Study Pulmonary hypertension (PH) is a devastating condition with high morbidity/mortality. Early detection is critical and simple biomarkers of disease are urgently needed. Red cell distribution width (RDW) is a commonly obtained lab parameter that is elevated in various cardiovascular diseases. The purpose of this study was to determine if RDW is elevated in different forms of PH and to compare RDW values in patients with PH vs. those at-risk for PH.

Methods Used We conducted a retrospective cross-sectional analysis of patients seen at the University Medical Center Comprehensive Pulmonary Hypertension Center in New Orleans from August 2014-August 2015 who had an RDW measurement (PH=112, at risk for PH=49). PH was defined based on right heart catheterization (RHC, mean pulmonary artery pressure ≥ 25 mmHg). At-risk for PH patients either did not have a diagnosis of PH based on RHC or lacked echocardiographic features suggestive of PH but did have risk factors:

Summary of Results PH patients had the following WHO group classifications: I=61, II=27, III=14, IV=10. The most common at-risk condition was Sick Cell Disease (SSc; n=29). RDW was not significantly different among the WHO group classifications ($p=0.08$). There were significant correlations between RDW and 6-minute walk distance (6 MWD, $r=-0.35$, $p=0.001$), as well as between RDW and BNP ($r=0.32$, $p=0.001$). RDW was significantly higher in patients with PH compared to disease-free controls ($15.4 \pm 2.2\%$ vs. $14.1 \pm 1.2\%$, $p<0.0001$). There was no difference in RDW between those with PH and the group at-risk for PH ($15.5 \pm 2.2\%$ vs. $14.8 \pm 2.3\%$, $p>0.05$), but SSc patients with PH had significantly higher RDW values compared to SSc patients without PH ($16.2 \pm 2.1\%$ vs. $14.2 \pm 2.0\%$, $p=0.02$).

Conclusions PH patients had significantly higher RDW values compared to controls, but RDW values were not different across WHO groups. RDW moderately correlated to markers of disease severity (6 MWD and BNP). SSc patients with PH had higher RDW values compared to SSc patients without PH. This suggests the potential use of RDW as a biomarker to identify SSc patients with PH.

539 PULMONARY ARTERY ENLARGEMENT IS ASSOCIATED WITH PULMONARY HYPERTENSION AND PULMONARY ARTERIAL COMPLIANCE IN SEVERE CYSTIC FIBROSIS

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10.1136/jim-2016-000393.542

Purpose of Study Pulmonary arterial enlargement, defined as a pulmonary artery (PA) diameter to ascending aorta (A) diameter (PA:A) ratio >1 on computed tomography (CT), has become increasingly recognized as a non-invasive marker of pulmonary vascular disease in lung diseases, and may suggest pulmonary hypertension (PH) in obstructive lung diseases. Recently, a PA:A >1 was shown to be highly prevalent in adults with cystic fibrosis (CF). We hypothesize that PA:A will correlate to hemodynamic measures and will identify underlying PH in CF.

Methods Used We conducted a cohort study of all adults with CF referred for lung transplant evaluation at UAB from 2000 to 2011. Subjects were included if they had CT, right heart catheterization, and echocardiogram data. We calculated the PA:A ratio using the PA diameter measured at the level of the bifurcation and the aortic diameter measured from the same CT slice. Using linear regression analyses, we explored the associations between PA:A ratio and hemodynamic parameters including mean pulmonary artery pressure (mPAP), pulmonary arterial compliance (PAC) and pulmonary vascular resistance (PVR), and echocardiographic indices including right ventricular (RV) systolic pressure, RV size and ejection fraction (RVEF). We used logistic regression models to determine associations between PA:A and PH defined by mPAP >25 mmHg.

Summary of Results Of the 38 adults with CF analyzed, 58% were male. The mean age was 28 ± 9 years. PA:A was 1.05 ± 0.20 ; mPAP was 28 ± 3 mmHg; and PAC was 2.25 ± 1.04 ml/mmHg. PA:A >1.15 was associated with mPAP

>25 mmHg (OR 13.3, 95%CI 1.28–139, 0.03). In univariate linear regression models, PA:A was associated with mPAP (β 0.60; p 0.001) and PAC (β -0.49; p 0.037), and negatively associated with FVC (β -0.40; p 0.04) and RVEF (β -0.42; p 0.04). In multivariate analysis adjusting for age, sex, and FEV₁%, PA:A remained associated with mPAP (β 0.60; p 0.002). PA:A ratio was not associated with RV size, PVR, or transplant-free survival.

Conclusions Elevated PA:A ratio is associated with mPAP and is a reliable non-invasive marker of PH in patients with severe CF. Given prior evidence that PA enlargement is associated with poor outcomes in CF, this may be an important biomarker for advanced disease.

540 **PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA ENHANCES HUMAN PULMONARY ARTERY SMOOTH MUSCLE CELL APOPTOSIS SUSCEPTIBILITY THROUGH REGULATION OF MICRORNA-21 AND PDCD4**

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10.1136/jim-2016-000393.543

Purpose of Study Pulmonary vascular remodeling is a central pathophysiological phenomenon in pulmonary hypertension (PH) that develops in association with enhanced proliferation of pulmonary artery smooth muscle cells (PASMC) in the medial vascular compartment. Cellular resistance to apoptosis is an increasingly recognized phenomenon in vascular remodeling and PH. Programmed cell death 4 (PDCD4) is a prototype apoptosis mediator which may influence apoptosis activity in pulmonary vascular wall cells. We recently demonstrated that activation of peroxisome proliferator-activated receptor gamma (PPAR γ) enhanced PDCD4 expression and attenuated proliferation in hypoxia-exposed human pulmonary artery smooth muscle cells (HPASMC). The current study examines interactions between PPAR γ , microRNA-21 and its gene target, PDCD4 to further explore the influence of PPAR γ on apoptosis susceptibility in HPASMC.

Methods Used The effects of hypoxia, PPAR γ , miRNA-21 and PDCD4 on HPASMC apoptosis susceptibility were determined using the ApoAlert[®] Caspase Colorimetric Assay Kit (Clontech). In parallel, apoptosis was examined using an Annexin V Apoptosis Detection Kit (BD Biosciences) and fluorescence-activated cell sorting (FACS) analysis. To determine the effects of hypoxia on the expression of a major mediator of apoptosis, PDCD4 levels were examined in the mouse lung in vivo and in HPASMC in vitro.

Summary of Results PDCD4 protein and mRNA expression were reduced in the hypoxic mouse lung and in hypoxia-exposed HPASMC. Apoptosis activity was reduced in hypoxia-exposed HPASMC and in response to microRNA-21 overexpression or siRNA-mediated PPAR γ and PDCD4 depletion. Activation of PPAR γ using a PPAR γ -encoded adenovirus restored apoptosis activity to baseline levels. Pharmacological activation of PPAR γ with

rosiglitazone demonstrated a dose dependent increase in annexin V detection by flow cytometry.

Conclusions Collectively, these findings identify microRNA-21 and PDCD4 as key mediators that regulate the susceptibility of HPASMC to undergo apoptosis in response to PPAR γ . Our findings demonstrate that an additional mechanism through which PPAR γ inhibits proliferation in hypoxia-exposed HPASMC occurs through augmentation of apoptosis activity.

541 **MITOCHONDRIAL FUNCTION IN ALVEOLAR MACROPHAGES IS IMPAIRED IN HIV-1 TRANSGENIC RATS VIA A PPAR γ -DEPENDENT PATHWAY**

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10.1136/jim-2016-000393.544

Purpose of Study HIV impairs alveolar macrophage (AM) antioxidant defenses and innate immunity. HIV-1 transgenic rats have defects in AM phagocytic function, hydrogen peroxide scavenging, and inflammatory cytokine production. As these processes depend on mitochondrial function, we hypothesized that HIV-1 transgene expression dysregulates mitochondrial function via down-regulation of peroxisome proliferator-activated receptor gamma (PPAR γ) coactivator 1-alpha (PGC-1 α), a key mitochondrial metabolic regulator known to be modulated by PPAR γ .

Methods Used To model the alveolar space of an individual living with HIV, we used an HIV-1 transgenic rat model in which the same HIV-related viral proteins seen in the alveolar spaces of infected patients are expressed. AM isolated from whole-lung lavage of HIV-1 transgenic rats and their wild-type littermates were cultured for 24 hrs \pm 10 μ M of the synthetic PPAR γ ligand pioglitazone. Basal respiration, ATP production, maximal respiration, and spare capacity were determined via mitochondrial stress testing in a Seahorse extracellular flux analyzer. Gene expression of PGC-1 α was determined by qRT-PCR in AM from wild-type and HIV-1 transgenic rats.

Summary of Results AM from HIV-1 transgenic rats demonstrated significant impairments in basal respiration, ATP production, maximal respiration, and spare capacity. PGC-1 α gene expression was significantly decreased in HIV-1 transgenic rat AM, relative to expression in wild-type controls. In contrast, pioglitazone treatment reversed the AM derangements in HIV-1 transgenic rats.

Conclusions The significant impairments in mitochondrial bioenergetics identified in this study offer a novel pathway by which HIV-related viral proteins can compromise a range of downstream AM functions. PGC-1 α suppression by HIV-1 transgene expression may contribute to AM immune dysfunction through dysregulation of mitochondrial function. Although further experiments are necessary to confirm our findings and determine the effects of pioglitazone on other AM functions, these experiments offer an exciting new avenue of investigation in HIV and suggest a possible role for PPAR γ agonists as adjunctive therapy in individuals living with HIV.

542 **PSEUDOMONAS AERUGINOSA QUORUM SENSING MOLECULES ATTENUATE PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR (PPAR) GAMMA AND PPAR GAMMA COACTIVATOR 1 (PGC1)-ALPHA, AND SUPPRESS EPITHELIAL MITOCHONDRIAL RESPIRATION**

NM Maurice,¹ B Bedi,^{1,2} JJ Varga,¹ Z Yuan,^{1,2} JB Goldberg,¹ M Hart,^{1,2} RT Sadikot^{1,2}. ¹Emory University, Atlanta, GA; ²Atlanta VA Medical Center, Decatur, GA.

10.1136/jim-2016-000393.545

Purpose of Study *P. aeruginosa* is a major cause of multi-drug resistant infections, especially in immunocompromised and hospitalized patients. The pathogenic profile of *P. aeruginosa* is related to its ability to secrete a variety of virulence factors. Quorum sensing (QS) is a mechanism wherein *P. aeruginosa* secretes small diffusible acyl-homoserine lactone molecules such as N-3-oxododecanoyl homoserine lactone (3-oxo-C₁₂-HSL), which promote inter-bacterial communication, virulence, and biofilm formation. There is a growing body of evidence that QS molecules can also modulate host biology through actions on human cells. Mitochondrial respiration is one possible target of these molecules. The purpose of this study was to determine whether 3-oxo-C₁₂-HSL affects host mitochondrial function, and, if so, whether this effect is associated with modulation of PPAR γ and PGC1- α , a transcription co-activator that is known to enhance mitochondrial biogenesis and cellular respiration.

Methods Used BEAS-2B cells were treated for 6 and 16 hours with 3-oxo-C₁₂-HSL (100 μ mol) or PAO1 (MOI 1 or 30). Mitochondrial function was assessed using the Seahorse XF Cell Mito Stress Test. Levels of PPAR γ and PGC1- α mRNA and protein were quantified using qRT-PCR and western blotting, respectively.

Summary of Results Treatment with 3-oxo-C₁₂-HSL induced a dose-dependent decrease in basal oxygen consumption rate (OCR), maximal OCR, and ATP production. There was no significant change in spare respiratory capacity. 3-oxo-C₁₂-HSL and PAO1 also caused a significant decrease in PPAR γ and PGC1- α mRNA and protein levels. **Conclusions** *P. aeruginosa* QS molecules suppress mitochondrial respiration and decrease PPAR γ and PGC1- α levels in bronchial epithelial cells. These findings suggest that modulation of host mitochondrial function and inhibition of PPAR γ signaling contribute to the pathogenicity of *P. aeruginosa*. Pharmacological PPAR γ activation may provide a complementary therapeutic approach to the treatment of *P. aeruginosa* infection.

543 **POST-EXTUBATION NONINVASIVE VENTILATION AFTER CONGENITAL HEART SURGERY IN INFANTS**

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10.1136/jim-2016-000393.546

Purpose of Study We sought to describe the epidemiology and determine the impact of postoperative noninvasive ventilation (NIV) on extubation failure and other clinical

outcomes when compared to nasal cannula (NC) oxygen in infants following cardiopulmonary bypass (CPB) surgery.

Methods Used 358 infants <200 days undergoing cardiac surgery requiring CPB from 7/2012–12/2015 were included. Patient characteristics/outcomes considering first planned extubation were compared between two cohorts: NIV (BiPAP or CPAP) or supplemental oxygen [including high flow nasal cannula]. Retrospective Propensity Score Analysis (PSA) [logistic regression 1:2 matching nearest neighbor, 0.2 caliper] was performed; 10 patients with missing PSA variables excluded. Extubation failure was defined up to 72 hrs.

Summary of Results Extubation to NIV occurred in 102/358 (28%); median duration of NIV 44 hrs. 43/256 (17%) extubated to NC were 'rescued' by NIV, 19 of which required reintubation. Analysis demonstrated NIV was empirically chosen for younger, higher risk patients. To control treatment bias, PSA using pre-extubation variables identified 42 NIV and 65 NC subjects. In the PSA cohort, patients extubated to NC had median initial flow of 5LPM. Median duration of NIV was 47.4 hrs (25.4, 96.6). 19 (29%) patients in NC group escalated to NIV. Extubation failure occurred in 12 (11%) and was not different between groups; median time to reintubation was 18.6 hrs for NIV vs. 20.7 hrs for NC. Patients extubated to NC were weaned to 2LNC sooner, achieved full enteral feeds and had first oral attempt sooner, and had shorter hospital length of stay (LOS).

Conclusions When controlling for patient characteristics and management parameters present at extubation with PSA, there was no difference in extubation failure rate between patients extubated to NIV vs. NC in infants after congenital heart surgery requiring CPB. However, NIV was associated with increased respiratory resource utilization, delay in nutrition delivery, and increased hospital LOS. Prospective efforts to help select patients that would best benefit from NIV and utilization of NIV weaning protocols could lead to improved postoperative outcomes.

**Renal, Electrolyte and Hypertension I
Concurrent Session**

2:00 PM

Sunday, February 12, 2017

544 **IMPAIRED FUNCTIONAL SYMPATHOLYSIS IN END-STAGE RENAL DISEASE**

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10.1136/jim-2016-000393.547

Purpose of Study Chronic renal failure patients have reduced exercise tolerance contributing to increased cardiovascular risk. Reflex activation of sympathetic nervous activity (SNA) during exercise increases cardiac output and vasoconstricts nonworking skeletal muscle. However, within exercising skeletal muscle, local metabolites are generated that oppose SNA-mediated vasoconstriction to

preserve blood flow and oxygenation within the working muscle, termed functional sympatholysis. We hypothesized that chronic kidney disease (CKD) and end-stage renal disease (ESRD) patients have impaired functional sympatholysis resulting in reduced oxygenation of exercising muscle which may contribute to exercise dysfunction.

Methods Used In 33 subjects (10 CKD, 10 ESRD, 13 controls) muscle oxygen tissue saturation index (TSI) was measured using near-infrared spectroscopy (NIRS) positioned over the flexor digitorum profundus in the forearm. Lower-body negative pressure (LBNP) was applied at -20 mmHg to induce increased SNA without arterial blood pressure changes. Continuous measurements were made at baseline, during LBNP, and during LBNP with concomitant rhythmic handgrip exercise performed at 30% of maximum voluntary contraction.

Summary of Results Baseline TSI was significantly lower in ESRD compared to controls and CKD ($p=0.004$). There was a reduction in muscle TSI in all groups during SNS activation induced by LBNP at rest (LBNP_{rest}). During LBNP with handgrip exercise (LBNP_{ex}), there was a significant improvement in muscle TSI when compared to LBNP_{rest} in controls ($-15.20 \pm 3.05\%$ vs. $-5.01 \pm 2.62\%$, $p=0.049$) and in CKD ($-15.74 \pm 7.66\%$ vs. 2.26 ± 4.28 , $p=0.003$), suggesting preserved functional sympatholysis. However, there was no improvement in muscle TSI with concomitant exercise in ESRD ($-11.94 \pm 2.04\%$ vs. $-6.25 \pm 1.82\%$, $p=0.330$).

Conclusions ESRD patients have impaired functional sympatholysis that may contribute to exercise intolerance. Further studies are needed to elucidate the mechanisms underlying impaired functional sympatholysis in ESRD.

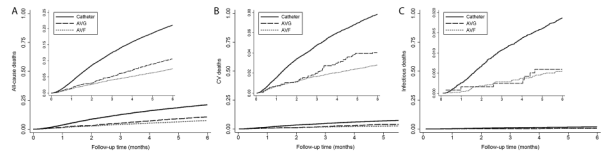
545 VASCULAR ACCESS AND MORTALITY IN INCIDENT ESRD

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10.1136/jim-2016-000393.548

Purpose of Study The purpose of the study is that fistula is the general recommendation for all hemodialysis patients, but creating a mature AV fistula can be challenging in elderly individuals. It is unclear if elderly incident HD patients derive a survival benefit from an AV fistula over an AV graft or a tunneled catheter.

Methods Used We examined a nationwide cohort of 52,172 US veterans with advanced CKD transitioning to hemodialysis during 2007–2011. The association of vascular access type at hemodialysis initiation (arteriovenous fistula, arteriovenous graft or tunneled catheter) with all-cause, cardiovascular and infectious mortality during the 6-month post-dialysis period was assessed using Cox models and competing risk regressions with adjustment for potential confounders. Effect modification by age was examined by examining associations in pre-specified age subgroups (<50, 50-<60, 60-<70, 70-<80 and ≥80 years old), and by including interaction terms.

Summary of Results 8,944 (19%) patients started HD with an AVF, 1,233 (3%) with an AVG, and 36,616 (78%) with a TDC. During the 6-month post-transition period, a total of 8,500 all-cause, 3,021 cardiovascular, and 702



Abstract 545 Figure 1

infection-related deaths were observed. Compared to patients with a mature AVF, those with AVG and TDC had a higher overall risk of all-cause mortality (adjusted hazard ratio [HR]: 1.38; 95% confidence interval [CI] 1.14–1.67 and HR: 2.71; 95%CI 2.50–2.93, respectively) and cardiovascular mortality (subhazard ratio [SHR] and 95%CI: 1.42, 1.04–1.94 and 2.47, 2.16–2.82, respectively). Only TDC use was associated with higher infection-associated mortality (SHR and 95%CI for AVG vs. AVF: 1.03, 0.47–2.30 and for TDC vs AVF: 3.04, 2.24–4.13, respectively). These associations were not modified by age (interaction $p=0.42$, $p=0.38$ and $p=0.23$ for all-cause, cardiovascular and infectious mortality).

Conclusions A mature AVF is associated with the best outcomes in incident hemodialysis patients of all ages during the immediate post-transition period, and the use of TDCs with the worst outcomes. A catheter-last approach should be advocated even in the most elderly incident HD patients.

546 PRE-DIALYSIS IVC DIAMETER PREDICTS ULTRAFILTRATION GOAL IN HOSPITALIZED DIALYSIS PATIENTS

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10.1136/jim-2016-000393.549

Purpose of Study Estimates of hemodialysis(HD) ultrafiltration(UF) goals are based on volume status. UF goals are usually empiric, with hypotension on HD indicating a ‘dry weight.’ Bedside ultrasonography can determine inferior vena caval diameter (IVCD) which may predict right ventricular (RV) pre-load. We theorized that IVCD may enhance assessment of volume status and help guide UF goals for HD.

Methods Used End stage renal disease inpatients on dialysis without known right heart failure were studied. Prior to HD, hypertension (HTN) (SBP> 140 mmHg) and presence of edema were recorded and UF goal assigned. A nephrology fellow, trained to assess IVCD using a GE Sonosite machine, measured the IVCD at its entry into the right atrium prior to and following HD. Linear regression (LR) was used to examine the association between pre-IVCD and volume removal.

Summary of Results 20 patients were studied from Jan-May 2016. Physical findings: edema (65%), HTN (70%) and both (45%). Groups were defined as euvolemic (no edema, no HTN N=3) or hypervolemic (edema and HTN N=10). Table shows pre and post-dialysis SBP

Abstract 546 Table 1

Group (Mean±SD)	Pre SBP (Mean±SD)	Post SBP (Mean±SD)	Pre IVCD (Mean±SD)	Post IVCD (Mean±SD)	Change in IVCD (Mean±SD)	UF removed (Mean±SD)
Euvolemic	113±13	114±9	1.47±0.3	1.33±0.4	0.1±0.1	0.3±0.6
Hypervolemic	168±23	142±16*	2.44±0.4	2.01±0.4*	0.4±0.2	2.07±0.5
All patients	152±27	133±17*	1.74±0.4	2.07±0.5*	0.3±0.2	3.75±0.98

*p<0.05 when compared to pre-dialysis levels

(mmHg), IVCD (cm), change in IVCD (cm) and UF removed (L). In edematous patients LR showed for every one cm change in pre IVCD the amount of volume removed increased by 1.43 kg controlling for edema and pre-SBP.

Conclusions IVCD is a non-invasive, objective marker of pre-load in HD inpatients, is well tolerated, and correlates with UF removal. IVCD augments volume assessment and may help guide determination of UF goals in HD.

547 HYPONATREMIA IN PATIENTS WITH WEST NILE INFECTION: A RETROSPECTIVE ANALYSIS OF 23 CASES

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10.1136/jim-2016-000393.550

Purpose of Study To identify prevalence of hyponatremia in patients with WN infection; explore possible mechanisms, and its impact on length of hospital stay and mortality.

Methods Used We conducted a retrospective review of patients treated with WN virus infection from 01/2011 until 04/2016 at the TTUHSC. An institutional database was searched for diagnosis of WN infection diagnosis codes. Patients were included if they had clinical and laboratory evidence active infection. Patients were classified as having neurologic WN infection and WN fever, and hyponatremia: mild (130–134 mmol/l), moderate (125–129 mmol/l), and severe (below 125 mmol/l).

Summary of Results 23 Patients met the inclusion criteria, of which 18 patients (78%) had hyponatremia and 17 of these patients (94%) had a neurologic form WN infection. It was found that 77.7% of the patients with hyponatremia were over 50 years, and all survived. The average

Abstract 547 Table 1 Demographic

	Percentage
<25	8.7
25–49	21.7
50–75	60.9
>75	8.7
Female	52.1
Male	48
Mortality	8.6

Abstract 547 Table 2 Sodium Levels in Patients with WN

Sodium level	Percentage
>134	21.7
130–134	56.5
125–129	13.0
<125	8.7

hospitalization length was 24 Days for severe hyponatremia, 14 Days for mild, and 10 Days for moderate. All patients with moderate and severe hyponatremia required rehabilitation.

Conclusions Hyponatremia is a common finding in patients with WN infection (78%). Decreased level of consciousness and concurrent medications could result in transient hyponatremia. A moderate or severe level of hyponatremia was seen in 27.1% of the patients. Mechanistically some cases of hyponatremia exhibited features of SIADH (3) while others appeared to be volume-related. The severity of hyponatremia and infection, as well as comorbid conditions seem to be independent determinants of neurologic sequelae and the length of stay in patients with WN infection.

548 SOLUBLE HUMAN LEUKOCYTE ANTIGEN-G LEVELS AND PROLONGED ALLOGRAFT SURVIVAL: A DEMOGRAPHIC ANALYSIS

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10.1136/jim-2016-000393.551

Purpose of Study Human leukocyte antigen-G (HLA-G) is a tolerogenic protein that contributes to allograft survival. Dimerized, soluble HLA-G (sHLA-Gd) has been shown to significantly prolong allograft survival and correlate with reduced levels of pro-inflammatory cytokines. Our goal was to determine if subject's sHLA-Gd levels correlate with patient demographics, allowing clinicians to better predict a patient's immunogenicity and likelihood of rejecting a transplanted organ.

Methods Used Blood samples collected from 122 renal transplant recipients, with no history of rejection (NR, n=90) or with a history of biopsy confirmed acute cellular rejection (ACR, n=32), were analyzed by immunoprecipitation and western blot. The sHLA-Gd level was determined and categorized based on participant's rejection status,

gender, ethnicity, age, cause of renal disease, type of transplant donor, number of Class I and Class II HLA mismatches, as well as class I and class II panel reactive antibody (PRA) levels.

Summary of Results Our data show sHLA-Gd levels are significantly higher ($p=0.0015$) in NR than ACR. Higher sHLA-Gd levels were found in NR than ACR females ($p=0.006$), African-Americans ($p=0.0039$), Caucasians ($p=0.0067$), deceased-donor transplants ($p=0.0166$), living-donor transplants ($p=0.0293$), and those with Glomerular Disease ($p=0.0058$) or Polycystic Kidney Disease ($p=0.0229$). No significant difference in sHLA-Gd levels were found between NR and ACR males or those with diabetes mellitus or hypertension. Higher sHLA-Gd levels correlate with better class I and class II HLA matches between donors and recipients. Moreover, lower class I PRA and class II PRA correlate with high sHLA-Gd levels.

Conclusions Data demonstrates that higher sHLA-Gd levels correlate with prolonged allograft survival in most demographic populations. sHLA-Gd is an agent which modulates the allogenic and inflammatory response, serving as a biomarker for immunogenicity. Measuring sHLA-Gd levels may assist clinicians in tailoring immunosuppression regimens to improve renal allograft survival in patient with differing degrees of immunogenicity.

549 GENDER DIFFERENCES IN MRI CONTRAST-INDUCED FIBROSIS

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10.1136/jim-2016-000393.552

Background Magnetic resonance imaging (MRI) contrast-induced systemic fibrosis (also known as ‘nephrogenic’ systemic fibrosis, NSF) exclusively occurs in patients with impaired renal function. Gadolinium has been detected in human skin biopsies by various methods including induction-coupled plasma mass spectrometry (ICP-MS) and scanning electron microscopy with electron dispersive spectroscopy (SEM-EDS). Based on our experience with rodents, we suspected males are more susceptible to gadolinium-based contrast toxicity

Methods Used Rats were gender-, age-, and weight-matched. One group was treated with gadodiamide (2.5 mmol/kg intraperitoneally) and another served as control. Skin, liver and lung were paraffin-embedded or flash-frozen. Tissue gadolinium was measured by ICP-MS.

Summary of Results Males demonstrated more severe disease and earlier onset than females. Regardless of gender, gadolinium was detectable in skin, liver and lung. Male rats treated with gadodiamide had greater gadolinium

levels in skin compared to female counterparts. Both male and female groups had similar skin thickness and dermal nuclei on dermal histology.

Conclusions Male rats are much more susceptible to the toxic effects of gadolinium-based contrast with respect to females. That there is greater retention of gadolinium in the skin suggests that biodistribution differs between the genders. This may explain the earlier onset and greater severity in males.

550 ASSESSMENT OF INPATIENT DIALYSIS ADEQUACY USING ON-LINE CLEARANCE: A FELLOW QUALITY IMPROVEMENT PROJECT

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10.1136/jim-2016-000393.553

Purpose of Study A Hemodialysis (HD) single-pool Kt/V target of >1.4 (Kt/V) is widely accepted as the minimum standard for outpatients dialyzing thrice weekly. Studies evaluating HD adequacy in hospitalized patients suggest worse outcomes when Kt/V is below standard outpatient goals. However, HD adequacy is rarely assessed in hospitalized settings. Online clearance monitoring (OCM) by sodium dialysance can accurately estimate urea clearance. In this project, we assessed OCM derived adequacy in hospitalized ESRD patients treated with HD.

Methods Used Data were prospectively collected on all ESRD patients treated over a 2 week period. HD was performed on a Fresenius 2008T machine with Optiflux 180 dialyzer at $Q_b=400$ ml/min & $Q_d=800$ ml/min. Session durations were based on outpatient prescriptions or 4 hours when not available. Urea volume of distribution (Vd) was estimated by the Watson formula. OCM derived Kt/V values were recorded at the end of each HD session. Data are mean +/- (SEM).

Summary of Results 21 patients were treated with 62 HD sessions. There were 10 AVF, 2 AVG, and 9 CVC responsible for 30, 8, and 24 treatments respectively. Treatment times were 227 ± 31 min. OCM data indicated only 42% (26/62) of treatments achieved $Kt/V \geq 1.4$ with 22% (14/62) having $Kt/V < 1.2$. Analysis of patients’ initial HD treatment suggests high Vd and CVC access are associated with failure to meet Kt/V goal.

Conclusions These data suggest that inpatient HD frequently fails to achieve adequacy standards. OCM was easy to perform and only required calculation of Vd. We postulate that OCM directed therapy has the potential to improve HD delivery in the inpatient setting and possibly improve outcomes. Based on our results, we plan to utilize OCM in future determinations of dialysis session length.

Abstract 550 Table 1

Kt/V Goal	Access	Vd (L)	Time (min)	UF vol (L)	spKt/V	eKt/V
Met n=10	20% CVC	36.7 (1.1)	232 (6.3)	2.1(0.4)	1.65 (0.07)	1.43 (0.06)
Fail n=11	64% CVC	49.7 (2.7)	228 (8)	2.8 (0.5)	1.20 (0.06)	1.03 (0.05)
P-value	0.04	0.0003	0.34	0.16	0.06	0.05

551 DIGITAL URINE SEDIMENTS: KEEPING THE ATTENDING IN THE LOOP

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Purpose of Study Nephrology fellowships often need that fellows perform analysis of the urine sediment (U-Sed) in the absence of the faculty. Solo assessment of the U-Sed dilutes the educational value and may lead to erroneous interpretation of findings. To address this deficiency, we theorized that smart phone digital pictures of the U-Sed, taken by fellows and texted to the faculty, may enhance educational and clinical value. To address this question, we assessed a random group of images for quality, discrimination of elements, and diagnostic utility.

Methods Used Three fellows submitted U-Sed images from the inpatient consult service for assessment, this were photographed through the microscope eye piece. In a group session, fellows and faculty (blinded to the diagnosis) scored each image for 17 variables: image quality (acceptable or not), diagnostic utility (yes/no), casts (presence+5 types), cells (presence+3 types), and other (yeast, crystals, or debris).

Summary of Results Forty-five images were assessed by a group of 5 faculty (FAC) and 5 fellows (FEL). Several images were used as controls and carefully classified by two faculty prior to the session.

Conclusions Most smart phone images of U-Sed are of good quality. Muddy brown casts, crystals, and red cells can be recognized, but candida is less obvious. Sampling error may occur based on the experience of photographer. Keeping faculty in the loop by sharing U-Sed images may be of educational and clinical utility.

PARAMETER	PARAMETER RECOGNIZED OR SCORED		
	ALL	FACULTY	FELLOWS
Image quality (acceptable)	73%	80%	66%
Diagnostic use (useful)	44%	44%	44%
Elements seen			
Casts	42%	39%	45%
Cells	24%	21%	28%
Crystals	16%	16%	15%
Debris	37%	66%	30%
Candida	4%	6%	2%
Control images			
Muddy brown casts	NA	100%	96%
Crystals	NA	100%	88%
Debris	NA	100%	60%
Red cells	NA	100%	100%
Candida	NA	88%	20%

Abstract 551 Figure 1

552 NITRIC OXIDE REGULATES RENIN SYNTHESIS AND SECRETION IN THE COLLECTING DUCT

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Purpose of Study Regulation of renin synthesis and release by the juxtaglomerular cells has been extensively studied. However, the mechanisms regulating renin derived from the principal cells of the collecting duct are largely unknown. Renin synthesis and secretion in the collecting duct are stimulated by a calcium dependent PKC and activation of cAMP/PKA/CREB pathway. The present study aimed to examine the mechanism by which nitric oxide (NO) regulates renin in collecting duct cells.

Methods Used To examine the effects of NO on collecting duct renin synthesis, we measured mRNA by qRT-PCR and protein levels by western blot in mouse collecting duct M-1 cells treated for 8h with either NONOate (NO-donor; 1 mM) or L-NAME (NO synthase inhibitor; 1 mM). To further determine the role NO on renin secretion, renin amount was measured by ELISA in supernatants of cells treated as indicated above. These experiments were complemented by immunofluorescence studies using a rabbit anti-renin antibody (1:400 dil; RT, ON).

Summary of Results In M-1 cells, either NONOate or L-NAME treatments both increased intracellular renin protein levels (1.1 ± 0.1 vs. 0.97 ± 0.0 a.u.; $P < 0.05$) compared to vehicle (PBS)-treated cells (0.445 ± 0.1). However, renin mRNA levels only increased in response to NO synthase inhibition with L-NAME ($P < 0.05$) but not after NONOate. Interestingly, the amount of extracellular renin was augmented in response to L-NAME but not to NONOate or PBS (371 ± 25.7 vs. 218 ± 25.2 and 251 ± 11.3 pg/ml; $P < 0.05$). The stimulation of intracellular renin protein expression in response to NONOate and L-NAME was confirmed by immunofluorescence.

Conclusions In M-1 cells: 1) NO directly inhibits renin secretion as reflected by the accumulation of renin intracellularly and the lack of renin secretion into the extracellular space. 2) Inhibition of NO synthase by L-NAME stimulates renin synthesis and secretion likely due to reduced levels of intracellular soluble guanylate cyclase, cGMP, and PKG, allowing for a positive stimulation of PKA on renin synthesis and secretion. Further studies will delineate this pathway.