2015, which he refused resection. He elected to initiate radiation & chemotherapy instead. He was then found to have a right upper lung and left lower lung masses concerning for metastatic disease.

A diagnostic biopsy was performed and revealed SqCC. He was started on pembrolizumab (keytruda™) 200 mg IV every 3 weeks in 10/2016 in outpatient setting. On routine outpatient blood work, he was found to have severe hyponatremia. Patient was hospitalized, his serum sodium was 117 mmol/L, urine osmolality 158 mosm/kg, urine analysis specific gravity <1.005, serum osmolality 241 mosm/kg, urine sodium 62 mEq/L, Thyroid stimulating hormone 80.6 mIU/L. After initiating Levothyroxine and Tolvaptan his urine osmolality 383 mosm/kg and serum sodium improved to 130 mmol/L by hospital day five. Hyponatremia is the most common electrolyte abnormality in cancer patients. In the US the direct costs of treatment hyponatremia annually are estimated to be \$1.6-\$3.6 billion.

Hyponatremia is an independent predictor of poor outcome in cancer patients. Pembrolizumab could play a role in causing immune mediated hypothyroidism especially in patients who suffer from head and neck SqCC. Hypothyroidism leads to decrease cardiac output, increase ADH release, decrease free water excretion by up regulating V2 receptors expression in principle cells similar to Syndrome of inappropriate ADH. Treatment with Levothyroxine and Tolvaptan improved free water excretion, allowed a safe hyponatremia correction, decreased hospital stay and permitted chemotherapy future administration.

Southern Society for Clinical Investigation and Southern American Federation for Clinical Research

Plenary session

SSCI young investigator award finalists

SSCI poster award finalists

SAFMR/SSCI/ young faculty award

SAFMR/SSCI/ trainee research award

8:00 AM

Friday, February 23, 2018

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IMPAIRED ARTERIAL BAROREFLEX SENSITIVITY IN PREHYPERTENSION

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10.1136/jim-2017-000697.501

Purpose of study Prehypertension is associated with increased risk of hypertension and cardiovascular disease (CVD), the mechanisms of which remain unclear. Prior studies have shown increased resting sympathetic nerve activity (SNA), and augmented blood pressure (BP) responses during mental stress, suggesting autonomic dysregulation at rest and during stress.

We hypothesized that compared to normotensives ($\leq 120/80$ mmHg), prehypertensives (120/80–139/89 mmHg) have impaired arterial baroreflex sensitivity (BRS) leading to autonomic dysregulation, and increased neurocardiovascular reactivity to mental stress.

Methods used 22 participants were studied: 12 otherwise healthy prehypertensives (35 ± 6 years) and 10 matched normotensive controls (32 ± 6 years). We recorded muscle SNA (MSNA) using microneurography, beat-to-beat BP, and continuous EKG during 5 minutes of supine rest and 3 minutes of stress via mental arithmetic. Arterial baroreflex sensitivity (BRS) was measured via *modified oxford technique* using IV boluses of nitroprusside and phenylephrine to manipulate arterial BP. The slope of the linear relationship between diastolic BP and MSNA (sympathetic BRS), and systolic BP and R-R interval (cardiovagal BRS) were assessed.

Summary of results As expected, baseline systolic BP (130 ± 7 vs 117 ± 8 mmHg) and diastolic BP (87 ± 7 vs 74 ± 8 mmHg) were significantly higher in prehypertensives ($p < 0.001$). Resting MSNA (25 ± 12 vs 18 ± 10 bursts/min) tended to be higher in prehypertensives ($p = 0.08$). Sympathetic BRS was comparable between the groups, but cardiovagal BRS (13 ± 10 vs 22 ± 10 ms/mmHg) was significantly lower in prehypertensives ($p = 0.03$). During mental arithmetic, minute by minute increases in BP and MSNA did not differ between the groups. However, there was a significant correlation between diastolic BP reactivity to mental stress and resting cardiovagal BRS ($r = 0.703$, $p = 0.016$), as well as with resting sympathetic BRS ($r = 0.795$, $p = 0.010$) in the prehypertensive group. In contrast, in normotensive controls, there was no correlation between BP responses to stress and cardiovagal ($r = 0.126$, $p = 0.766$) or sympathetic BRS ($r = 0.287$, $p = 0.581$).

Conclusions These findings suggest that early impairment of arterial BRS may be present in prehypertension and may modulate BP responses to stress, contributing to increased hypertension and CVD risk.

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NATIONAL TRENDS OF SICKLE CELL DISEASE RELATED ADULT HOSPITALIZATIONS

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10.1136/jim-2017-000697.502

Purpose of study Sickle cell disease (SCD) is an increasing global health problem. Data pertaining to contemporary trends of patient characteristics with SCD is limited. Hence, we studied national trends of patient characteristics admitted with a primary diagnosis of SCD from 2003 to 2014 across United States.

Methods used Using 2003 to 2014 Nationwide Inpatient Sample (NIS) database of the Healthcare Cost Utilization Project (HCUP), we examined the contemporary trends for patient demographics, hospitalization characteristics, in-hospital complications and healthcare resource utilization of SCD related hospitalizations in the US.

Summary of results Overall there were 770,000 SCD hospitalizations between 2003 and 2014 with an increase in annual frequency from 52,741 in 2003 to 72,930 in 2014, p trend < 0.001 . There was a significant decrease in mean age (31.94 to 31.53, years) and proportion of females (55.0% to 53.8%) (all p trend < 0.001). While the frequency of hospitalizations for

African Americans decreased (94.8% to 93.4%), there was an increase in SCD hospitalizations for Hispanics (2.9% to 3.4%). There was an increase in the admissions to hospitals located within western US (7% to 8.4%) and teaching status (60.4% to 77.0%). Mean length-of-stay decreased from 6.2 to 5.4 days, but there was an increase in mean hospital charges from \$17,926 to \$32,147. In-hospital mortality decreased from 0.5% to 0.3%; while there was a consistent increase in the complications of cerebral vascular accident (2.0% to 2.6%), acute chest syndrome (0.7% to 7%), renal failure (2.5% to 7.1%) and pulmonary hypertension (2.5% to 5.5%). There was a significant increase in patients with a co-existing diagnosis of opioid dependence (0.9% to 3.5%) (all p-trends <0.001).

Conclusions Number of hospitalizations, costs, and complications associated with sickle cell disease are significant. We observed significant changes in hospitalization characteristics and further research is warranted to better understand and improve the hospitalization outcomes of SCD patients.

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UTILITY OF LUNG ULTRASOUND B-LINES IN VOLUME ASSESSMENT OF END STAGE RENAL DISEASE PATIENTS ON HEMODIALYSIS

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10.1136/jim-2017-000697.503

Purpose of study Volume assessment in end stage renal disease (ESRD) patients on hemodialysis (HD) can be sometimes challenging. Lung ultrasound to look for B-lines, which indicate interstitial edema, is an emerging tool in assessing bedside volume status, and may assist in setting ultrafiltration (UF) goals for dialysis. We performed a quality assurance project to assess the utility of lung ultrasound in determining UF goals.

Methods used ESRD patients were studied before and after HD. Clinical parameters of volume status including systolic blood pressure (SBP) and presence of edema were recorded pre-dialysis, and target UF was set accordingly. We counted the number of B-lines pre and post HD using two portable ultrasound machines, GE V-scan and GE Sonosite. For each patient, the ultrasound probe was placed at the same mid-axillary or mid-clavicular intercostal space to visualize B-lines pre and post HD. Linear regression or ANOVA was used to examine the association between the number of B-lines and fluid removed by UF.

Summary of results 24 ESRD patients were studied for the number of lung B-lines pre and post HD. B-lines were categorized as 0, 1–2, and 3 or more. For all patients, UF removed trended with the number of B-lines, but there was no significant association. There was a non-significant decrease in the number of B-lines with UF from 3.4 ± 2.1 to 0.7 ± 1.0 ($p=0.53$). Patients with ≥ 3 B-lines tended to get more volume removal with mean UF volume of 2.4 ± 0.9 L. Mean UF removal in patients with 1–2 B-lines was 1.3 ± 0.9 L, and with 0 B-lines was 1.4 ± 0.6 L. Interestingly, four patients who did not have any B-lines could not tolerate target UF set pre-HD on the basis of SBP and edema.

Conclusions Lung ultrasound may be a useful tool for bedside volume assessment of hemodialysis patients and help in deciding UF goals to achieve dry weight. Our pilot project shows a trend that higher number of B-lines may correlate with higher

UF tolerance but the data is non-significant. A larger sample size and more sophisticated portable ultrasound machines may give a better idea of any association between B-lines and the determination of UF goals in HD.

503A

MICRORNA-224 PROMOTES THE METASTASIS OF HEPATOCELLULAR CARCINOMA THROUGH INHIBITING THE TUMOR SUPPRESSOR NON-METASTATIC CELL 2

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10.1136/jim-2017-000697.503A

Introduction MicroRNAs (miRNAs) can control the expression of targeted genes through the degradation of mRNAs or the inhibition of protein translation.¹ Hence, miRNAs can exert the pro-metastatic activity through targeting the tumor suppressor genes. MicroRNA-224 has been demonstrated as an oncogenic microRNA in different type of cancers. Here, we demonstrate the pro-metastatic characteristic of microRNA-224 through inhibiting tumor suppressor non-metastatic cell 2 (NME2).

Methods The microRNA-224 was constructed into Luciferase Plasmid PGL4.13. Subsequently, the plasmid was transduced into the hepatocellular carcinoma cell lines Huh7 and Hucct1. Next, the Scratch assay and Invasion assay were performed to study the phenotype. Meanwhile, the online bioinformatics was used to predict the binding target of miR-224. Then, the Luciferase reporter assay was conducted to verify the miR-224 binding site on the predicted target. Finally, the qRT-PCR and Western Blot were performed to show the influence of miR-224 on the expression of its target. All data are presented as means $\pm$ SD. Student's t-test was performed for evaluating statistically significance.

Results

- The experimental overexpression of miR-224 was established in the hepatocellular carcinoma cell lines Huh7 and Hucct1.
- The migration and invasion of Huh7 and Hucct1 were enhanced by miR-224 comparing to the control ($P<0.05$).
- MiR-224 was predicted to bind to NME2 to exert the pro-metastatic characteristics. The miR-224 binding site on NME2 was confirmed through the mutagenesis assay.
- The expression of NME2 was suppressed by miR-224 in the Huh7 and Hucct1 which was verified by PCR and Western Blot.

Conclusion Previously, a majority of studies have been conducted to verify the oncogenic characteristics of miR-224.^{2–4} Here, we demonstrated NME2 as the downstream factor to express the pro-metastatic behavior of miR-224. NME2 is one of the family members of the first discovered metastatic suppressor gene non-metastatic 23 (NM23).^{5,6} The expression of NME2 has been shown to be inverse proportional to metastasis. The suppressive expression of NME2 has been found in regionally invasive and metastatic carcinomas.⁵ Here, we show the metastatic promoter characteristic of miR-224 promote invasion and migration of tumor cells can be explained by inhibiting non-metastatic cell 2 (NME2) which is a metastatic suppressor gene (MSG).⁵ Taken together, the over expression of miR-224 is correlative with stronger metastatic propensity of tumor cells. The possible mechanism of miR-224 mediating metastasis is through inhibiting the metastatic suppressor NME2.

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503B DOES PKC MEDIATE THE HIGH RISK OF PREECLAMPSIA IN PREGNANT WOMEN WITH DIABETES?

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10.1136/jim-2017-000697.503B

Purpose of study Preeclampsia (PE) is a leading cause of pregnancy-related mortality and morbidity, and its prevalence is 4-fold higher in women with diabetes vs those without, but the underlying mechanism is unclear. The anti-angiogenic factor soluble fms-like tyrosine kinase-1 (sFlt1) plays an important role in the pathogenesis of PE. Evidence suggests that PKC activation, which is associated with the development of diabetic vascular complications, may mediate the enhanced sFlt1 release in non-trophoblast cell types; but it is unclear whether this mechanism occurs in the placenta and thus mediate the high risk of PE in diabetes. We aimed to determine:

- the role of PKC in the regulation of sFlt1 expression in a human placental trophoblast cell line.
- whether diabetes-relevant conditions promote sFlt1 expression via the PKC pathway.

Methods used Quiescent human trophoblast HTR-8/SVneo cells were treated with the PKC activator phorbol-12-myristate-13-acetate (PMA), or the diabetes stimuli 'heavily oxidized, glycated' low-density lipoproteins (HOG-LDL) vs native LDL $\pm$ glucose, over 24 hrs, with or without PKC inhibitor GF109203X. Both sFlt1 mRNA expression (RT-PCR) and protein release (ELISA) were measured.

Summary of results We found that 5 nM PMA increased sFlt1 mRNA expression ($p \leq 0.001$ for sFlt15a) and protein release ($p \leq 0.001$) in HTR-8/SVneo cells; this effect was abrogated by the pre-treatment of 50 μ M GF109203X ($p \leq 0.001$ for sFlt15a expression, $p \leq 0.001$ for protein). Similarly, 50 μ g/ml HOG-LDL increased sFlt15a expression ($p \leq 0.001$) and protein release ($p \leq 0.001$), which were attenuated by GF109203X. However, glucose did not appear enhance the effect of HOG-LDL.

Conclusions The results are consistent with the possibility that modified lipoproteins may promote PE development in women with diabetes, likely via a PKC-mediated up-regulation and release of sFlt1. These findings provide new insights into the disease mechanism, and potential targets for developing preventative and interventional measures for PE.

503C

L1 EXPRESSION ANALYSIS IN INDUCED PLURIPOTENT STEM CELLS

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10.1136/jim-2017-000697.503C

Purpose of study Long interspersed element-1s (L1s) are autonomous, mobile elements that are able to copy and insert themselves throughout the genome with their own reverse transcriptase and endonuclease. These elements make up 17% of the human genome with over 500,000 copies, though the vast majority of these elements are defective and only a few dozen are potentially responsible for L1 activity. It is reported that there is increased retrotransposon activity in induced pluripotent stem cells (hiPSCs) and human embryonic stem cells (heESCs). hiPSCs hold the promise of broad application in the biomedical field including regenerative treatment. However, there is an increased risk of tumorigenesis when these reprogrammed cells are implanted. As L1 has the potential to contribute to tumor progression through insertional mutagenesis and increased genomic instability, we investigated its expression in hESCs and hiPSC.

Methods used To better understand the potential of L1-mediated mutagenesis in stem cells, it is imperative to first identify the few culprit L1s at specific loci that are actively transcribing to RNA. Our lab has developed a novel approach in detecting full length L1 expression by PacBio sequencing 5'RACE-selected full length L1 RNAs and mapping sequence results to the reference genome using our in-house bioinformatics pipeline.

Summary of results Here we provide proof of concept with the application of this novel method in characterizing full-length expressed L1s in 2 human cord blood derived endothelial cell lines (hCBEC), 1 fibroblast cell line (hFF), 3 hESC lines, and 8 iPSC lines. We characterized L1 expression patterns at the specific locus level in the four types of cell lines and saw an increase in L1 expression in hESC and iPSC cell lines.

Conclusions As there is an increase in L1 expression in induced pluripotent stem cells, there is greater potential for L1-mediated mutagenesis. This is important when considering induced pluripotent stem cells as potential therapy. Future directions will focus on identifying the functional impact of L1 retrotransposition in induced pluripotent stem cells.

503D

PATIENT-DERIVED TRIPLE NEGATIVE BREAST CANCER XENOGRAFTS TO DISCOVER NOVEL KINASE PATHWAYS

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10.1136/jim-2017-000697.503D

Purpose of study Triple negative breast cancers (TNBCs) have an aggressive clinical presentation due to high rates of metastasis, recurrence and chemoresistance; Louisiana, specifically New Orleans, has among the highest incidences of TNBC in the country. Targeted therapy remains elusive in TNBC and discovery of novel therapeutic targets are necessary. Current models in target discovery research cannot accurately recapitulate the complex architecture and heterogeneity of TNBC.

Immortalized cell lines have been selected in a 2D environment and may have lost important features of original tumors. Our primary objective was to dissect and evaluate the various components that drive complex interactions within TNBC tumors using patient-derived xenografts from New Orleans hospitals.

Methods used We analyze relevant transcript (qRT-PCR) and protein (flow cytometry, immunohistochemistry) expression patterns that are unique to each PDX model. Using qRT-PCR and 3D culture, we examine effects of the pan-deacetylase inhibitor, LBH589 on mammospheres, in vivo tumorigenesis and collagen expression. We also generated cell lines and mammospheres (TU-BcX-2K1, TU-BcX-2O0, TU-BcX-49S, TU-BcX-4IC) from each PDX model. Finally, we utilize novel techniques such as tissue decellularization to examine extracellular matrix components and evaluate the necessity of the scaffold in TNBC tumorigenesis.

Summary of results Our laboratory has established four TNBC PDX models representing various patient ethnicities, response to chemotherapy, and TNBC molecular subtypes and metastatic behavior. We demonstrate these models can be used in therapeutic discovery research and recapitulate results observed in preliminary studies using immortalized TNBC cell lines. Finally, we dissect these models using various techniques to examine aspects of this complex tumor that can be targeted by developing therapeutics, including specific cell populations, the extracellular matrix, and cancer stem-like cells.

Conclusions Our aim is to leverage novel patient-derived models from under-studied patients with a range of clinical presentations to guide the selection of therapeutically targetable pathways in specific molecular subtypes of TNBC.

503E

ASSESSING THE IMPACT OF NEOINTIMAL LESIONS ON ELASTICITY AND BLOOD FLOW THROUGH PULMONARY ARTERIES

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10.1136/jim-2017-000697.503E

Purpose of study Pulmonary arterial hypertension (PAH) is a defined as a chronic increase in blood pressure of the pulmonary artery (>25 mmHg). Medial hypertrophy and hyperplasia, and adventitial thickening occur in early stages of the disease process. With progression, neointimal lesions develop in pulmonary arterioles, leading to narrowed vessel lumens and vascular occlusion. It was originally thought that the lesions are uncommon, and contribute little to increases in pulmonary artery pressure (Ppa). However, recent 3-D

reconstruction of hypertensive arterioles suggests that lesion density is more widespread than previously thought. Presently, physiological approaches do not discriminate whether or not neointimal lesions impact Ppa. Here, we test the hypothesis that retrograde perfusion will enable quantitative assessment of the impact of neointimal lesions on pulmonary arterial pressure.

Methods used PAH was induced in male Fischer rats via a single injection of SUGEN 5416 (20 mg/kg) followed by hypoxia exposure (10% O₂). The animals were studied after 1 and 3 weeks in hypoxia, and after 3 weeks of hypoxia plus 2 additional weeks in normoxia. To examine pulmonary vascular resistance and elastic recoil, the heart and lungs were isolated, ventilated, and perfused with 6% whole blood in forward and retrograde orientations at 8 mL/min. Thereafter, flow rates were increased by 8 mL/min every 5 minutes until tracheal edema occurred. Pulmonary artery and venous pressures were measured continuously via physiograph recorder, and double occlusion pressures were measured following each 5-minute interval. Note that double occlusion pressures were used as a serogate for pulmonary capillary wedge pressure.

Summary of results In experimental PAH, Ppa, Fulton Index, and elastic recoil of pulmonary arteries increase with disease progression. PAH lungs accommodated forward perfusion over the entire 5-week time course. However, only 1 and 3 week lungs accommodated retrograde flow. Retrograde flow was unsuccessful in 5 week animal, indicating that neointimal lesions had become prominent.

Conclusions Experimental PAH is a progressive disease due to medial and adventitial remodeling and neointimal lesion formation. These occlusive lesions appear to prevent retrograde perfusion, suggesting they are more prominent than previously thought.

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HIGH INTENSITY STATIN USE AFTER ACUTE VASCULAR EMERGENCIES VARIES BY SPECIALTY

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10.1136/jim-2017-000697.504

Purpose of study High intensity statin (HIS) therapy is advocated to reduce atherosclerotic events in high risk patients especially those with acute vascular emergencies. We studied trends in high intensity statin use by different specialties managing vascular emergencies

Methods used A random sample of patients (every 3rd discharge) admitted with a diagnosis of acute myocardial

Abstract 504 Figure 1 Patients admitted with MI

infarction (MI), ischemic stroke (IS) and peripheral arterial disease (PAD) requiring intervention at a single center between June 2014 to December 2015 were included. By institutional practice, these vascular emergencies are managed primarily by cardiologists, neurologists and vascular surgeons respectively. Statin use was classified as low, medium and high intensity according to the 2013 ACC/AHA guidelines. Age, gender, race, insurance status, dialysis status, heart failure, statin use at admission, LDL level less than 75 mg/dL and type of vascular emergency were included in a logistic regression model to study determinants of HIS prescription

Summary of results A total of 360 patients (134 MI, 126 stroke, 100 PAD) were analyzed. 42% of the entire cohort were on HIS on admission (23% MI vs 9.5%IS vs 20%PAD; $p=0.011$). At discharge, HIS use was significantly higher in patients managed by cardiologists (75%MI vs 27%IS vs 23% PAD; $p<0.001$). In regression analysis, admission for MI (managed by cardiologists) was the only independent predictor of HIS prescription at discharge (OR 9.8, 95% CI: 4.5 to 20.9; $p<0.0001$).

Conclusions Our findings show that patients admitted with MI (managed primarily by cardiologists) were more likely to be discharged on HIS compared to patients with stroke managed by neurologists and PAD managed by vascular surgeons. Despite the similar pathophysiology shared between these vascular emergencies, adoption of guidelines varies among specialties

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IDENTIFICATION OF A HUMAN CARTILAGE MICROBIOME AND CHARACTERIZATION OF DISTINCT CARTILAGE MICROBIOME PROFILES ASSOCIATED WITH OSTEOARTHRITIS

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10.1136/jim-2017-000697.505

Purpose of study Osteoarthritis (OA) is both the most common form of arthritis and the leading cause of chronic disability in the US. Genetic contributions to OA have been identified, but carry a low risk. Environmental factors including epigenetics have been implicated; however, a cartilage microbiome has not been explored. In this study, we set out to determine whether a constituent cartilage microbiome exists and whether changes in it are associated with human OA.

Methods used Discarded tissue samples were obtained from patients undergoing total knee and hip ($n=22, 34$) arthroplasty in an initial discovery and later confirmatory cohort, along with 20 disease-free cadaveric hip and knee samples. Grossly eroded and intact sections were harvested and confirmed by histology. DNA was isolated and bacterial 16S ribosomal gene deep sequencing performed. Operational taxonomic units (OTUs) were assigned using QIIME ver. 1.9. via open-reference OTU picking with alignment to the Green-Genes database. Group significance was determined using a Kruskal-Wallis nonparametric ANOVA test, and p-values calculated ($\alpha\leq 0.5$ considered significant). Linear discriminant analysis (LDA) effect size (LEfSe) was performed to identify taxa most characteristic of groups.

Summary of results Discovery and confirmatory cohorts of both knee and hip samples were highly similar. A distinct microbiome pattern was found among eroded sections

compared to intact and cadaver control cartilage sections (figure 1) irrespective of location, including reduced Actinobacteria, increased Firmicutes, and increased Proteobacteria. LDA identified the order Actinomycetales as one of several characteristic of intact cartilage (LDA 4), whereas class Bacilli were among those characteristic of eroded cartilage (LDA 2.5).

Conclusions In this study, we identify for the first time a microbiome of human knee and hip cartilage. Distinct patterns were noted in control, intact, and eroded cartilage sections, and similar patterns were shared among both knee and hip samples. We further identified several specific families and genera that are highly characteristic of each group.

Southern Society for Pediatric Research

Plenary session

Young investigator award finalists

8:00 AM

Friday, February 23, 2018

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IMPROVING GROWTH WITH AN EXCLUSIVE HUMAN MILK DIET IN THE NICU WITHOUT NEGATIVELY IMPACTING BODY COMPOSITION AT 2 YEARS OF AGE

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10.1136/jim-2017-000697.506

Purpose of study To evaluate post-discharge growth, body composition, and neurodevelopment of preterm infants ≤ 1250 g birth weight (BW) fed an exclusive human milk (HM)-based diet.

Methods used A prospective cohort study of extremely premature infants fed an exclusive HM-based diet. Subjects were studied for growth at 12–15 and 18–22 months corrected gestational age (CGA), body composition by dual energy x-ray absorptiometry (DXA) 18–22 months CGA, and neurodevelopment by Bayley Scales of Infant Development III (BSID-III) scores at 18–22 months CGA.

Summary of results We followed 51 infants (gestational age 27.8 ± 2.6 weeks and BW 893 ± 204 g) at 12–15 months CGA and 44 infants at 18–22 months CGA. At 12–15 and 18–22 months CGA, z-scores were not significantly different from birth for all growth parameters. In-hospital growth significantly correlated with growth parameters at 12–15 and 18–22 months CGA and improved bone mineral content, lean mass, and fat free mass at 18–22 months CGA. Increasing amounts of Mom's milk received was also significantly correlated with decreased fat mass, fat percentage, and fat mass index at 18–22 months CGA. No significant body composition differences existed between the preterm infants and age-, weight-, and height-matched term controls. No infants had cognitive composite BSID-III scores <70 . 18.2% of language and 4.5% of motor composite scores were <70 .

Conclusions Preterm infants fed an exclusive HM-based diet had normal growth patterns, a low rate of postnatal growth failure, normal body fat and lean masses, and appropriate bone mineralization at 18–22 months CGA. Improved in-

hospital growth and receipt of Mom's milk correlated with a favorable body composition. BSID-III scores were comparable to those found in the literature for infants ≤ 1250 g BW.

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A PILOT PROSPECTIVE COHORT STUDY ON BILIRUBIN BINDING CAPACITY AND INTRALIPID INFUSION RATE

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10.1136/jim-2017-000697.507

Purpose of study Very low and extremely low birthweight (VLBW) newborns are at risk of bilirubin induced neurologic dysfunction despite exposure to only moderate serum bilirubin. A previous study reported that intralipid (IL) can cause elevated levels of free fatty acids which bind to albumin and decrease bilirubin binding capacity (BBC). We hypothesized that IL infusion rate and BBC would vary inversely in VLBW newborns.

Methods used In a prospective cohort study of 60 newborns < 32 wks GA (30 BW < 1 kg and 30 BW 1–1.5 kg), we used hematofluorometry to measure BBC from blood samples obtained as IL infusion rates increased from 0 to 3 g in increments of 1 g/kg/d, and again as IL dose decreased from 3 to 0. The association of IL infusion rate and BBC was analyzed using multilevel regression to account for within-patient correlation.

Summary of results Preliminary results are reported from 244 blood samples from 35 patients: 14 BW < 1 kg and 21 BW 1–1.5 kg. Samples were obtained on 7.1 ± 1.3 days per patient (min 3, max 10). The BBC-IL association differed by IL dose phase (interaction term $p < 0.01$). In the IL increasing phase there was a significant positive BBC-IL association, with BBC increasing by 1.2 per 1 g/kg/d increase in IL ($p < 0.001$). At infusion rates of 0, 1, 2, and 3 g/kg/d, the mean BBCs were 18.0, 19.2, 20.4, and 21.7 mg/dL. The positive association was present and statistically significant in both BW strata, and was not diminished by adjusting for day of age. In the IL decreasing phase there was no evidence of a BBC-IL association ($p = 0.5$). The ability to adjust for serum albumin (SA) was limited because SA was not measured regularly. Still, there was a strong association between SA and BBC: BBC increased 7.1 (3.9, 10.4) mg/dL for each SA increase of 1 g/dL ($p < 0.001$). However, there was no association between SA and IL dose, and adjusting for SA did not affect the BBC-IL associations.

Conclusions In these data there is no evidence that IL causes clinically significant decreases in BBC in VLBW newborns. The magnitude of the positive BBC-IL association as IL rates were increased was small and may be due to confounding factors.

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CAN EARLY PROGRESSIVE FEEDING INCREASE THE NUMBER OF DAYS ALIVE ON FULL ENTERAL FEEDING IN EXTREMELY PRETERM INFANTS?

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10.1136/jim-2017-000697.508

Purpose of study Extremely preterm infants (≤ 28 weeks of gestation) rarely receive early progressive feeding (small increments of feeding volumes between 1 and 4 days after birth). The primary objective of this trial was to test the hypothesis that progressive feeding without trophic feeding compared to a 4-day course of trophic feeding followed by progressive feeding results in an increased number of days alive on full enteral feeding during the first 28 days after birth in extremely preterm infants receiving human milk

Methods used This parallel-group randomized trial with 1:1 allocation included infants with gestational ages of 22 weeks 0 days through 28 weeks 6 days who were enrolled within 48 hours after birth between September 2016 and June 2017. Extremely preterm infants were randomly assigned to receive either early progressive feeding without trophic feeding (intervention group) or a 4-day course of trophic feeding followed by progressive feeding (control group) before or on day 1 of feeding. The primary outcome was number of days alive on full enteral feeding in the first 28 days after birth. Secondary outcomes were death, necrotizing enterocolitis (NEC), late-onset sepsis (LOS), use of parenteral nutrition (PN), and need for central venous access.

Summary of results Sixty infants were enrolled. Mean birthweight of study participants was 832 g. The primary outcome differed between groups (median difference favoring the early progressive feeding group: +2 days; 95% CI: 0 to 3; $p = 0.02$). Early progressive feeding reduced the use of PN (4 vs 8 days; $p \leq 0.01$) and the need for central venous access (9 vs 13 days; $p \leq 0.01$). The outcome of LOS (10% vs 27%; $p = 0.18$) and the composite outcome of NEC or death (27% vs 20%; $p = 0.74$) did not differ between the groups.

Conclusions In extremely preterm infants, early progressive feeding increased the number of days alive on full enteral feeding in extremely preterm infants. Though underpowered to detect differences in NEC, this trial does not suggest that early progressive increases the risk of NEC. This trial was partially supported by The Gerber Foundation. ClinicalTrials.gov: NCT02915549.

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PRE B CELL RECEPTOR: A CRITICAL COMPONENT FOR B CELL DEVELOPMENT THAT AFFECTS BONE HOMEOSTASIS

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10.1136/jim-2017-000697.509

Purpose of study B cell development begins in the fetal liver then switches after birth to the bone marrow (BM). During development, B cells pass through a series of quality control checkpoints that test the integrity and function of their immunoglobulin. The first checkpoint tests for the formation of pre B cell receptor (preBCR), which requires the successful association of a surrogate light chain with a nascent heavy chain (μ HC). B cells and osteoblasts are in close physical proximity at this stage of development. Reciprocal cross-talk between osteoblast and bone marrow resident cells is known to occur, however, specific interactions between B cells and osteoblasts are not known. The objective of this study is to investigate the interplay between early B cell subsets and bone homeostasis.

Methods used Bone homeostasis was analyzed in three strains of mutant mice, including those with global deletion of

Lambda 5 ($\lambda 5$), membrane bound IgM heavy chain (μ MT), and CD19 genes.

Summary of results All of these mutant mice lack B cell maturation but survive to adulthood without overt bone pathology. At six months of age, where postnatal bone development is complete, femurs were harvested from female mice. Trabecular bone was significantly decreased in $\lambda 5$ and μ MT mutant mice. However cortical bone in both mutants was comparable to wild-type mice. Histological analysis revealed an increase in both osteoblast and osteoclast numbers, suggesting accelerated bone remodeling in the mutant mice. Rate of bone synthesis was then compared using double calcine injection. There was a significant decrease in synthesis of both trabecular and cortical bone in the $\lambda 5$ and μ MT mutant mice. Similar impairment in bone synthesis was noted in $\lambda 5$ mutant mice on a Balb/C background. Interestingly, deletion of CD19 gene that blocks the mature B cell compartment in spleen has minimal effect on bone.

Conclusions Taken together, our data shows that blockage of early developmental stages of B cells in bone marrow affects osteoblast function and bone synthesis. This suggests that pre B cells in the bone marrow play an important role in regulating development and maintenance of trabecular and cortical bone.

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MATERNAL IMMUNE ACTIVATION SENSITIZES NEUROINFLAMMATORY RESPONSES TO NEONATAL HYPOXIA-ISCHEMIA IN OFFSPRING BRAINS

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10.1136/jim-2017-000697.510

Purpose of study Epidemiological evidence suggests that intrauterine infection is a risk factor for autism spectrum disorders (ASD), which is supported by ASD-like deficits in animal models of maternal immune activation (MIA). However, because not all human MIA offspring develop ASD, 'second hits' may be instrumental to produce severe brain damage and cognitive deficits. We hypothesize that prenatal rodent MIA amplifies neuroinflammatory responses to a secondary neonatal hypoxic-ischemic (HI) insult in the offspring, leading to greater production of pro-inflammatory cytokines and brain tissue destruction.

Methods used MIA was induced by intraperitoneal injection of Poly I:C (20 mg/kg), a synthetic analogue of double-stranded RNA that activates Toll-like receptor 3, in C57BL/6 mice in mid pregnancy (E12.5). Offsprings were challenged by the Rice-Vannucci model of HI (unilateral common carotid artery

ligation followed by 90-min exposure to 10% oxygen at 37°C) at 10 days of age. Controls include age-matched sham and singularly MIA- or HI-injured B6 pups. Mouse brain tissues were isolated at 24 h post-HI to compare NFkB signaling activity, mRNAs for pro-inflammatory cytokines ($n > 6$ for each group), and the morphology of microglia. Another cohort of sham, MIA-, HI-, and MIA/HI-challenged mice were sacrificed 7 days post-HI to compare the extent of brain atrophy.

Summary of results We found that MIA alone caused elevated NFkB signaling and higher basal levels for IL-6 and IL-17 mRNA, but only a few clusters of activated microglia in the offspring brain. At 24 h post-HI, the MIA offspring brains developed significantly higher NFkB activity (as shown by more nuclear p55/ NFkB and less cytoplasmic IkB) and more mRNAs for pro-inflammatory cytokines, including IL-6, IL-17, and IL-1b, when compared to HI alone. Moreover, at 7 d recovery, the MIA/HI-injured mice showed greater brain atrophy than HI-injured mice ($p < 0.05$; $n > 10$).

Conclusions These preclinical data suggest that MIA elevates basal inflammatory activity in the offspring brain, and acts as a primer to amplify neuroinflammation responses and brain damage after a secondary HI insult. This two-hit model may explain why only a subset of MIA offspring develop ASD-like cognitive deficits. Future studies are needed to unravel the mechanisms of MIA-induced neonatal immune dysregulation.

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ZIKA VIRUS IS ASSOCIATED WITH FETAL GROWTH RESTRICTION AND A GESTATIONAL WINDOW OF SUSCEPTIBILITY IN A MURINE MODEL

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10.1136/jim-2017-000697.511

Purpose of study Vertical transmission of Zika virus (ZIKV) leads to neuroprogenitor infection and destruction of brain parenchyma. However, it is unclear whether timing of infection (early or mid-gestation) bears equivalent risk for abnormal neural development. Using an established model of interferon alpha receptor 1 (IAR1) suppressed susceptible mice, we sought to determine if the timing of ZIKV inoculation yielded phenotypic differences at birth and adolescence.

Methods used Pregnant Swiss-Webster dams ($n = 9$) were i.v. inoculated with 1×10^4 PFU of first passage contemporary ZIKV strain or a mock injection on embryonic day 4 (E4), E8, or E12, with IAR1 suppressing antibody administered i.p. days pre- and proceeding inoculation. On postnatal day 1 (P1), pups were weighed and biparietal head (BPD) diameters

Abstract 511 Figure 1 (A) microcephaly appears in mid-gestation (e8) infection group but not in other group (e4 or e12) revealing a window of susceptibility to in-utero ZIKV infection (student's t-test). (B) vertical transmission of mother to a pup results in IUGR phenotype and postnatal infection; image shows ZIKV affected pup and normal size littermate. (C) recovery of ZIKV from moribund pup by RT and qPCR

assessed. Brain weights were obtained for half the pups, while the other half assessed weekly for BPD and symptoms until 6 weeks of age. Viral levels were assessed for both groups.

Summary of results ZIKV infected dams at e8 had IUGR pups with smaller BPD ($p<0.0001$) and brain weights ($p<0.001$) compared to control ($n=14$ and 12 , respectively) (figure 1). When pregnant dams were ZIKV infected at e4, BPD ($p<0.0001$) and pup weight ($p=0.027$) were smaller, although there was no difference in brain weights. The e12 infected mice did not have IUGR pups. Of note, a subset of e8 ZIKV-infected pups demonstrated moribund lethal findings including arrest of growth and hind-limb paralysis later in juvenile life; this was accompanied by multi-organ infectivity with ZIKV (figure 1).

Conclusions This is the first animal model to show the timing of gestational infection to be related to postnatal microcephaly and mortality. The finding of more severe congenital ZIKV syndrome-like symptoms in mid gestation suggests a window of susceptibility.

Allergy, immunology, and rheumatology I

Concurrent session

2:00 PM

Friday, February 23, 2018

512 RITUXIMAB FOR CHRONIC STEROID-DEPENDENT HENOCH-SCHONLEIN PURPURA

E Eloiseily, CB Crayne*, M Mannion, S Azerf, P Weiser, T Beukelman, M Stoll, D Feig, P Atkinson, R Cron. *University of Alabama Birmingham, Birmingham, AL*

10.1136/jim-2017-000697.512

Purpose of study Henoch-Schonlein purpura (HSP) is a small vessel vasculitis characterised by non-thrombocytopenic purpura, abdominal pain, arthritis, and glomerulonephritis. HSP is usually self-limited, but more severe cases may require corticosteroids (CS). Rarely, a subset has persistent disease despite CS treatment or has disease recurrence on CS tapering. Refractory HSP has been effectively treated with a variety of CS sparing therapies. Rituximab (RTX) has been reported as beneficial in refractory HSP with substantial renal involvement. RTX use for children with less severe HSP but chronic CS dependent disease refractory to other immunomodulatory agents is not well explored. We describe 8 children treated with RTX for chronic HSP and report a reduction in recurrent hospitalizations and subsequent CS discontinuation.

Methods used Children diagnosed with HSP treated with RTX during 2008–2012 at a single institution were retrospectively reviewed. Data were abstracted, including the presenting symptoms, the type and duration of treatment received, and the number of hospitalizations prior to and after RTX. Data were analysed using StataCorp 2015.

Summary of results Eight children, not previously reported, treated with RTX for chronic CS-dependent HSP were identified. In addition to palpable purpura, they suffered gastrointestinal distress, hematuria and/or proteinuria, and arthritis. Seven received long-term CS use, and 7 received various other CS-sparing immunomodulatory therapies. All 8 received RTX with B cell depletion. The incidence rate of hospital admission

before and after receiving RTX was 1.78 vs 0.68 per year, respectively, yielding an incidence rate ratio of 0.38 (CI of 0.11–1.1, $p=0.06$). Six achieved full remission off CS. The mean total oral steroid burden after RTX revealed a non-statistically significant reduction ($p=0.668$). No serious adverse events were noted.

Conclusions RTX appears to be a safe and effective therapy for chronic CS dependent HSP refractory to other immunomodulatory agents. Future prospective analyses of RTX use for the treatment of chronic CS dependent HSP will be worthwhile.

513 SINONASAL AND LARYNGEAL SARCOIDOSIS; A RARE CHALLENGING ENTITY

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10.1136/jim-2017-000697.513

Case report A 55-year-old woman with history of cutaneous sarcoidosis presented with nasal obstruction. Physical exam revealed stridor, skin plaques involving the nose in a butterfly distribution, the nasolabial folds, cheeks 'Lupus Pernio'. Oral cavity examination revealed tender swollen gums and loose premaxillary teeth. CT of the neck revealed complete opacification of the left maxillary antrum with outward expansion of the sinus walls, bilateral maxillary destruction of the sinuses. Sinonasal endoscopy showed cobblestone mucosa and extensive destruction of the nasal vestibules. Biopsy of the nasal vestibule revealed chronic non-caseating granuloma. Laryngoscopy revealed an edematous and pink epiglottis with a subglottic nodular lesion. High-dose corticosteroid, oral methotrexate, and azelastine-fluticasone nasal spray were initiated with no benefit. Oral prednisone was difficult to reduce due to rebounds in her symptoms. A weekly s/c injection of methotrexate 25 mg and hydroxychloroquine 400 mg PO daily were started then with modest improvement. Two months later, subcutaneous injections of 250 mg (2 mg/kg) of golimumab (SIMPONI[®], Janssen Biotech, Inc.) were started. She reported more improvement in her nasal symptoms and shortness of breath.

Discussion Sinonasal and laryngeal sarcoidosis are rare, poorly understood, and difficult to diagnose. The extent of the disease is variable, and the response to systemic corticosteroids is often poor. Clinicians should consider anti-TNF α inhibitors, early in the course when the response to usual therapy is poor.

514 PAEDIATRIC MIGRATORY POLYARTHRITIS AND GRANULOMATOSIS WITH POLYANGIITIS

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10.1136/jim-2017-000697.514

Purpose Rare in children, granulomatosis with polyangiitis (GPA), formerly named Wegener's granulomatosis, is a chronic antineutrophil cytoplasmic antibody (ANCA) associated vasculitis affecting small and medium arteries. Childhood GPA characteristically involves the upper and lower respiratory tracts and the kidneys. The rare incidence of GPA in children makes diagnosis more challenging.

Case series Two eleven year old children presented with fever, weight loss, and migratory polyarthritis with associated periarthritic rash. Patient 1 is an eleven year old Caucasian female who presented with a two week history of migratory polyarthritis involving ankles, knees, and wrists. Each episode of arthritis resolved within 24 hours and was associated with an erythematous-violaceous annular rash, sometimes with petechiae. Within a week, her haemoglobin dropped from 11 to 5, with positive stool hemocult. Associated symptoms included fever, weight loss, cough, and bilateral conjunctivitis. Patient 2 is an eleven year old Caucasian male who presented with a several month history of large joint migratory polyarthritis; each episode lasted about 48 hours. Associated symptoms included recurrent fever, weight loss, sinus congestion, and a maculopapular rash overlying only the joints. He later progressed to have bilateral conjunctivitis and anaemia. He was found to have sinus disease and had a renal biopsy with focal necrotizing ANCA glomerulonephritis with rare epithelial crescent and patchy interstitial inflammation. Both patients were positive for c-ANCA and PR3, this combined with proteinuria and pulmonary disease confirmed diagnosis of GPA.

Conclusion This case series explores the common differential diagnosis of fever and migratory polyarthritis, specifically acute rheumatic fever, inflammatory bowel disease related arthropathy, polyarteritis nodosum, and reactive arthritis. It highlights the diagnostic criteria for GPA, detailing the clinical manifestations of disease and specifying labs, pathology, and imaging needed to guide diagnosis and management. While GPA is rare in children, prompt recognition of disease is important in improving prognosis.

515 IL-23 REGULATES RECRUITMENT OF CD40L INTO THE B: T IMMUNOLOGICAL SYNAPSE IN AUTOIMMUNE BXD2 MICE

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10.1136/jim-2017-000697.515

Purpose of study Targeting IL-23 to treat autoimmune disease and chronic inflammation is currently in development based on its pro-inflammatory function and regulation of Th17 cell development. IL-23 was previously shown to be important for promoting pathogenic autoantibody production in Fas deficient B6-Fas^{lpr/lpr} mice, suggesting a positive role of IL-23 in mediating Fas-independent germinal centre (GC) responses. We determined if IL-23 regulated development of spontaneous GCs and autoantibody production in BXD2 mice.

Methods used BXD2-p19^{-/-} mice were generated by crossing the B6- p19^{-/-} with the BXD2 for 10 generations. ELISA was performed to measure the sera levels of RF, anti-DNA and anti-histone autoantibodies. The expression and distribution of CD40L, activation-induced cytidine deaminase (AICDA) and plasmablasts were evaluated at 120 nM resolution by super-resolution SIM microscopy.

Summary of results There was significantly decreased total IgG, but increased total IgM and IgM anti-DNA and RF autoantibodies in BXD2-p19^{-/-} mice compared to BXD2 mice. There was a significant increase in GC size (3.4 fold) but a decrease

in size and number of CD4 T cells in the GC light zone (LZ). The expression of AICDA, a master gene regulating antibody affinity maturation, was decreased in PNA +germinal centre B cells in BXD2-p19^{-/-} mice. Super-resolution imaging revealed that decreased expression of AICDA in GC B cells was associated with impaired recruitment of CD40L into the TCR synapse of CD4⁺ T follicular helper cells (Tfh) cells interacting with PNA⁺ B cells in the light zone (LZ) of the GC.

Conclusions Our data revealed a novel role of IL-23 in the regulation of CD40L-mediated germinal centre B-T cell interaction in the LZ of autoimmune BXD2 mice. IL-23 plays a unique role in the class-switch response of GC B cells due to a disruption of the distribution of CD40L which is distinct from the role of IL-21 to upregulate CD40L expression on Tfh. These results suggest a novel mechanism of action of anti-IL-23 therapies to inhibit adaptive immune responses in addition to its known inhibitory role of innate response in autoimmune diseases.

516 17,20S(OH)₂PD SUPPRESSES TOTAL COLLAGEN SYNTHESIS IN THE BLEOMYCIN MODEL OF FIBROSIS

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10.1136/jim-2017-000697.516

Purpose of study Systemic sclerosis (SSc) is a chronic and often fatal disease characterised by widespread fibrosis of the skin and internal organs. TGF-β1 contributes to the fibrotic process in this disorder. Vitamin D deficiency in SSc correlates with the degree of fibrosis and is associated with increased morbidity and mortality. This study was designed to use murine models of fibrosis to determine whether 17,20S(OH)₂pD suppresses collagen synthesis, cytokines, and mediators of the TGF-β1 pathway in the bleomycin (BLM) model of fibrosis.

Methods used Fibrosis was induced into the skin of female C57BL/6 mice subcutaneously with BLM. Mice received daily oral gavage with either vehicle (propylene glycol) or 17,20S(OH)₂pD at 5,15, or 30 µg/kg, for 21 days. The skin was biopsied and examined for total collagen, dermal thickness, and mRNA expression of MMP-13, BMP-7, MCP-1, Gli1, and Gli2. Serum cytokine levels were tested using the Bio-Plex cytokine array.

Summary of results 17,20S(OH)₂pD [similar to 1,25(OH)₂D₃ and non-calcemic 20(OH)₂D₃] suppressed net total collagen production and showed a decrease in dermal thickness after treatment with 17,20S(OH)₂pD at 5, 15, and 30 µg/kg doses. 17,20S(OH)₂pD also decreased MMP-13, BMP-7, MCP-1, Gli1, and Gli2 expression *in-vivo*. Cytokine panel revealed that 17,20S(OH)₂pD suppressed production of: IL-12p70, IL-13, IL-17, IL-1β, IL-2, IL-6, and TNF-α and increased production of IL-12p40.

Conclusions 17,20S(OH)₂pD modulates mediators of fibrosis *in-vivo* and suppresses total collagen production and dermal thickness. Treatment with 17,20S(OH)₂pD favours reduction of fibrosis offering a new therapeutic approach for treating disorders of fibrosis like SSc.

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THE SUPPRESSION OF COLLAGEN INDUCED ARTHRITIS BY TYPE I COLLAGEN

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10.1136/jim-2017-000697.517

Purpose of study Studies suggest that Leukocyte-associated Immunoglobulin-like receptor 1 (LAIR-1) may have a role in the treatment of Rheumatoid Arthritis (RA). LAIR-1 is a trans-membrane glycoprotein and is an inhibitory receptor on immune cells that has collagen as its ligand.

Methods used In order to develop novel methods for the treatment of autoimmune arthritis, we used type I collagen to treat mice using the collagen-induced arthritis (CIA) model. We wanted to determine whether the mechanism of suppression involved T cell tolerance or stimulation of LAIR-1. These experiments were performed using the murine model of collagen induced arthritis in both DR1 wild type (WT) mice and LAIR-1 knock-out (KO) mice.

Summary of results Our data showed that immunisation of mice with CII/CFA caused LAIR-KO mice to have a more severe arthritis than DR1 wild type mice ($p \leq 0.005$). On the other hand, both LAIR-1KO and WT mice treated with 30 μ g of I BI/per dose by oral gavage had a significant suppression of arthritis compared to either DR1WT or DR1 LAIR-1KO PBS controls ($p < 0.02$). When we examined anti-collagen -antibody production, we found that the IgG antibody levels to type II collagen were significantly decreased in the CI fed LAIR -/- mice compared to the PBS treated controls

Conclusions These data reveal that the absence of LAIR-1 amplifies the severity of autoimmune arthritis. Moreover, administration of type I collagen by oral gavage significantly decreased arthritis in both DR1 WT and DR1 LAIR-KO mice compared to PBS controls. Our data supports the conclusion that treatment with type I collagen may be a promising therapy for the treatment of autoimmune diseases although the mechanism is not specific to the LAIR-1 receptor, and may involve T cell tolerance.

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AN APPROACH TO SKIN TESTING IN A PATIENT WITH STEROID ALLERGY

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10.1136/jim-2017-000697.518

Purpose of study Steroid allergy is rare but likely under-recognised as this medication is often used to treat conditions in which symptoms of an allergic reaction might be attributed to the primary condition. Immediate hypersensitivity reactions have been described with limited data on cross-reactivity between individual agents. Skin testing for hypersensitivity reactions to steroids is not validated, but as lifelong avoidance of all steroids is impractical, testing is recommended. Here we describe a case of a woman with a reported allergy to steroid and the testing we performed to characterise her allergy. A 66-year-old female reported an eczematous rash at the end of a course of oral Methylprednisolone. The same medication was prescribed to treat this rash with subsequent worsening of

rash a few days into her course as well as shortness of breath and diaphoresis for which she presented to the hospital. During her hospitalisation, she was given IV Methylprednisolone for a possible allergic reaction and again developed shortness of breath, diaphoresis, and facial swelling. She was treated with Epinephrine.

Methods used Patch testing, skin prick testing, intradermal skin testing, oral drug challenge

Summary of results We performed testing for steroid allergy by skin prick and intradermal testing for type I hypersensitivity reaction and patch testing for type IV hypersensitivity reaction to various steroids. Patch testing was negative to all tested steroids. Skin prick testing was negative to six tested corticosteroids. Intradermal testing was positive to Methylprednisolone, Prednisolone, and Hydrocortisone and negative to other tested steroids. Oral drug challenge was then performed to Dexamethasone and was well-tolerated.

Conclusion Steroid allergy is rare, but when a history suggestive of a hypersensitivity reaction is present, testing should be performed to multiple steroid agents given unclear patterns of cross-reactivity. Oral challenge should be performed to ensure tolerance of the chosen agent. When steroid allergy is suspected, patients should avoid all preparations and agents until testing can be completed. It may be necessary to perform graded challenge or desensitisation to steroids in an inpatient facility if testing is not available.

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TRENDS AND OUTCOMES OF VENOUS THROMBOEMBOLISM IN HOSPITALISED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM NATIONWIDE INPATIENT SAMPLE DATABASE

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10.1136/jim-2017-000697.519

Purpose of study Venous thromboembolism(VTE) is a major cause of mortality and morbidity in hospitalised patients particularly with autoimmune disorders. Nationwide Inpatient Sample (NIS) database was analysed to determine rate of hospitalisation and mortality from VTE in systemic lupus erythematosus(SLE) patients.

Methods used 2003–2011 NIS database was queried to identify adults (age ≥ 18 years) hospitalised with SLE and VTE. Demographic characteristics and in-hospital outcomes of this population were compared to SLE patients without VTE. Multivariate logistic regression analysis was used to obtain adjusted odds ratio (OR).

Summary of results The total number of patients with SLE was 2 99 595 of which 9175 (3.06%) had VTE. Mean age was 50 years and 89% were females. Age of SLE patients with VTE was lower than those without VTE (48 vs 51 years). Rate of VTE was higher in African Americans as compared to Caucasians (3.8% vs 2.8%) and in males when compared to females (4.3% vs 2.9%).

After adjusting for potential confounders, SLE patients with VTE had significantly higher inpatient mortality, greater disability at discharge, longer length of stay(LOS) and higher cost of hospitalisation (table 1).

The rate of VTE in SLE patients have increased as shown in figure 1.

Conclusions Hospitalised SLE patients with VTE is associated with higher mortality, greater disability, increased LOS and higher cost of hospitalisation. Male sex and African-American race may be associated with an increased risk of VTE. This study would help in the development of appropriate prophylactic strategies in high risk SLE population.

Abstract 519 Table 1 Outcomes

Variable	All Patients	VTE	No VTE	OR	p-Value
Inpatient Mortality	6132 (2%)	429 (5%)	5703 (2%)	2.35 (CI 2.10 – 2.62)	<0.001
Moderate to severe disability at discharge	77904 (26%)	3117 (34%)	74787 (26%)	1.53 (CI 1.46 – 1.62)	<0.001
Variable	All Patients	VTE	No VTE	Co-efficient	p-Value
LOS Median (IQR), Days	4	6	4	3.57 (CI 3.32 – 3.83)	<0.001
Total Charges (\$10,000) Median (IQR)	23100	36100	22800	2.54 (CI 2.30 – 2.79)	<0.001

Data are presented as Number of patients (%) or Median ($\pm$ IQR).

Abbreviations: OR = Odds Ratio (95% Confidence Intervals (CI)); LOS = Length of stay; VTE = Venous Thromboembolism; IQR = Interquartile range

Abstract 519 Figure 1 The rate of VTE in SLE patients have increased

520 SWOLLEN JOINTS IN LUPUS PATIENT? THERE IS MORE TO THIS LUPUS FLARE

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10.1136/jim-2017-000697.520

Introduction Systemic lupus erythematosus (SLE) patients are immunocompromised due to iatrogenic immunosuppression and the disease itself. Joint pain and swelling in these patients is often presumed to be SLE flare, but signs and symptoms of infection may be overlapping, making it difficult to distinguish them. Here we report a case of a young female with SLE who developed disseminated gonococcal infection (DGI), with diagnostic dilemma on presentation.

Case presentation A 21-year-old African American female with SLE (+ANA, SSA, ds-DNA, anti-Sm Ab, anti-RNP), non-compliant with treatment (hydroxychloroquine) presented to the emergency room with worsening pain and swelling in her right knee, bilateral ankles and wrists. This was initially diagnosed as cellulitis and treated with clindamycin, however she returned with worsening of symptoms associated with myalgias and fatigue. Initial temperature was 99.3 °F, pulse 139, blood pressure 155/88. She had swelling and tenderness of the right knee and tenosynovitis of both hands. Arthrocentesis was

performed and labs returned with a leukocytosis, high c-reactive protein, low complements, and high ds-DNA. A diagnosis of SLE flare was made for which she was started on solumedrol and hydroxychloroquine. However, she did not improve and had a high fever on day 2. Synovial fluid grew *Neisseria gonorrhoea*. At this point, a diagnosis of DGI was made along with active SLE. She was started on intravenous ceftriaxone, azithromycin and metronidazole. Despite the antibiotics, the patient developed septic shock, was transferred to the ICU and was started on vasopressors. Shortly after, she had open drainage of the right knee. Following the procedure, she improved with complete recovery in 3 days.

Conclusion This case highlights that SLE flare and infection often coexist. In particular, SLE patients are at high risk for Neisserial infections due to acquired complement deficiency making the patient more susceptible to such infections. Therefore, the physician should be prudent to perform a careful history and physical exam as well as rule out infection during any SLE flare due to the potential comorbidity of any untreated infection.

521 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-2017-000697.521

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 recognises antigen and includes all of the D β 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 hypothesise that alterations to the D region will alter T cell 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 2KO as a deletion control and a replacement of the D β locus with a hydrophobic D β (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 analysed using IMGT junction analysis program. Ovalbumin and ovalbumin tetramers were used to interrogate the antigen specific response of the altered T cells.

Summary of results We have data comparing the T cell repertoires of the altered D β mutants. When compared to control mice, the D β YTL mice have an altered T cell repertoire in terms of CDR β 3 amino acid composition and these differences can be attributed to the changes in the germline sequence. We also found that these differences are at distinct CDR β 3 positions. Certain hydrophobic and other normally non-represented amino acids were actually tolerated in the mutant mice and were not deleted through somatic mechanisms; while leucine was highly selected against. Changing the D β also changes the total T cell number in both developing and mature T cells, with an altered D β being selected against. The

altered D β mice also have reduced antigen specific recognition after OVA immunisation.

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.

522 ALKAPTONURIC OCHRONOSIS

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10.1136/jim-2017-000697.522

Case report Alkaptonuria is a rare autosomal recessive disorder that causes deposition of excess homogentisic acid in intra- and extra-articular connective tissue. The classic clinical triad seen in these patients is homogentisic aciduria, ochronosis, and ochronotic arthropathy. This excess deposition causes weakening, ultimately resulting in tissue degeneration and osteoarthritis often seen by the fourth decade in life.

A 48-year-old female was referred to rheumatology for early onset advanced osteoarthritis and degenerative disc disease suspicious for a secondary cause. Patient had suffered from progressive, non-inflammatory pain in her lower back, right knee, and right shoulder for about 5 years. Her shoulder x-ray showed advanced osteoarthritis, requiring a right total shoulder replacement with improvement in her symptoms. Thoracolumbar x-ray showed intervertebral disc calcification with severe degenerative disc disease. She was referred to rheumatology for further evaluation for an underlying cause. She denied any early onset diabetes, bronze skin, liver problems, or history of parathyroid disorders. She also denied any dark colour cartilage but did admit that urine turned dark upon standing. Workup for causes of crystal deposition disease, including hemochromatosis, hyperparathyroidism, hypomagnesemia, and hypophosphatemia, was negative. Urine homogentisic acid was ordered and returned elevated at 5046 mmol/mol creatinine, which is diagnostic for alkaptonuria. She was subsequently referred to genetics and continued on symptomatic therapy for her joint pain.

Alkaptonuria results in accumulation of homogentisic acid due to a deficiency in homogentisate 1,2-dioxygenase enzyme. The excess acid can deposit in collagen-rich connective tissues, such as joints, valves, cartilage, and skin, leading to ochronosis. These deposits can lead to joint degeneration early in life, resulting in ochronotic arthropathy. Most often it is seen in the lumbar spine, knee, hip, and shoulder joints. Diagnostic radiologic findings are narrowing of the intervertebral spaces and wafer-like disc calcification. Dietary protein restriction and vitamin C supplementation have shown some benefit in treatment of the disease. Ochronotic arthropathy is an often-overlooked cause for secondary osteoarthritis and should be considered in young patients who develop severe degenerative joint disease.

Cardiovascular I

Concurrent session

2:00 PM

Friday, February 23, 2018

523 ALDOSTERONE EXCESS AND ATRIAL FIBRILLATION IN A LARGE COHORT OF EUROPEAN AMERICAN AND AFRICAN AMERICAN PATIENTS WITH APPARENT RESISTANT HYPERTENSION

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10.1136/jim-2017-000697.523

Purpose of study Atrial fibrillation (AF), one of the most common cardiac arrhythmias, increases mortality and morbidity across the United States. Furthermore, primary aldosteronism (PA) is found in approximately 20% of patients with resistant hypertension (RHTN) who are disproportionately affected by higher cardiovascular morbidity and mortality independent of blood pressure (BP). The aim of this study was to analyse the relationship of aldosterone excess and the occurrence of atrial fibrillation in a diverse cohort of patients with RHTN.

Methods used This cross-sectional study examines the prevalence of AF of a cohort of 2375 apparent resistant hypertension patients referred to the Hypertension Clinic at the University of Alabama at Birmingham. RHTN was defined as BP $>140/90$ mmHg despite treatment with ≥ 3 antihypertensive medications, including a diuretic, if tolerated. PA was defined as aldosterone-renin ratio (ARR) >20 and 24 hour urinary aldosterone (UAldo) >12 mcg. Non-PA was defined as plasma renin activity >1 ng/ml/h and UAldo <12 mcg.

Summary of results The prevalence of AF was 6.96% for the entire cohort. Patients with AF had more hyperlipidemia, heart failure, obstructive sleep apnea, chronic kidney disease, and coronary artery disease compared to non-AF patients (table 1). Biochemical analysis showed a non-significant trend to higher plasma aldosterone levels, lower renin levels (2.4 ± 4.9 vs 3.9 ± 9.2 ng/ml/h, $p=0.0011$) and a higher ARR than non-AF patients (14.7 ± 15.3 vs 12.1 ± 14.5 , $p=0.044$), suggesting that aldosterone excess may play a role. When stratified to PA vs non-PA, patients >60 years with PA had a significant higher prevalence of AF (18.5% vs 6.9%, $p=0.009$) compared to non-PA resistant hypertensive patients by univariate analysis (table 2). There was no difference in comorbidities between the groups, except for more chronic kidney disease in the PA group ($p=0.0004$).

Conclusions These results suggest that activation of the cardiac mineralocorticoid system may play an important role in patients with atrial fibrillation.

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SINGLE CENTRE EXPERIENCE WITH PATIENTS HAVING PRIMARY ALDOSTERONISM

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10.1136/jim-2017-000697.524

Purpose of study Autonomous aldosterone production is a well recognised, but an underdiagnosed cause of secondary hypertension. The incidence of primary aldosteronism has yet to be fully established and therefore differences in presentation and demographics likely exist among patients. Herein, we reviewed the profiles of patients diagnosed with primary aldosteronism to determine if certain variables were characteristic of such patients, who were followed on the cardiology service at this medical centre.

Methods used We performed a retrospective review of 39 patients with primary aldosteronism followed at an urban medical centre from 2003 to 2017. The following variables were analysed: age, sex, electrolytes (potassium, sodium, magnesium, calcium), aldosterone/renin ratio, thyroid stimulating hormone, serum creatinine, race, body mass index and comorbidities. Variables were compared to patients diagnosed with aldosteronism from the National Inpatient Sample (NIS) database.

Summary of results In our single centre population, the majority of patients with primary aldosteronism were female (92.3%) and African American (79.5%). The average age was found to be 45.9 (SEM 2.2) years with an average body mass index of 43.3 (SEM 2.6) kg/m². The average serum potassium was 3.4 (SEM 0.1) mEq/L, magnesium was 1.8 (SEM 0.1) mEq/L, creatinine was 1.1 (SEM 0.1) mg/dL and aldo/renin ratio was 38.6 (SEM 8.6). Of the 39 patients 15.4% had a history of diabetes, 5.1% with chronic kidney disease and 7.7% with coronary artery disease.

Conclusions When compared to the NIS database, our single centre cardiology experience in hypertensive patients with primary aldosteronism having hypokalemia and hypomagnesemia differs in several aspects: there are significantly more females and African Americans. In addition our population was on average younger with a lower prevalence of diabetes and chronic kidney disease.

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LIPID FRACTION CHANGES AFTER ROUX N-Y, GASTRIC BYPASS AND SLEEVE GASTRECTOMY SURGERY-THE ROLE OF INFLAMMATION

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10.1136/jim-2017-000697.525

Purpose of study Obesity has been recognised as a word epidemic. In response to this epidemic, multiple surgical interventions have been developed for weight reduction. Contemporary bariatric surgical techniques produce significant changes in serum lipids, but changes vary widely likely due to anatomic alterations unique to each procedure. Differences in the degree of HDL changes have been describe among interventions with similar effects on Roux N-Y (RYGB) and Sleeve Gastrectomy theorised to be related to intestinal contribution and synthesis of apolipoprotein A-IV and A-I.

Methods used A non-randomised retrospective study of Puerto Rican patients (P) was performed to compare the changes after undergoing either SG or RYGB to evaluate the differences on metabolic parameters before and one year after surgery with special attention to changes in lipid fractions. A total of 34 P. of SG and 102 from RYGB groups were included for analysis. The parameters evaluated were, Body Mass Index (BMI), Total cholesterol (T.C.), LDL-C, HDL-C and Triglyceride levels, before and one year after surgery.

Summary of results In P. undergoing bariatric surgery TYNGP or SG no significant differences intergroup were found in pre-operative BMI, T.C., triglycerides, LDL or HDL levels. One year post surgery, no significant intergroup differences were found on BMI (30.4%–30.08%), triglycerides (24%–25%). The HDL increased 11%–23% between RYGB-SG group respectively (p<0.05). Cholesterol reduction (10.4%–1.80%) (p<0.05) between RYNGP-SG, respectively; as well as LDL reduction (15%–7.32%) respectively (P<0.05). The F.B.S. was normalised in both type of surgeries.

Conclusions Bariatric surgery is an effective way of losing weight and improving some metabolic abnormalities. The effects of RYGB on total cholesterol and LDL-C are greater than SG. SG is more effective in increasing HDL-C. We think this elevation of HDL-C in both procedures reflects a more inflammatory process of S.G. than RYGB surgery or changes in the genes controlling lipid production.

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THERAPEUTIC POTENTIAL OF STEM CELLS IN RIGHT VENTRICULAR DYSFUNCTION: A SYSTEMATIC REVIEW OF PRECLINICAL STUDIES

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10.1136/jim-2017-000697.526

Purpose of study Critical congenital heart disease (CHD), or defects that require early invasive intervention represent approximately one third of all CHDs and account for a high rate of infant mortality. Right ventricular dysfunction caused by pressure/volume overload, is a common complication in patients with critical CHD. Advances in regenerative medicine demonstrate that the use of stem cells as novel therapeutic agents in animal models of right ventricular dysfunction (RVD) have a promising future. For that reason, we propose to conduct a systematic review to (i) methodically review the current literature describing the effects of stem cells on animal models of RVD, (ii) quantify the effect of stem cells on RVD, and (iii) identify limitations/research gaps that should be addressed for future preclinical and clinical studies.

Methods used We performed a systematic search of English randomised and non-randomised studies using MEDLINE's database through PubMed, Web of Science, and Google Scholar with the search terms 'stem cells', 'right ventricular function', 'animal' and any of their synonyms. Two investigators independently identified eligible studies and collected data on study specifics, stem cell characteristics, and outcome measures.

Summary of results A total of 6 studies met inclusion in the current systematic review. The studies are in mice, sheep, and pig. Four of the studies (67%) underwent pulmonary artery banding to induce RVD. Two (33%) studies derived their stem cells from human umbilical cord, while other investigators

used other sources. The conductance catheter was the most common (50%) measure of RV function after inducing RVD. Four of the studies (67%) demonstrated marked improvement of the RV after stem cell therapy. RV function was assessed by using end systolic elastance (Ees), RV fractional area change (FAC), and RV chamber size and volume.

Conclusions This review is limited by the small data set and publication bias; however, results suggest a promising role for stem cells in preclinical studies of RVD. Future translational studies and ongoing early phase clinical trial will help elucidate the clinical safety and efficacy of stem cells in RVD.

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RECIPROCAL ST SEGMENT CHANGES IN MYOCARDIAL INFARCTION: ISCHEMIA AT DISTANCE VS MIRROR REFLECTION OF ST-ELEVATION

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10.1136/jim-2017-000697.527

Purpose of study Reciprocal ST-depression in the ECG's of patients with ST-elevation myocardial infarction (STEMI) results from either true ischemia at a distance via collateral circulation diverting blood to the infarcted region or an electrical phenomenon that results from a mirror reflection of ST-elevation. We aimed to identify the role of reciprocal ECG changes in predicting collateral circulation to the infarcted area determined angiographically.

Methods used In a retrospective study, ECG and angiography of 53 STEMI patients admitted to SUNY Upstate Medical University in 2014 were reviewed independently by experts blinded to the results of ECG and coronary angiography.

Summary of results Reciprocal changes (RC) in ECG were present in 41 patients (77%) and on angiography, 14 patients (26%) exhibited collateral vessels to the ischaemic areas. No correlation was found between the presence of RC and collateral circulation ($p=0.384$), or between the depth of reciprocal ST-depression and the degree of the collateral circulation ($p=0.195$).

However, 84% patients without collaterals exhibited resolution of RC after successful coronary intervention (PCI) ($p=0.036$), suggesting that the ST depressions that resolved after reperfusion were directly caused by the culprit vessel. Patients without RC presented late after symptom onset (9.25 vs 3.83 hours, $p=0.004$), also suggesting time related resolution.

Conclusions RC had no relation to or predictive value for collaterals on angiography. Among late presenting patients, RC were less frequent. Thus, reciprocal ST-depression may represent sub-endocardial ischemia from the primary coronary event or simply an electrical phenomenon, rather than ischemia at distance from impaired collateral circulation.

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HEART FAILURE WITH RECOVERED EJECTION FRACTION AT AN URBAN MEDICAL CENTRE

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10.1136/jim-2017-000697.528

Purpose of study Heart failure with recovered ejection fraction (HFrecEF) is considered a new HF phenotype. However, it is uncertain if myocardial contractility is truly recovered or merely in remission with improved EF a response to medical therapy or the removal of a negative inotropic stimulus. Herein, we monitored patients having HFrecEF at our urban medical centre.

Methods used Retrospective review of our cardiology clinic patients with prior HF with reduced EF (HFrEF) (<40%) who subsequently had recovered EF (>40%) between March, 2015 and April, 2017. The baseline characteristics, medical history and echocardiogram of these patients were analysed.

Summary of results A total of 32 patients (mean age $\pm$ SEM 49.4 ± 10.5 years; 50% female; and 100% African Americans (AA)) were identified; 68.8% had nonischemic (NICM) and 31.3% ischaemic cardiomyopathy (ICM). 78.9% presented with decompensated HF and baseline EF $26.0 \pm 6.5\%$ which improved to $53.4 \pm 8.6\%$ at recovery on average of 518.7 ± 399.9 (85–1676 days). In keeping with reversible causes of their CM, 7 were former alcohol, 4 former cocaine and 2 former marijuana abusers; 1 energy drink consumer; and 4 with peripartum CM. 100%, 87.5% and 59.4% were taking a beta-blocker, an angiotensin converting enzyme inhibitor and an aldosterone receptor antagonist, respectively. Seventy percent of patients with ICM had percutaneous coronary revascularisation. A reversible cause of HFrEF was not identified in 8 patients (5 NICM and 3 ICM), however, they were on optimal medical therapy suggesting EF recovery may be related to their medical management.

Conclusions In the present study, 75% of our AA patients with HFrecEF had withdrawal of a negative inotropic stimulus, while all were receiving optimal medical therapy, which may have contributed to their recovery in ventricular function to suggest HF in remission rather than a new HF phenotype. Prospective studies and a scheduled regimen of serial echocardiograms are needed to understand the characteristics and rate of recovery of patients with impaired EF to determine if they are a distinctive HF phenotype.

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QUALITY OF ANTICOAGULATION CONTROL IN PATIENTS WITH HISTORY OF ATRIAL FIBRILLATION

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10.1136/jim-2017-000697.529

Purpose of study This study evaluates the use of anticoagulation in admitted patients with a prior diagnosis of atrial fibrillation to assess appropriate therapy.

Methods used Patients ($n=175$) with a pre-existing diagnosis of atrial fibrillation admitted between 2016–2017 to cardiac telemetry were studied to assess anticoagulation (AC) status on admission, with consideration of clinical data, CHA₂-DS₂-VASc score, and HAS-BLED score.

Summary of results The study population was 53% male, mean age 75.4 years. The mean EF was 45.9%, mean INR 1.88, and mean serum creatinine 1.52. The mean CHA₂-DS₂-VASc score for the entire group was 4.1 and mean HAS-BLED score was 2.4. There was no difference in mean CHA₂-DS₂-VASc between patients on AC at admission (AC+, $n=126$) and those not on AC at admission (AC-, $n=44$).

Admission CHA₂-DS₂-VASc score was low (0) in 3% of AC +patients, intermediate (1) in 7%, and high (≥ 2) in the

remaining 90%. Of the AC- patients, 42/44 (95.5%) had a CHA₂-DS₂-VASc score ≥ 2 . The reasons for AC- included 17/44 (38.6%) with a history of bleeding, 8/44 (18.2%) due to fall risk, and 16/44 (36.4%) due to unclear reasons; 1/44 patients reported cost as the reason for not taking AC.

The HAS-BLED bleeding risk scores included 5% of patients with a score of 0 (low), 49% with a score of 1–2 (moderate), and 46% with a score ≥ 3 (high risk). While non-NOAC use (ie VKA or enoxaparin) was stable between moderate and high HAS-BLED risk groups, NOAC use declined steeply by 48% moving from moderate to high bleeding risk groups.

The percentages of AC- patients for various CHA₂-DS₂-VASc scores are seen in the table.

Conclusions 90% of all patients fell into the high CHA₂-DS₂-VASc stroke risk group, underscoring the indication for AC. However, high proportions of patients at nearly every CHA₂-DS₂-VASc level ≥ 2 were not on AC. 95.5% of patients not on AC at admission had a CHA₂-DS₂-VASc score ≥ 2 and would ideally be treated with AC to reduce annual stroke risk. Contraindications to AC, such as history of bleeding or falling, often prohibit AC use in this group. However, there may also be a subset of these patients in whom AC would be indicated who are not receiving optimal therapy.

Abstract 529 Table 1 AC- patients

	CHA ₂ -DS ₂ -VASc 0 n=6	CHA ₂ -DS ₂ -VASc 1 n=9	CHA ₂ -DS ₂ -VASc 2 n=17	CHA ₂ -DS ₂ -VASc 3 n=27	CHA ₂ -DS ₂ -VASc ≥ 4 n=111
% not on AC	33%	0%	41%	19%	27%

530 ATRIAL FIBRILLATION IN THE INTENSIVE CARE UNIT

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10.1136/jim-2017-000697.530

Purpose of study Atrial fibrillation (AF) remains the most common sustained tachyarrhythmia worldwide with evidence suggesting an increase in incidence and prevalence. Herein, we compared the profiles of intensive care unit (ICU) patients to patients hospitalised to the medical floor and who on admission were diagnosed with AF to determine if certain variables were characteristic of ICU patients.

Methods used A retrospective review of 160 patients with AF at an urban medical centre from November 1, 2015 to July 1, 2017, of which 41 were admitted to the ICU. The following variables were analysed: sex, electrolytes (potassium, magnesium, calcium), brain natriuretic peptide, serum creatinine, race, body mass index, left ventricular hypertrophy present on electrocardiogram, corrected QT interval and presence of rapid ventricular response. Variables were compared with identical features in those admitted to the medical ward (n=119).

Summary of results The ICU population was slightly older (67.5 $\pm$ 2.3) with a higher incidence of females (39% vs 35%)

in both populations noted to have atrial fibrillation. The ICU population did have an elevated brain natriuretic peptide (1112 pg/mL vs 852 pg/mL) as well as an expected higher incidence of rapid ventricular rate (63% vs 45%). The ICU population was noted to have a statistically significant elevation of BMI (32.8 vs 24.8, $p < 0.01$) in the obese range as well as a statistically lower serum calcium (8.5 mg/dL vs 8.9 mg/dL, $p < 0.01$) when compared to patients admitted to the medical ward.

Conclusions In ICU patients with atrial fibrillation, an older age, elevated BMI, lower serum calcium, and increased serum brain natriuretic peptide were noted when compared to patients admitted to the medical ward. ICU patients have a higher incidence of atrial fibrillation with rapid ventricular response, likely due a hyperadrenergic state associated with their underlying disease process requiring ICU level of care.

531 TEN YEAR FOLLOWUP OF PATIENTS WITH DISEASE OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY WITH AND WITHOUT RENAL DISEASE

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10.1136/jim-2017-000697.531

Purpose of study The purpose of this observational study was to compare the survival of patients with disease of the left anterior descending with and without renal disease.

Methods used Patients referred for coronary artery disease in 2003–2004 with left anterior descending disease were selected for two groups. based on a serum creatinine of 1.2 milligrams per deciliter or less (group 1), and patients with a serum creatinine 1.3–2.5 milligrams per deciliter (group 2). All patients were offered a program of risk factor management and revascularisation when indicated, and ICD implantation by accepted guidelines. All cause mortality was compared using Kaplan-Meier logrank analysis, and hazard ratios were calculated by the Cox proportional hazards method

Summary of results

- 81 patients in group 1 with a mean age of 60.96 $\pm$ 10.31 years and serum creatinine 1.00 $\pm$ 0.145 were compared over a followup period of at least 10 years with 31 patients in group 2 with a mean age of 66.71 $\pm$ 8.78 years with a mean serum creatinine of 1.57 $\pm$ 0.27 milligrams/deciliter.
- Patients in group 2 had decreased survival with 19/31 deaths (61.3%) compared with 34/81 (42.0%) in group 1 patients with normal renal function. Comparison of survival curves by the Kaplan-Meier logrank method showed decreased survival in group 2 ($p = 0.0095$).

And analysis by the Cox proportional hazards method showed a hazard ratio of 2.07 ($p = 0.011$), consistent with an increased risk for mortality in the patients with decreased renal function.

Conclusions

- Patients with left anterior descending disease and elevated baseline serum creatinine within the range of 1.3–2.5 milligrams per deciliter have decreased survival over a 10 year period when compared with patients with left

anterior descending disease and normal serum creatinine. A program of risk factor treatment and revascularisation did not reduce the mortality risk to the level present in patients with a normal baseline creatinine.

- A larger study with additional followup may help to identify reversible factors that can be treated to improve survival in patients with coronary and renal disease.

532 A RETROSPECTIVE CASE-CONTROL STUDY ON THE EFFECTS OF PHARMACIST INTERVENTION ON A1C IN AN AMBULATORY SETTING

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10.1136/jim-2017-000697.532

Purpose of study To identify the impact of physician and pharmacist collaboration on lowering A1C in diabetic patients in a primary care clinic.

Methods used

- IRB approved retrospective, case-control study of all diabetes patients in the IM clinic from July 2013 to March 2015.
- Inclusion Criteria: Age 18–65, Baseline A1c >6.5%.
- Exclusion criteria: No baseline or follow-up A1c in the chart, referral to endocrine specialist.
- Cases included patients referred to and seen by the pharmacist in at least 1 pharmacotherapy clinic visit.
- Controls included age-matched patients seen by the primary care physician as part of usual care.
- Data collected include baseline A1c, followup A1c after pharmacy visit or most recent A1c in control group and number of visits to the pharmacotherapy clinic.

Summary of results

- 35 patients in the case group and 46 age-matched control patients were included in this analysis.
- Baseline A1c was higher in the cases (9.4%; range 6.8%–16.6%) than the control group (8.1%; range 6.5%–15.6%).
- More patients were controlled at A1c goals at baseline in the control group (17 vs 2).
- The mean decrease in A1c was higher (1.2% vs 0.7%) in patients referred to the pharmacist.
- The absolute increase in patients at goal at follow-up was higher in patients referred to the pharmacist (9 vs 5).
- The median number of visits to the pharmacist was 1 with a range of (1–8).

Conclusions Physician and pharmacist collaboration within the Internal Medicine clinic resulted in greater decreases in A1c and a greater increase in patients achieving A1c goals than usual care within the clinic during this time. Although this is a retrospective study with a small sample size, our findings are consistent with other studies in circulation that show a benefit in cardiovascular outcomes in patients seen by a pharmacist in collaboration with a physician in an ambulatory setting.

Gastroenterology

Concurrent session

2:00 PM

Friday, February 23, 2018

533 SUCCESSFUL HEPATITIS C TREATMENT WITH DAAS IMPROVES HEPATIC FIBROSIS

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10.1136/jim-2017-000697.533

Purpose of study The advent of DAAs has revolutionised the treatment of HCV infection with cure rates ≥98%, however there is limited data on the effect of successful virologic cure on hepatic fibrosis. The aim of this study was to compare hepatic fibrosis scores and staging that is measured non-invasively using Ultrasound elastography (UE) between patients without HCV viremia post-SVR and patients who did not receive treatment or with prior treatment failure.

Methods used Clinical data was extracted from medical records of patients with HCV who were referred to a tertiary referral centre. The sampling frame was comprised of HCV patients who received care from 1/1/2015 to 10/31/2016. Patients with at least 2 UEs were included in the sample and those without were excluded. The sample (n=69) was stratified into two groups: 1) those without HCV viremia post-SVR, and 2) those with HCV viremia who did not receive treatment or with prior treatment failure. The Paired samples t-test was used to compare the two patient groups on liver fibrosis scores and liver fibrosis staging (METAVIR).

Summary of results The majority were male (55%), non-Hispanic white (63%), genotype 1 (85%) patients with a mean age of 57. Forty-nine (71%) patients were without viremia post-SVR and 20 (29%) were with HCV viremia who did not receive treatment or with prior treatment failure.

In group 1 patients, the mean fibrosis score decreased significantly from 7.57 before treatment to 6.14 after treatment ($t=4.35$, $p=0.00$). Conversely, the mean fibrosis score increased significantly from 5.99 to 6.36 ($t=-1.13$, $p=0.27$) in group 2 patients. In patients of group 1, 37% had categorical reductions in hepatic fibrosis staging, 62% had no change and 2% had worsening progression; whereas, only 25% of patients in group 2 had categorical reductions in hepatic fibrosis staging, 55% had no change, and 20% had worsening progression.

Conclusions Patients who were successfully treated with DAAs had greater reductions of hepatic fibrosis compared to those without DAA treatment or with treatment failure. More studies are needed to assess and establish liver histology improvements associated with viral eradication pharmacodynamics of DAAs.

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THE EFFECT OF HEPATITIS C TREATMENT ON RENAL FUNCTIONS IN LIVER TRANSPLANT PATIENTS

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10.1136/jim-2017-000697.534

Purpose of study Recurrent Hepatitis C virus (HCV) post liver transplant (LT) is associated with higher mortality. It is estimated that 10%–20% of all HCV-infected patients have some degree kidney disease. This percentage may be even higher in LT patients, secondary to immunosuppressive medications toxicity. The presence of kidney disease presents a challenge for HCV treatment in LT patients. The aim of this study is to evaluate the impact of HCV treatment on the renal function in LT patients.

Methods used This is a prospective study including sixty LT patients who received HCV treatment between 2015 and 2016. There were two outcomes: difference in serum creatinine levels and in glomerular filtration rates (GFR) measured at treatment initiation and at 24 weeks after. We examined the proportions of patients who experienced an increase, a decrease, or no change between these two measurements. In addition, we performed paired T-test to examine whether the difference between serum creatinine at baseline and 24 weeks is statistically significant.

Summary of results Patients were 70% males, 88% Caucasians, age 60 (SD 7.2) yrs., 15% cirrhotics and 45% treatment experienced. Treatment duration ranged between 8 to 24 weeks. All patients received Sofosbuvir/Ledipasvir without Ribavirin. All patients achieved sustained virologic response at 12 weeks after treatment (SVR12). 45% of patients had baseline renal impairment as defined by GFR <60%. Among those patients, 8.33% had improved GFR, in 10% GFR has not changed, and in 26.67% GFR has worsened. 55% of patients had normal renal function as defined by GFR >60%. Among those patients, 10% had improved GFR, in 36.67% GFR has not changed and in 8.33% GFR has worsened. 52% of patients had improved or stable creatinine and 48 had worsened creatinine. The average amount of change in serum creatinine between baseline and 24 weeks was 0.038 (24 weeks minus baseline) and the difference was not statistically significant ($p=0.25$).

Conclusions This study showed improvement or unchanged renal function in 65% and worsened renal function in 35% in LT patients who achieved SVR12. Worsening of GFR was more frequently encountered in those with impaired renal function prior to treatment. Caution should be entertained in treating HCV in LT patients especially those with baseline of renal impairment.

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SUSTAINED VIRAL CLEARANCE FOLLOWING INTERRUPTED THERAPY FOR HEPATITIS C

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10.1136/jim-2017-000697.535

Purpose of study This study evaluated the rate of sustained viral response following four weeks of interrupted antiviral therapy.

Methods used Retrospective chart review of patients with Chronic Hepatitis C who completed four weeks of Direct Acting Antiviral Therapy between January, 2015 and September,

2017. These patients' Hepatitis C RNA levels were followed over three months after the cessation of treatment.

Summary of results Between January 2014 and September 2017, 1187 patients were treated with Hepatitis C antiviral therapy. The sustained viral response was confirmed in 95.8%. Since January 2015, fifteen patients completed only four weeks of treatment. Mean age 54 (range 30–74), 15 males, 12 African-Americans, 3 Caucasians, 3 failed previous antiviral therapy: 1 had received Pegylated interferon + Ribavirin, 1 Sofosbuvir + Ribavirin, 1 Ledipasvir + Sofosbuvir. Fibrosis Level: F1: 6, F2: 1, F3: 4, F4: 2, Untested: 2; Genotype 1: 12, Genotype 2: 2, Genotype 3: 1. Viral Load $\leq 1,000,000$ IU 7, $> 1,000,000$ IU 8; The fifteen patients were treated with the following: Sofosbuvir + Ledipasvir 8, Dasabuvir/Ombitasvir/Paritaprevir/Ritonavir + Ribavirin 4. Sofosbuvir + Velasvir 2, Sofosbuvir + Ribavirin 1. Eight patients had a sustained viral response. Seven had relapse following interruption of therapy. Patients with negative HCV RNA over three months after cessation of treatment were followed a mean of 11 months (range: 3–15) and sustained clearance of Hepatitis C was confirmed.

Conclusions In this small series of patients with four weeks of interrupted antiviral therapy, a high success rate was observed with multiple antiviral agents despite variation in viral load and level of fibrosis. The viral clearance following interrupted antiviral treatment was sustained. Interruption of care should not be assumed to be a failure of antiviral therapy.

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PSOAS MUSCLE DENSITY IMPROVES SURVIVAL PREDICTABILITY FOLLOWING TIPS

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10.1136/jim-2017-000697.536

Purpose of study Cirrhosis is associated with loss of skeletal muscles mass and density. The aim of the study was to examine the role of psoas muscle density (PD) measurement in predicting survival when combined with MELD score.

Methods used This is a retrospective study of 287 patients who had TIPS between 2005 and 2015. Patients had TIPS placed for management of variceal bleed (VB) or intractable ascites. PD was measured in Hounsfield Units (HU) by creating

Abstract 536 Figure 1 Life-table survival curves

a region of interest on the muscle on CT prior to TIPS, and MELD score was calculated. The primary endpoint was to determine a threshold sensitivity of pre-TIPS PD for assessing mortality in each group and measure its correlation with survival following TIPS. The secondary endpoint was to determine if combining the PD threshold with MELD can improve survival predictability following TIPS, compared to MELD alone.

Summary of results Patients were 62% males, 88% Caucasians, age 56 ± 9.8 years, with average MELD score of 12.4 ± 7.5 . The threshold of PD measures for discriminating survival was 29.4 HU ($p=0.0026$). PD <29.4 HU was associated with higher risk of mortality. Compared to using MELD alone, adding PD significantly decreased the -2 Log Likelihood of the model ($p=0.0022$). A higher PD was associated with lower risk of mortality [HR=1.64, 95% CI: 1.14 to 2.35, $p=0.0081$].

Conclusions When used in conjunction with MELD score, PD improves overall survival predictability. The best survival outcome was reported in patients with MELD <15 , psoas density >29.4 .

537 TREATMENT OF PATIENTS WITH DECOMPENSATED CIRRHOSIS WITH DAAS IMPROVES CLINICAL SYMPTOMS WITHOUT AFFECTING THEIR MELD SCORE

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10.1136/jim-2017-000697.537

Purpose of study There is currently a paucity of data as to whether treatment of patients with decompensated cirrhosis with DAAs will lead to a reduction in the manifestations of hepatic decompensation, namely, ascites, hepatic encephalopathy (HE) and variceal bleed (VB). Primary outcomes were the proportion of decompensated HCV cirrhotic patients with ascites, HE, and VB 3 months post treatment and 12 months post treatment. Secondary outcomes were pre- and post-treatment MELD and CP scores and AFP levels.

Methods used A retrospective analysis was performed on all patients with HCV cirrhosis who began DAA treatment at a large tertiary medical centre. Manifestations of hepatic decompensations which were investigated included ascites, HE and VB, recorded as present or absent. McNemar's test was used to test change from before treatment to 3 months and 12 months after treatment.

Summary of results The majority of patients were male (57%), Caucasian (84%), treatment naïve (60%), genotype 1 (78%), and mean age of 59 years. 65% of patients received 12 weeks of treatment followed by 32% and 3% receiving 24 weeks and 16 weeks of treatment respectively. 81% of patients were treated with ledipasvir/sofosbuvir. Ascites was resolved in 38% of patients 3 months post-treatment (66% vs 28%, $p=0.01$) and in 36% of patients 12 months post-treatment (66% vs 30%, $p=0.05$). HE was resolved in 52% of patients 3 months post-treatment (68% vs 16%, $p<0.01$) and in 46% of patients 12 months post-treatment (68% vs 22%, $p=0.01$). VB was resolved in 31% of patients 3 months post-treatment (34% vs 3%, $p<0.01$) and in 26% of patients 12 months post-

treatment (34% vs 8%, $p=0.07$). There were no differences of statistical significance between pre- and post-treatment MELD and CP scores (15 ± 5.5 vs 15 ± 6.6 ; 7 ± 1.6 vs 7 ± 2.5). AFP levels were significantly lowered from pre to post-treatment (9.0 ± 8.8 vs 4.8 ± 3.4 , $p<0.01$) mean decrease of 4.7.

Conclusions Patients with decompensated HCV cirrhosis exhibit a significant reduction of manifestations of hepatic decompensation following treatment with DAAs. Further studies are needed to assess sustained benefit of this reduction over time and its effect on need for liver transplantation.

538 ARE WE MISSING CELIAC DISEASE?

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10.1136/jim-2017-000697.538

Purpose of study We calculate the prevalence of celiac disease among patients that present to the primary care setting with symptoms that are suggestive of celiac disease. We then aim to identify any demographic or clinical bias in screening of children that present with symptomatology that is characteristic of celiac disease. We then assess the local clinicians' knowledge of celiac disease through a verified questionnaire.

Methods used We retrospectively reviewed medical records of children who met the following criteria: Children ages 1–18 who visited the primary care services at the University of South Alabama Children's and Women's Hospital from July 2015 – June 2017 with the ICD-10 diagnosis of constipation, diarrhoea, Iron deficiency anaemia, abdominal pain, weight loss and failure to thrive (symptoms seen with celiac). We recorded demographics and data using a clinical abstraction form. We identified the number of (tissue transglutaminase) TTG- IgA screening tests and the number of celiac diagnosis in that period. We tried to identify any trends or factors that raise the clinician's suspicion for celiac disease within our local population. We then created a questionnaire to assess the clinical knowledge of the healthcare providers at our primary care centres.

Summary of results Out of 2570 patients seen at the outpatient primary care setting with symptoms suggestive of celiac disease, 83 TTG-IgA tests were ordered and no celiac diagnosis was made. 65% of these tests were ordered among African American patients and 16% among Caucasians. 46% of these tests were ordered on males and 54% among females. 46% of these tests were ordered in children over 13 years of age.

A questionnaire sent to the primary care physicians (Residents, mid-levels and attendings) had a 58% response rate. 70% of the health care providers did not feel comfortable in their ability to diagnose celiac disease.

Conclusions Despite the high national prevalence of celiac disease no cases were identified in our local population during the two-year study period. A Questionnaire sent out to the healthcare providers identified a knowledge gap in celiac disease screening and diagnosis. This knowledge gap likely attributes to the low prevalence of celiac disease within our primary care clinics with concern of missed celiac disease cases.

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THE RELATIONSHIP BETWEEN SLEEP DISTURBANCES, QUALITY OF LIFE, AND SYMPTOM SEVERITY IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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10.1136/jim-2017-000697.539

Introduction Paediatric inflammatory bowel disease (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) is a waxing and waning disease with symptomatic alternating with remission periods. Sleep disturbances impose adverse effects on host defense mechanisms, and the inflammatory response. We hypothesise that sleep disturbances may occur in proportion to disease activity in children with IBD.

Objective This aim of this prospective questionnaire study was to assess the prevalence of sleep disturbances and quality of life in children with IBD.

Methods used Sleep Habits were assessed by the Child Sleep Habits Questionnaire (CSHQ) for parents, the Pittsburgh Sleep Quality Index (PSQI), Paediatric Daytime Sleepiness Scale (PDSS), and Adolescent Sleep Wake Scale (ASWS) for adolescent. Quality of Life was evaluated using the KINDLR questionnaire. Disease activity for CD was determined by the Paediatric Crohn's Disease Activity Index (PCDAI). The Paediatric Ulcerative Colitis Activity Index (PUCAI) was used to define disease activity in UC/indeterminate colitis patients.

Summary of results Fifty-three children with IBD (38 CD, 12 UC, and 3 indeterminate colitis) were screened for participation in the study. There was a significant association between the CSHQ and PCDAI ($p=0.002$) and the PSQI and PUCAI ($p=0.04$). Children with UC and indeterminate colitis had more sleep disturbances than patients with CD significantly based on the PSQI, PDSS, and ASWS ($p=0.03$, 0.05 , and 0.04 , respectively). In addition to the above correlations with active disease, CSHQ scores correlated with paediatric CD patients in remission ($p=0.002$), while PSQI results best correlated with paediatric UC/indeterminate colitis patients in remission ($p=0.033$).

Conclusions The results of this study showed that sleep disturbances occur in paediatric IBD patients whether they are in remission or have active disease. We speculate that adverse affects on sleep quality may affect quality of life and possibly disease activity. Based on the results of this study, we propose that paediatric IBD patients should be screened for sleep disturbances.

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EFFECT OF EARLY AMPICILLIN TREATMENT ON THE NEONATAL MURINE MICROBIOME

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10.1136/jim-2017-000697.540

Purpose of study There is increasing evidence that the neonatal microbiome plays a major role in maintaining a balanced immune response and influencing disease development such as sepsis and necrotizing enterocolitis. Several factors can influence the preterm gut microbiome, including antibiotic treatment. In this study, we have focused on the influence of maternal antibiotic exposure and early antibiotic administration on the neonatal murine gut microbiome. We hypothesised that pre- and postnatal antibiotic treatment in neonatal mice would

induce a sustained depletion and/or alteration of the intestinal microbiome, which may impact neonatal disease susceptibility. **Methods used** Pregnant C57BL/6 wild type mice were treated with ampicillin (AMP) 100 mg/kg oral gavage from E17–19 to simulate clinically-relevant prenatal antibiotic exposure and control pregnant dams received no antibiotic treatment. Mouse pups were then treated with either AMP (100 mg/kg) or phosphate-buffered saline (PBS) (control) once daily via intraperitoneal injection for 3 consecutive days to simulate postnatal antibiotic exposure. Intestinal and lung tissue were collected on postnatal day (PND) 6 and 21. Intestinal and lung tissue were then subjected to 16S rRNA gene sequencing.

Summary of results We identified a significant difference in β -diversity of the intestinal microbiomes between the AMP and PBS-treated groups at PND 21. The PBS control mice had higher levels of Lactobacillus compared to the AMP treated group at PND 6, while the AMP treated group had higher levels of Corynebacterium and Staphylococcus at PND 6. However, these effects were not observed at PND 21. There was not a significant difference in α -diversity between AMP and PBS treatment groups at either PND 6 or 21. In both treatment groups, microbial diversity increased between PND 6 and 21.

Conclusions Our data suggests that a clinically-relevant antibiotic dosage has a sustained effect on the intestinal microbiome at PND 21 in a mouse model. Future studies will focus on potential cross talk between the gut and lung microbiomes and the effect of antibiotic treatment on common preterm outcomes such as bronchopulmonary dysplasia and sepsis.

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RUMINATION SYNDROME THE SPECTRUM OF CLINICAL PRESENTATION AND EFFICACY OF TREATMENT OPTIONS-A SINGLE CENTRE EXPERIENCE

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10.1136/jim-2017-000697.541

Purpose of study Rumination syndrome (RS) is an under-recognised disorder characterised by regurgitation of swallowed food and liquids within minutes after ingestion accompanied by abdominal pain. We describe a large single-centre series of adults with RS emphasising the spectrum of presentation as well as treatment and outcomes.

Methods used RS was identified in patients referred to a tertiary care centre for unexplained regurgitation/vomiting and upper abdominal pain from 2015 to 2017. Data was collected regarding their diagnosis of RS from medical records, clinic visits, and phone interviews. All patients received diaphragmatic breathing/relaxation techniques and pharmacotherapy with tricyclic antidepressants (TCAs)-doses from 20–125 mg, antiemetics, pain management and nutritional support as indicated.

Summary of results Twelve patients, age range 17 to 82 years (mean 40), 50% male, met criteria for RS. Time to diagnosis ranged from 4 months to 17 years. The working diagnoses were achalasia, gastroparesis, and GERD. The abdominal pain was attributed to gastritis, peptic ulcers, and cholelithiasis. Gastric emptying studies were normal in 11 with one had associated gastroparesis. Treatment outcomes are summarised: 1 patient was able to tolerate symptoms without any treatment; 2 had the greatest improvement with breathing/

relaxation techniques; 2 reported the most help by combining breathing with TCAs, and 2 attributed their response to TCAs. 50% required surgically placed J-tubes because of clinical instability: severe weight loss (14–80 lbs), frequent ED visits and dehydration. Nocturnal enteral feedings were given while practicing breathing during daily meals. J-tubes were removed within 2–6 months when energy improved, along with tolerance of PO intake, and stable weight. Pain management focused on reducing abdominal wall pain by breathing techniques and using tramadol and xylocaine patches.

Conclusions Highlights:

- Diagnosis is delayed or missed extensively due to confusion with many other entities.
- Treatment is focused on mastering of breathing techniques that can take up to 12 weeks for full efficacy, combined with TCA therapy.
- Enteral feeding via J-tube may be necessary in order to stabilise a subset suffering from severe weight loss and dehydration while they respond to therapy.

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GASTRIC ELECTRIC STIMULATION COMBINED WITH SURGICAL PYLOROPLASTY IS CLINICALLY EFFECTIVE IN THE TREATMENT OF REFRACTORY GASTROPARSIS EVEN WHEN THERE IS DEPLETION OF THE INTERSTITIAL CELLS OF CAJAL IN GASTRIC SMOOTH MUSCLE

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10.1136/jim-2017-000697.542

Purpose of study Current literature indicates that the symptom improvement after chronic gastric electrical stimulation (GES) is suboptimal in patients with gastroparesis (GP) and depleted numbers of ICC. Combining GES and surgical pyloroplasty (PP) in order to maximise symptom outcome is a new therapeutic option for severe GP. Our aim was to investigate if clinical efficacy with this new therapy is influenced by the ICC status of patients

Methods used GP patients received GES and PP to control their symptoms and improve quality of life. During surgical implantation of GES system, full-thickness biopsies from the gastric antrum were obtained. The tissues were stained with H and E, C-kit for ICC and trichrome to identify fibrosis. Depletion of ICC was defined as less than 10 cell per high power field (HPF) in the antral smooth muscle. Total GP symptoms score (TSS) before and after GES and PP were evaluated by adding scores for nausea, vomiting, early satiety, postprandial fullness, bloating and abdominal pain assessed by a 4-point Likert scale. Data is presented as mean $\pm$ SD, and statistical analyses was based on t-test

Summary of results Overall, 21 GP patients (16F; 17 diabetics (DM), 4 idiopathic (ID); mean age 41.3 received GES+PP. Based on the numbers of ICC/HPF, subjects were divided into 2 groups:

Patients with ICC <10/HPF: 7 GP patients; 5 DM, 2 ID; mean duration of GP 5.4 $\pm$ 3.1 years; duration of GES+PP 28.3 $\pm$ 12.1 months; mean number of ICC 5.7 $\pm$ 2.1/hpf.

Patients with ICC $\geq$ 10/HPF: 14 GP patients; 11F; 12 DM, 2ID; Mean duration of GP 3.0 $\pm$ 1.6 years; mean duration of GES 25 $\pm$ 13.8 months; mean number of ICC 13.1 $\pm$ 2.4/hpf

Group 1 had TSS of 20.4 $\pm$ 3.5 before and 9.4 $\pm$ 3.4 after GES+PP (p <0.01), while Group 2 recorded 19.1 $\pm$ 3.1 TSS before and 8.5 $\pm$ 6.1 after GES+PP (p <0.001).

Baseline TSS, duration of active GES stimulation were similar in both groups, but the duration of GP symptoms was longer in group 1 with more depleted status of ICC vs group 2 (p <0.05)

Conclusions A depleted ICC status had no negative influence on successful symptom outcome in GP patients treated with combining GES and PP, unlike the reduced symptom outcome of GES therapy alone for severe GP patients

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UTILITY OF PERFORMING ESOPHAGOGASTRODUODENOSCOPY AT THE TIME OF ENDOSCOPIC ULTRASOUND

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10.1136/jim-2017-000697.543

Purpose of study Esophagogastroduodenoscopy (EGD) at the time of endoscopic ultrasound (EUS) is not routinely performed unless there is a clear indication for EGD. Little is known whether significant incidental upper gastrointestinal lesions are missed when using non-forward viewing endoscopes without completing a forward-viewing exam. The purpose of this study is to examine the prevalence of clinically significant incidental upper gastrointestinal tract lesions that were found when using a standard forward-viewing scope at the same time of EUS exam and whether this led to change in the management.

Methods used A retrospective analysis of all consecutive patients who underwent EGD and upper EUS during the same visit from January 2011 to December 2013 was performed. EGD and EUS findings were recorded separately. EGD findings were considered significant if it led to change in patient's management. EGD findings are recorded and reviewed separately from EUS indication and findings.

Summary of results A total of 155 patients who underwent EGD at the same time of EUS are included. Abnormal esophageal findings include Barrett's oesophagus in 6 patients, small esophageal varices in 2 patients, stricture/ring with dilation in 2 patients and candida esophagitis in 3 patients. Abnormal stomach findings include gastritis with positive *Helicobacter pylori* on biopsies in 14 patients, gastric xanthoma in 2 patients, gastric ulcers in 2 patients and gastric adenocarcinoma in 1 patient. Abnormal duodenal findings include duodenitis in 3 patients. The most striking finding of this analysis is incidental finding of gastric adenocarcinoma in a patient who had EUS for biliary abnormalities.

Conclusions Our results have shown that performing an EGD at the time of EUS can lead to increased yield of finding incidental upper gastrointestinal lesions. Gastroenterologists should strongly consider performing an EGD at the same time of EUS.

Haematology and oncology I

Concurrent session

2:00 PM

Friday, February 23, 2018

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OBESITY CONTRIBUTES TO BREAST CANCER METASTASIS IN PRECLINICAL MODELSR Sabol*, A Bowles, A Cote, M Matossian, B Collins-Burow, M Burow, B Bunnell. *Tulane University, New Orleans, LA*

10.1136/jim-2017-000697.544

Purpose of study Breast cancer (BC) is the second leading cause of cancer deaths in the United States. Obesity is an established risk factor for BC. Obese women have an increased incidence and mortality of BC, however the mechanisms through which obesity promotes tumour progression are not well understood. Current models used to study BC *in vivo*, specifically immortalised cell lines or orthotopic xenografts, are limited by the lack of tissue architecture and human stromal components. Passaging immortalised cell lines results in irreversible alterations of genetic information and behavioural characteristics. Patient-derived xenografts (PDX) have emerged as a novel translational tool for cancer research with the potential to more accurately recapitulate the molecular and behavioural aspects of cancer. Further, PDX represent primary patient tumours providing evidence in the context of humans *in vivo*.

Methods used Our team has developed a system to investigate the obesity-BC axis. The protocol involves implanting PDX tumour line 2 K1 coated in matrigel alone or co-transplanted with adipose-derived stem cells from lean (lnASCs) and obese (obASCs) donors. 2 K1 is a triple negative breast cancer (TNBC) PDX. 2 K1 PDX tumours were implanted bilaterally into the mammary fat pad of female SCID/Beige mice with pooled ASC donors until the tumour volume grew to 750–1000 mm³.

Summary of results Tumours with obASCs show decreased expression of CD326, aka epithelial cell adhesion molecule and increased circulating HLA1+ ‘human cells’ as well as increased CD44 +CD24 cancer stem cells in the blood. Metastatic evaluation revealed increased number of metastases in the lungs of the obASC group. These data suggest that obASCs promote increased circulating tumour cells leading to increased metastasis of TNBC.

Conclusions Metastasis accounts for 90% of tumour related deaths; however, the mechanisms through which metastasis is promoted are not well characterised. This study demonstrates that obesity contributes to breast cancer metastasis through adipose stem cells (ASCs).

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MUTATIONAL ANALYSIS OF HNSCCM Botros*, DR Marshall. *Meharry Medical College, Nashville, TN*

10.1136/jim-2017-000697.545

Purpose of study Head and neck cancers begin in the mucosal squamous cell linings of the mouth, nose and throat and are collectively known as head and neck squamous cell carcinomas

(HNSCC). HNSCC is further defined by anatomical site as oral cavity cancer (OCa), oropharyngeal cancer (OPC) and laryngeal cancer (LCa). African American (AA) males having at least 2-times greater mortality than their European American (EA) counterparts. There are many reasons for these disparities, including genomic. The purpose of this study is to identify genes with differing mutation rates for EA and AA individuals, that are associated with cell proliferation and movement.

Methods used The Cancer Genome Atlas (TCGA) contains mutational analyses of 528 cases of HNSCC. Filters within the TCGA interface allowed the grouping of HNSCC subsites by ICD-10 codes. Likewise, data was filtered by race. Resulting gene lists were analysed to identify genes whose mutation rate was >10%.

Summary of results HNSCC cases by location and race are: 121 LCa (EA=95, AA=19), 118 OCa (EA=96, AA=11), 79 OPC (EA=73, AA=6), 70 overlapping sites at diagnosis (OLOP) (EA=62, AA=5), 131 cases of tongue not specified [(TNS) EA=118, AA=6]. As expected, TP53 was highly mutated in all subsites and for all races. For LCa, the one anatomical subsite that has a large AA representation, differentially mutated genes include TTN (EA=70% and AA=32%) and FAT1 (EA=24% and AA=16%). The trend for FAT1 continues for OCa (EA=32% and AA ≤10%) and TNS (EA=26% and AA=16%) and is present at <10% for both races for OPC. Interestingly, FAT1 mutations have been reported to be associated with a better prognosis for HNSCC. CDKN2A is also mutated at 23% vs 16% EA and AA patients respectively. Interestingly, it has been reported to be mutated to a higher degree in HPV negative tumours so this may correlate with reported disparities in HPV positivity of HNSCC for EA and AA.

Conclusions While this level of analysis is not robust enough to prove a role for FAT1, or other genes in HNSCC mortality disparities, the differences between EA and AA patients are intriguing. These data support future studies addressing the prevalence of these mutations in more HNSCC cases to determine if they will be useful markers of outcome and provide some insight into the racial disparities in HNSCC mortality.

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DETERMINATION OF TRENDS IN CARDIOMYOPATHY AND SUBCLINICAL CARDIAC PATHOLOGY IN SURVIVORS OF PAEDIATRIC CANCER

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10.1136/jim-2017-000697.546

Purpose of study The population of paediatric cancer survivors is experiencing late effects associated with their treatment. Children's Oncology Group established guidelines to monitor and screen for late effects, though not all survivors receive adequate screening. This study aimed to monitor cardiovascular (CV) late effects in survivors that had received anthracycline therapy.

Methods used In this retrospective analysis, 83 5 year survivors who received an anthracycline in their treatment were recommended to undergo an echocardiogram (ECHO). Data from ECHOs were collected with medical histories from survivorship clinic appointments. Patients were stratified by cumulative

anthracycline dose (CAD) to determine trends in subclinical CV pathologies.

Summary of results 83 patients received anthracycline chemotherapy in their treatment regimen. Of the 83 patients, 16 received a CAD below 100 mg/m², 29 received a CAD between 100–200 mg/m², 20 received a CAD between 200–300 mg/m², and 18 received a CAD over 300 mg/m². Presently, only 50 of the patients had follow-up ECHOs performed. ECHO revealed 12 (24%) patients showing cardiac abnormalities. Only one patient self-reported CV symptoms. Observed cardiac abnormalities included decreased or low-normal global longitudinal strain (n=2), interventricular dyssynchrony (n=2), anatomical abnormalities (n=4), lowered ventricular contractility or ejection fraction (n=5), and decreased left ventricular and septal diastolic function (n=1). Of the 12 patients with abnormal ECHOs, 5 received a CAD between 100–200 mg/m², 4 received a CAD between 200–300 mg/m², and 3 received a CAD over 300 mg/m². The patient reporting CV symptoms received a CAD of 245 mg/m².

Conclusions Echocardiography found 12 patients with evidence of a cardiac abnormality. Of these 12 patients, only one self-reported CV symptoms. Though current guidelines recommend frequent ECHOs for patients who receive CAD over 200 mg/m², 41.6% of patients receiving less than 200 mg/m² had abnormalities in their ECHOs. Paediatric cancer survivors receiving any CAD are at risk of having an abnormal ECHO; longitudinal monitoring of this population will determine whether abnormal ECHOs mean any difference in CV outcome.

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THE POOR RISK ASSOCIATED WITH TETRAPLOIDY IN AML OVERCOMES FAVORABLE-RISK FEATURES AND WARRANTS A CONSOLIDATION WITH ALLOGENEIC STEM CELL TRANSPLANT

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10.1136/jim-2017-000697.547

Purpose of study While tetraploidy (T) and near-tetraploidy (NT) confer favourable prognosis in B-cell lineage paediatric acute lymphoblastic leukaemia, their prognostic significance in acute myelogenous leukaemia (AML) remains ill-defined.

Combining data collected at our institution along with a review of the literature, we provide the most complete analysis of T and NT in AML.

Methods used A systematic literature search was performed using the key words tetraploidy, near-tetraploidy, acute myeloid leukaemia and AML. Data was tabulated regarding Fluorescence *in situ* hybridization (FISH) analysis, molecular analysis, karyotype, risk status, overall survival (OS), and history of allogeneic stem cell transplantation (Allo-SCT).

Summary of results Among 104 AML cases identified, incidence was similar between T (55/104) and NT (49/104). Median age at diagnosis was 54, male-to-female ratio of 2.2:1. Risk stratification included FISH and karyotype. Cases were stratified into favourable risk (inv(16), t(16;16), t(8;21) or t(15;17)), unfavourable risk (complex karyotype, monosomal karyotype, 5q-, 7q-, -5,-7, t(6;9), inv(3), t(3;3), 11q23 - non t(9;11), or t(9;22)), and intermediate risk (the rest). 13 patients (12.5%), all with t(8;21), had favorable-risk. 51 patients (49.0%) had unfavorable-risk, most of them with

complex karyotype. 40 patients (38.5%) had intermediate risk. We used the Kaplan–Meier method to stratify survival data, and the log-rank test to compare the survival between subgroups. The median OS (mOS) of the whole cohort was 6 months (M). The prognosis was poor for both T (mOS 6.2 M) and NT (mOS 6 M) (p=0.81). Risk stratification showed no impact on mOS (p=0.57) challenging current AML data and the favourable prognostic value of t(8;21) in tetraploid AML. The 21 patients (20.2%) who had Allo-SCT had better outcomes (mOS 17 M) than those who did not (mOS 4 M) (p=0.0085).

Conclusions The prognosis of T or NT AML is dismal and should be incorporated within the unfavourable risk group. Prompt evaluation for Allo-SCT should be initiated at diagnosis. Longer survival can be achieved with chemotherapy followed by Allo-HSCT.

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NATIONAL TRENDS OF SICKLE CELL DISEASE RELATED ADULT HOSPITALIZATIONS

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10.1136/jim-2017-000697.548

Purpose of study Sickle cell disease (SCD) is an increasing global health problem. Data pertaining to contemporary trends of patient characteristics with SCD is limited. Hence, we studied national trends of patient characteristics admitted with a primary diagnosis of SCD from 2003 to 2014 across United States.

Methods used Using 2003 to 2014 Nationwide Inpatient Sample (NIS) database of the Healthcare Cost Utilisation Project (HCUP), we examined the contemporary trends for patient demographics, hospitalisation characteristics, in-hospital complications and healthcare resource utilisation of SCD related hospitalizations in the US.

Summary of results Overall there were 770,000 SCD hospitalizations between 2003 and 2014 with an increase in annual frequency from 52 741 in 2003 to 72 930 in 2014, p-trend <0.001. There was a significant decrease in mean age (31.94 to 31.53, years) and proportion of females (55.0% to 53.8%) (all p-trend <0.001). While the frequency of hospitalizations for African Americans decreased (94.8% to 93.4%), there was an increase in SCD hospitalizations for Hispanics (2.9% to 3.4%). There was an increase in the admissions to hospitals located within western US (7% to 8.4%) and teaching status (60.4% to 77.0%). Mean length-of-stay decreased from 6.2 to 5.4 days, but there was an increase in mean hospital charges from \$17 926 to \$32 147. In-hospital mortality decreased from 0.5% to 0.3%; while there was a consistent increase in the complications of cerebral vascular accident (2.0% to 2.6%), acute chest syndrome (0.7% to 7%), renal failure (2.5% to 7.1%) and pulmonary hypertension (2.5% to 5.5%). There was a significant increase in patients with a co-existing diagnosis of opioid dependence (0.9% to 3.5%) (all p-trends<0.001).

Conclusions Number of hospitalizations, costs, and complications associated with sickle cell disease are significant. We observed significant changes in hospitalisation characteristics and further research is warranted to better understand and improve the hospitalisation outcomes of SCD patients.

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USING EJECTION FRACTION TO IDENTIFY CARDIAC LATE EFFECTS RISK IN PAEDIATRIC CANCER SURVIVORS

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10.1136/jim-2017-000697.549

Purpose of study Adverse cardiac outcomes are a common morbidity associated with paediatric cancer survivorship, especially in survivors who received anthracycline treatment. This study aimed to identify long-term survivors at risk of developing cardiotoxicity based on left ventricular (LV) contractile function.

Methods used In a single-centre retrospective analysis, 47 5 year survivors of paediatric cancer were evaluated at a survivorship clinic. Using late-effects guidelines, patients that received an anthracycline during their treatment underwent an echocardiogram (ECHO) at follow-up. This study examined ECHO based LV ejection fraction (EF). Evidence of cardiotoxicity was defined as EF below 55% at follow up or a decline in EF by more than 20% from baseline. Risk for cardiotoxicity was defined as a decline in EF by more than 15% from baseline.

Summary of results 47 patients were stratified into groups based on cumulative anthracycline dose (CAD). ECHO evaluation found 14 patients with evidence of cardiotoxicity and 9 patients at risk for cardiotoxicity. Of the patients with evidence of cardiotoxicity: 3 received a CAD below 100 mg/m², 5 received a CAD between 100 and 200 mg/m², 4 received a CAD between 200 and 300 mg/m², and 2 received a CAD above 300 mg/m². Of the patients at risk for cardiotoxicity: 1 received no anthracyclines, 1 received a CAD below 100 mg/m², 2 received a CAD between 100 and 200 mg/m², 4 received a CAD between 200 and 300 mg/m², and 1 received a CAD above 300 mg/m². In this population, patients with CADs over 200 mg/m² were 78% more likely to have evidence of cardiotoxicity or risk for cardiotoxicity (95% confidence interval 2, 209%). Clinical symptoms self-reported by patients included irregular heartbeat (n=5), chest pain (n=1), high cholesterol (n=1), and asthma (n=1).

Conclusions Echocardiography found 23 paediatric cancer survivors with evidence of manifest cardiotoxicity or risk for cardiotoxicity. There was a significant increase in risk of having abnormal or suspicious ECHO findings with CADs over 200 mg/m², though patients with CAD below 200 mg/m² also showed LV contractile dysfunction. This population should be monitored indefinitely to determine adverse cardiovascular outcomes.

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EVALUATING THE ROLE OF ROTATIONAL THROMBOELASTOMETRY (ROTEM) AS A PREDICTOR OF POSTPARTUM HAEMORRHAGE (PPH)

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10.1136/jim-2017-000697.550

Purpose of study To determine whether ROTEM findings during pregnancy could be an indicator for an increased incidence of PPH in patients who lack the traditional risk factors.

Methods used Samples were collected prospectively from pregnant women during routine blood draws after 20 weeks of gestation and within 24 hours post delivery(PD). These samples were studied using ROTEM, a visco-elastic study that

assesses hemostasis from a global standpoint, i.e, from initiation of the clot formation until the resolution of the clot and fibrinolysis. It measures clotting time(CT), clot formation time (CFT), maximum clot firmness(MCF), alpha angle, amplitude at 30 min(A30), and clot lysis at 30 min(LI30). Two different ROTEM assays were used: INTEM which assesses the intrinsic pathway of coagulation, and FIBTEM in which fibrin generation alone is examined after inhibiting platelets. PPH was determined by reviewing the electronic medical record and it was defined as a change of haemoglobin of greater than 1.7 mg/dL for vaginal delivery and 3.4 mg/dL for caesarean delivery. Data were analysed using Student's t-test and chi-square test.

Summary of results 38 patients were enrolled; 4 (10.5%) had PPH. When compared to patients without PPH, patients with PPH had significantly higher CT PD using INTEM (175.3 ±8.0 v/s 151.6±18.8, p=0.01), and significantly higher LI30 using FIBTEM in 3rd trimester(100% v/s 99% p=0.05).

There was no significant difference in the platelet counts between those with and without PPH (254.75±49.5 v/s 232 ±55.0 respectively). Overall, our mean values of CT (164.4 ±24.3; 57.0±7.7), CFT (56.4±17.7;478.54±596.7), MCF (70.6±5.0; 25.0±8.5), and alpha angle (78.6±3.3;75.5±3.8) by both INTEM and FIBTEM assays respectively were consistent with reference ranges reported in other studies.

Conclusions The CT in PD using INTEM, and more importantly the LI30 in 3rd trimester using FIBTEM are promising indicators to unmask patients who are at a higher risk to develop PPH. This highlights the importance of antifibrinolytics in the management of PPH. Larger studies (using more specific ROTEM assays to study the fibrinolysis system) are required to identify patients that might benefit from the prophylactic use of these drugs to prevent PPH.

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LYMPH NODE STROMAL CELLS SUPPORT TUMOUR GOWTH VIA BONE MARROW DERIVED EPITHELIAL CELLS IN HUMAN COLORECTAL CANCER

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10.1136/jim-2017-000697.551

Purpose of study Colorectal cancer (CRC) is the third leading cause of cancer death in US. Although mortality has decreased due to improved screening methods, patient prognosis is still severely affected by the formation of extranodal metastasis. A better understanding the mechanism of tumorigenesis is crucial for uncovering novel therapeutic interventions. It is known that infiltrating cells play an important role in tumour growth. Here, using an MHC-matched GFP⁺bone marrow (BM) transplantation model, we investigated the mechanism of how the infiltrating cells mediated CRC progression which is enhanced by lymph node stromal cells (LNSC).

Methods used BM cells from GFP⁺ donor mice were transplanted into lethally irradiated NOD/SCID recipient mice. After 4 weeks, the recipient mice were inoculated with human CRC cell lines (HT-29 or HT-116) in the presence or absence of LNSC in orthotopic xenograft model. A small molecule inhibitor targeting LNSC-derived SDF-1 (AMD3100) was tested. At the endpoint, the primary tumours were weighed, tumour cells were stained with antibodies against an array of infiltrating cell markers, and analysed by flow cytometry. The

BM-derived infiltrating cells were also evaluated by immunohistochemistry staining. These experiments were further validated by using CRC patient tumour specimen.

Summary of results In our orthotopic xenograft model, the addition of LNSCs significantly enhanced the CRC tumour weight ($p < 0.01$). BM-derived GFP⁺ cells were found in tumour cell suspension and tumour slides, indicating the migration of BM cells to tumour site. Co-localization of GFP and CD31 demonstrated that endothelial cells were derived from the BM. The frequency of CD31⁺ epithelial cell infiltrating to tumour site was increased by the co-inoculation of stromal cells with tumour cells, which can be significantly reduced by AMD3100 ($p < 0.05$).

Conclusions Host BM-derived epithelial cells participate in CRC tumour progression. LNSC recruits more endothelial cells from BM to the tumour site and accelerates angiogenesis and tumour growth, which is mediated by SDF-1.

552 UTILITY OF PLATELET AGGREGATION TESTING AS A DIAGNOSTIC TOOL IN PAEDIATRIC PATIENTS WITH BLEEDING PROBLEMS

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10.1136/jim-2017-000697.552

Purpose of study To document correlations/trends between less well-known platelet abnormalities and clinically significant bleeding at our institution over a 5 year period.

Methods used After appropriate IRB approval obtained, a retrospective chart review of 159 individuals with platelet aggregation tests from 2011 to 2015 was performed. Data collected included demographics (age, sex, race), personal and family history of bleeding, screening for coagulation defects and platelet aggregation test results. Patients with known bleeding diagnoses and those with incomplete medical records were excluded.

Summary of results Of the patients with epistaxis, 70% had abnormal platelet aggregation testing. For patients with heavy menses, abnormal platelet aggregation testing was found in only 36% of patients. In addition, abnormal platelet function assay (PFA-100) results or race did not appear to correlate with abnormal platelet aggregation testing.

Conclusions Our preliminary results suggest that platelet aggregation testing was more useful in predicting platelet defects in those with a clinical bleeding history of epistaxis as opposed to heavy menstrual periods. For other presenting symptoms, platelet aggregation testing did not offer diagnostic benefit. Abnormal response to ADP in the platelet aggregation test was the most common finding in our population; the clinical significance of which is not well understood.

Infectious diseases

Concurrent session

2:00 PM

Friday, February 23, 2018

553 LONG-TERM OUTCOMES OF PATIENTS WITH EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN THE COUNTRY OF GEORGIA

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10.1136/jim-2017-000697.553

Purpose of study TB is the leading cause of death globally due to an infectious disease. There are limited data on long-term outcomes among patients with extensively drug-resistant (XDR) TB (resistance to isoniazid, rifampin, a fluoroquinolone and injectable agent). The purpose of our study was to assess end of treatment and long-term outcomes and risk factors for poor outcomes among patients with XDR-TB in Georgia.

Methods used A retrospective population-based cohort study of patients with XDR-TB in the country of Georgia from 2011–2013 was performed. End of treatment and long-term outcomes were based on WHO defined treatment outcomes. Data were abstracted from the Georgian National TB Program surveillance database and medical charts. Additional long-term outcome data were obtained by contacting patients via telephone.

Summary of results 111 patients were diagnosed with XDR-TB; 59 (53%) had newly diagnosed TB. Median age at XDR-TB diagnosis was 34 years (IQR 26–49); 77 (69%) were male, 34 (31%) had a history of incarceration, 48 (44%) were smokers, and 23 (21%) had HCV infection. Among 101 patients with end of treatment outcome data, 35 (35%) had favourable outcomes (22 cured, 13 completed treatment), and 66 (65%) had poor treatment outcomes (14 died, 14 treatment failure, and 37 lost to follow-up [LFU]). For patients LFU, the median days of treatment were 189 (IQR 127–414), and 16 (43%) had a positive culture when LFU. In multivariable analysis, independent risk factors for poor end of treatment outcomes included age (OR 1.05, 95% CI: 1.01 to 1.08), tobacco use (OR 3.14, 95% CI: 1.04 to 9.44), history of incarceration (OR 4.79, 95% CI: 1.15 to 19.93) and a prior history of TB (OR 2.97, 95% CI: 1.01 to 8.75). An additional 12 patients died after treatment, all of who had poor end of treatment outcomes (8 LFU, 4 treatment failure). Total mortality was 27 (24%).

Conclusions In Georgia, just over half of XDR-TB cases had no prior history of TB, indicating primary transmission in the community. End of treatment and long-term outcomes were poor. A high proportion of deaths occurred after treatment, highlighting the need for enhanced post treatment surveillance.

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VIRULENT BACTERIA IN NORTHEASTERN TENNESSEE WATERSYu AJ*, R Miller, D Macariola. *East Tennessee State University Quillen College of Medicine, Johnson City, TN*

10.1136/jim-2017-000697.554

Purpose of study Over the past five years, there have been 634 cases of Shigatoxin producing *E. coli* (STEC) reported to Tennessee's Health Department. Each year the CDC estimates that STEC infections cause 2 65 000 illnesses, 3600 hospitalizations, and 30 deaths in the United States, with approximately 2.4% of US STEC cases occurring in Tennessee. At Niswonger Children's Hospital in Johnson City, Tennessee, there were 20 cases of STEC infection from September 2016 to September 2017, some of which progressed to hemolytic uremic syndrome, which can be life threatening. It is important to note that a number of these children did not have a history of food exposures that would place them at risk for STEC infection; however, there are other routes of infection such as exposure to water that we believe to be contaminated by nearby cattle farms. The purpose of our study was to determine whether bodies of water surrounding Johnson City neighbourhoods harboured STEC.

Methods used Fifty milliliter water samples were collected from selected areas in or around neighbourhoods of Johnson City, Tennessee. Water samples were inoculated to Sorbitol MacConkey (BD Diagnostic System) agar plates under sterile techniques, and incubated at 36°C for 18 hours under aerobic conditions.

Summary of results All sampled sites were positive for STEC, with all plates growing a larger number of colourless colonies (STEC) than pink colonies (non-STEC).

Conclusions STEC is a normal flora in the gastrointestinal tract of cattle, and cattle pastures surround many neighbourhoods in the region of Northeastern Tennessee as cattle farming is a major source of livelihood. It is likely that the water runoff from these cattle farms may be a source of contamination to the water sources around the city's neighbourhoods, water sources that are easily accessible to children year round. Public health measures should be undertaken to inform the public that these water sources may be contaminated with STEC to reduce paediatric STEC infections.

Abstract 554 Table 1 *E. coli* strains isolated from neighbourhood communities

Colony types	Founders park	Sinking creek	Carroll creek	Cherokee creek
Colourless (STEC)	14 (3.5)	24 (6)	32 (8)	35 (8.75)
Pink (Non-STEC)	8 (2)	3 (0.75)	7 (1.75)	4 (1)

Numbers in parentheses represent average number of colonies per plate

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THE ASSOCIATION BETWEEN BODY MASS INDEX AND OUTCOMES IN PATIENTS WITH SEPSIS AND ACUTE RESPIRATORY FAILUREJuarez Ramirez Tello E*, Edriss H, Sanchez AA, Nugent K, Yang S. *Texas Tech Health Science Centre, Lubbock, TX*

10.1136/jim-2017-000697.555

Purpose of study Patients with increased body mass indices (BMI) often present practical problems during their

management in intensive care units with acute medical disorders. Obesity does not appear to have a uniform effect on outcomes in patients with acute medical disorders. Some studies have suggested obese patients have longer ICU stays but lower mortality rates. This study considers the effect of BMI on outcomes in patients with sepsis requiring mechanical ventilation.

Methods used The electronic medical records of patients hospitalised between 2010 and 2016 with sepsis who required mechanical ventilation were reviewed to collect demographic characteristics, clinical information including BMI, pressures required for mechanical ventilation, management requirements, and outcomes including mortality and length of stay (LOS) in the ICU and in the hospital.

Summary of results This study included 173 adult patients. The mean age was 58.5±16.7 years; 53.2% were men. The mean BMI was 29.6±11.9. The mean white blood count was 14.3±8.0 k/μL, 43.9% of the patients had pulmonary infections, and 34.7% had extrapulmonary infections. The overall mortality was 44.5%. The mean LOS was 12.4±11.8 days in the ICU and 16.6±13.6 days in the hospital. The mortality rates were 42.9% in underweight the patients (<18.5), 49.1% in normal weight patients (18.5–24.9), 50.9% in overweight patients (25–29.9), and 34.0% in obese patients (>30). Using a multivariable model adjusted for age, gender, number of comorbid conditions, and APACHE 2 scores, BMI did not have an independent effect on mortality; overweight patients had an increased LOS in the ICU.

Conclusions This study demonstrates that patients with sepsis requiring mechanical ventilation have a high mortality rate. Obese patients had a reduced mortality rate compared with those with normal BMI but this did not reach statistical significance. The explanation for this trend requires a prospective study which considers differences in clinical characteristics, management requirements, and inflammatory parameters in normal weight and obese patients. Overweight patients had a longer ICU LOS.

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A RETROSPECTIVE CHART REVIEW ON MANAGEMENT OF SPINAL INFECTIONS INVOLVING HARDWAREN Beydoun*, S Kregel, S Tandon, E Johnson, A Dretler, M Moore, D Refai, N Roupheal. *Emory University, Atlanta, GA*

10.1136/jim-2017-000697.556

Purpose of study One to eight percent of patients undergoing spinal instrumentation surgeries develop infections which require prolonged parenteral antibiotic therapy. Little is known on the role of subsequent oral suppressive antibiotic therapy in the management of these infections. The aim of this study to determine the role of suppressive antibiotics in the management of spinal infections involving hardware.

Methods used This is a retrospective chart review based on ICD-9 and CPT codes relevant to spinal infections with hardware in patients ≥17 years of age within the Emory Healthcare System over a 10 year period with at least 3 months follow-up from completion of initial antibiotic therapy (mostly intravenous). Data was extracted on patient demographics, clinical presentation, laboratory markers, microbiologic results, and surgical and medical management including choice and duration of suppressive therapy.

Summary of results Of 869 records, 134 met the inclusion criteria for this analysis. Of these patients, 64% were males and 70% were Caucasians. The mean age of the study population was 58.6 years (range 17 to 85 years). Identification of causative agent was present in 87.9% of cases, either in blood or bone/disc/soft tissue cultures. 51.1% of patients had an infection that occurred after hardware placement, mostly occurring within 3 months post-surgery (64%), while the remainder had vertebral osteomyelitis as the primary process that necessitated subsequent hardware placement. Initial antibiotic therapy included intravenous antibiotics in all but one patient, and was administered for a median of 6 weeks (range 2 to 24 weeks). After initial treatment, 62.4% were given oral suppressive antibiotics per physician judgment, of whom 21.2% relapsed. Further analyses will be conducted via multiple regression.

Conclusions This is the largest retrospective observational study of vertebral infection with hardware in place assessing the optimal medical and surgical management. Rates of relapse were high, even among patients treated with prolonged suppressive therapy.

557 INCIDENCE OF HERPES SIMPLEX VIRUS INFECTION COMPARED TO SERIOUS BACTERIAL INFECTIONS IN INFANTS 3 MONTHS AND YOUNGER

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10.1136/jim-2017-000697.557

Purpose of study Herpes simplex virus (HSV) and serious bacterial infections (SBI) in very young infants are devastating illnesses. However, unlike in SBI, initiation of empiric evaluation and therapy for HSV infection is unclear resulting in variation in clinical practices. This ambiguity partly stems from scarcity of incidence data applicable to local settings. The purpose of this study is to determine the incidence of HSV infections relative to SBI's in infants 3 months and younger.

Methods used Medical records of infants <3 months evaluated at the ER and/or admitted to USA Children's and Women's Hospital (CWH) from January 1, 2014 through December 31, 2016 were reviewed. Infants with microbiologically-proven HSV infection and SBI, AND who were born at CWH were included in the study. Infected infants in the NICU and nursery, or those born outside of CWH were excluded. Laboratory results (bacterial cerebrospinal fluid [CSF], blood and urine cultures as well as HSV surface cultures and HSV CSF (PCR) were obtained from the hospital's laboratory database (Medmined). Results of serum HSV PCR were not readily available for review.

Summary of results Twenty (0.24%) of the infants born at CWH (n=8272) during the study period were found to have either HSV infection (n=2, meningitis) or SBI (meningitis n=0, bacteremia n=5, urinary tract infection [UTI], n=13). UTI was the most common SBI in this group of patients. The relative distribution of infections is similar when only <28 day old neonates were included in the review (table 1).

Conclusions HSV infection is more frequent than bacterial meningitis in our study population. Identification through serum HSV PCR may further increase cases of HSV infection.

Further study looking at cost-effectiveness of empiric evaluation and therapy for HSV infection is warranted.

Abstract 557 Table 1 Incidence of HSV and serious bacterial infections from 2014–2016 among children born at CWH

Infection	Incidence of infection, %	
	≤90 day old infants (r, age in days)	≤28 day old neonates (r, age in days)
HSV infection	0.024 (n=2, r 19–84)	0.012 (n=1, 19)
Bacterial meningitis	0	0
Bacteremia	0.060 (n=5, r 11–35)	0.036 (n=3, r 11–17)
Urinary tract infection	0.157 (n=13, r 16–80)	0.060 (n=5, r 16–25)
Total	0.242 (n=20)	0.109 (n=9)

558 IN VITRO SYNERGISM OF FLUCONAZOLE PLUS POLYMYXIN B AGAINST CANDIDA AURIS

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10.1136/jim-2017-000697.558

Purpose of study *Candida auris* is an emerging pathogen with intrinsic resistance to fluconazole (93%), amphotericin B (35%), and echinocandins (41%). To help overcome resistance in *Candida glabrata*, previous *in vitro* studies have demonstrated synergy using polymyxin B, a last resort antibacterial agent, in combination with fluconazole. The goal of the present study was to evaluate any *in vitro* synergism of fluconazole plus polymyxin B against *C. auris*.

Methods used A total of 10 unique clinical *C. auris* isolates were obtained from the CDC AR Bank. Using Etest, MICs for fluconazole and polymyxin B were determined in triplicate for each isolate. MICs were read at 24 hour and confirmed at 48 hour. The Clinical and Laboratory Standards Institute currently has no standard breakpoints for *C. auris*, but the CDC has published 2017 tentative breakpoints: fluconazole ≥32 resistant. Synergy testing was performed in triplicate, using a modified bacterial Etest MIC: MIC synergy method with each drug at 1×MIC. The summation fractional inhibitory concentration (ΣFIC) was calculated for each isolate (mean value used). To calculate ΣFICs, off-scale Etest MICs (fluconazole >256, polymyxin B >1024) were converted to the next two-fold dilution (512; 2048). Synergy was defined as ΣFIC ≤0.5; additivity, >0.5–1; indifference, >1–4; antagonism, >4.

Summary of results Etest MICs (μg/ml) were: fluconazole, 4 to >256 (70% resistant) and polymyxin B, >1024. With the Etest synergy method, 3/10 isolates (fluconazole MICs: 4, 8, and 12) demonstrated synergy with fluconazole plus polymyxin B (ΣFICs, 0.1–0.2). The remaining isolates showed indifference (ΣFICs, 1.3–2.4). No antagonism was seen.

Conclusions With rising emergence and few treatment options available for *C. auris*, additional testing should be performed to search for synergistic combinations. In this study, synergy was only found in the 3 fluconazole-susceptible *C. auris* isolates. It is unclear why, but this could be related to the limitation of the range of concentrations on the Etest strip. Further testing may include either antifungal-antibacterial combinations

or antifungal combinations. Any *in vitro* synergy/additivity may or may not correlate clinically.

559 CLINICAL OUTCOMES OF LASSA FEVER IN CHILDREN COMPARED TO ADULTS IN SIERRA LEONE

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10.1136/jim-2017-000697.559

Purpose of study Lassa fever is a viral haemorrhagic fever due to an arenavirus that causes febrile illness and is endemic to West Africa. The illness usually presents with fever and other nonspecific symptoms such as malaise, headache, sore throat, cough, nausea, vomiting, and myalgia. The clinical course can quickly progress to shock, multi-organ system failure, and death. This analysis uses recent data from Sierra Leone to characterise the clinical outcomes of children with Lassa Fever compared to adults.

Methods used We performed a retrospective cohort study of patients with suspected Lassa fever admitted to the Kenema Government Hospital Lassa Ward in Sierra Leone from 2010 to 2016. Lassa fever was confirmed via ELISA antigen or IgM. Children were defined as age 18 years or less and adults were defined as greater than 18 years.

Summary of results A total of 536 patients were included in the analysis, 223 (41.6%) of which were children. Of these children, 63 (28.3%) were positive for Lassa antigen and 61 (27.4%) were negative for Lassa antigen and positive for Lassa IgM. Ninety (48.4%) adults were positive for Lassa antigen and 96 (51.6%) were negative for Lassa antigen and positive for Lassa IgM. The group of children with laboratory-confirmed Lassa fever had 53 deaths, which was a case fatality rate (CFR) 42.7% compared to the adult group with 87 deaths, a CFR of 46.8%. When stratified by serology status, the CFR in antigen-positive children was 63.5% and antigen-negative and IgM-positive children was 21.3%, which was similar to adults at 66.7% and 28.1% respectively. Of note, children that were negative for Lassa antigen and IgM had a CFR of 40.4% compared to 26.8% in adults.

Conclusions The CFRs for laboratory-confirmed Lassa fever in children were similar to adults, particularly when stratified by serology status. However, the CFR in children with negative antigen and IgM testing compared to similar adult population were higher. While clinical outcomes were similar between adult and child Lassa patients, more research is needed in comparing clinical presentations between both groups in order to help predict mortality.

560 PREDICTORS OF PREP ELIGIBILITY AMONG AT-RISK WOMEN IN THE SOUTHERN UNITED STATES

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10.1136/jim-2017-000697.560

Purpose of study Women of colour in the South have disproportionately high rates of new HIV infections, but low use of HIV pre-exposure prophylaxis (PrEP). Identifying factors associated with PrEP eligibility could facilitate improved screening, offering, and uptake of PrEP among US women at risk for HIV.

Methods used We applied CDC criteria for PrEP use to at-risk HIV negative women enrolled in the Southern sites of the Women's Interagency HIV Study (WIHS) from 2014–2015 to estimate PrEP eligibility. PrEP eligibility was determined using number of male sex partners, partner HIV status, condom use, and injection drug use in the past 6 months. Factors associated with PrEP eligibility were assessed using unadjusted logistic regression models.

Summary of results Of 225 women, 187 (83%) identified as African-American with median age was 45 years. In the past 6 months, 43% reported ≥ 2 partners, 7.1% had a partner with HIV, and 11.1% reported a sexually transmitted infection. Overall, 72 (32%) women met CDC criteria for PrEP. Education of $\leq$ high school, experienced physical violence, sexual violence or engaged in transactional sex in the last 6 months, non-injection drug use in the last 6 months and any previous incarceration were associated with PrEP eligibility. Further, self-perception of HIV was highly predictive of PrEP eligibility.

Conclusions One-third of Southern HIV negative WIHS women were eligible for PrEP. Supplementing CDC eligibility criteria with questions about violence, transactional sex, incarceration, non-injection drug use and HIV risk self-assessment may enhance PrEP screening and uptake among US women.

561 BURDEN OF SERIOUS BACTERIAL INFECTIONS IN YOUNG FEBRILE INFANTS IN A MID SOUTH CHILDREN'S HOSPITAL

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10.1136/jim-2017-000697.561

Purpose of study To assess the incidence and time to identification of Serious Bacterial Infection (SBI) in infants 29–60 days in our population and determine if a risk stratification score can be used to identify low risk patients who can be safely discharged earlier to prevent unnecessary and potentially harmful hospitalisation and parenteral antibiotics.

Methods used We retrospectively reviewed the records of all infants, 29–60 days old, admitted to Le Bonheur Children's Hospital with an ICD-9 code for fever from September 2013 to September 2015. We collected demographics, pertinent medical history, clinical data (vital signs, laboratory and microbiology results, imaging), antibiotic use, and outcomes. Patients were separated into 'low risk' (LR) and 'non-low risk' (NLR) for SBI using Rochester Criteria. We determined the difference in the rate and time to diagnosis of SBI between the two groups.

Summary of results Among the 396 patients included, there were 90 LR and 306 NLR infants. There was a difference between LR and NLR in median temperature (37.4 C versus 38.1 C, $p < 0.0001$) and median length of stay (55.9 hours versus 58.1 hours, $p = 0.01$) but no difference in median age (42 days versus 44 days, $p = 0.09$). There were a total of 50 SBI in 44 patients (11 bacteremia, 3 meningitis, and 36

urinary tract infections). 4 patients had bacteremia with urinary tract infections and 2 patients had bacteremia with meningitis. There were a greater proportion of patients with SBI in NLR than LR 42/44 versus 2/44, $p=0.002$. Of the 2 LR SBI there was 1 bacteremia which resulted in 10 hours and 1 positive urine culture which resulted in 45 hours. There were no patients with an SBI that were discharged sooner than 36 hours. 286 patients without an SBI were discharged after 36 hours. Of those, 69 were LR patients who could have been discharged at 36 hours without a missed SBI.

Conclusions The overall incidence of SBI was low in our patient population and the Rochester criteria successfully identified LR infants. Using this data we feel we can safely discharge patients from the hospital with 36 hours of negative cultures without fear of missing an SBI in LR patients.

562 INCIDENCE AND RISK FACTORS OF SELECT MALIGNANCIES IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS AND END-STAGE RENAL DISEASE

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10.1136/jim-2017-000697.562

Purpose of study Individuals with human immunodeficiency virus (HIV) or end-stage renal disease (ESRD) are at increased risk for developing certain malignancies. Despite the prevalence of these conditions, little data is available on malignancies occurring in patients with both HIV and ESRD. This work aims to determine the incidence of select malignancies and identify potential risk factors for these malignancies in HIV +ESRD patients.

Methods used The United States Renal Data System was queried for all incident dialysis cases from 2005–2011 with an HIV diagnosis. ICD-9 codes were used to identify HIV status, comorbidities, and malignancies of interest. Descriptive statistics and generalised linear models were performed for the overall cohort and the most common malignancy diagnoses.

Summary of results The HIV+, ESRD patient cohort consisted of 6641 individuals (47.8±11.5 years old, 69.9% male). Of 1043 AIDS defining opportunistic infections (ADOIs) identified, *Pneumocystis jirovecii* pneumonia (295, 28.3%) and invasive candidiasis (268, 25.7%) were most common. Among the HIV +patient cohort, 543 (8.2%) carried a diagnosis of a specified malignancy. The most common malignancy diagnoses were Non-Hodgkin's lymphoma (NHL, 25%), Kaposi sarcoma (KS, 16%), and colorectal cancer (13%). Factors significantly associated with increased risk for any malignancy diagnosis included: history of prior cancer (adjusted relative risk, [aRR] 5.37), ≥2 ADOIs (aRR 3.11), 1 ADOI (aRR 2.23), cirrhosis (aRR 2.20), male sex (aRR 1.54), and hepatitis B infection (aRR 1.52). History of prior cancer (aRR 7.05) and ≥2 ADOIs (aRR 3.08) were strongly associated with increased risk of NHL diagnosis. For KS, ≥2 ADOIs (aRR 6.78) and male sex (aRR 5.56) greatly increased the risk of diagnosis. Those with a history of prior cancer (aRR 9.80) and ≥2 ADOIs (aRR 5.82) had the highest risk for a colorectal cancer diagnosis.

Conclusions Over 8% of HIV +dialysis patients developed a malignancy. History of prior cancer and AIDS defining infections were major risk factors, underscoring the importance of immune dysregulation. Awareness of factors affecting malignancy risk in this population may influence screening practices.

563 GUIDELINES FOR MATERNAL CHORIOAMNIONITIS EVALUATION REDUCE ANTIBIOTIC USE IN NEONATES

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10.1136/jim-2017-000697.563

Purpose of study Chorioamnionitis (CA) complicates up to 4% of all births in the US, however, the diagnosis varies. CDC guidelines (2010) require a CBC, blood culture, and IV antibiotics (ABX) for minimum of 48 hour for a neonate born to a mother with CA. With maternal fever as the prevailing clinical diagnostic sign of CA, over diagnosis leading to unnecessary tests and antibiotics in the newborn is an issue. New guidelines by NICHD suggest replacing the term 'CA' with the term 'Triple I' (Intrauterine infection, inflammation, or both) and provide specific criteria for diagnosis and management. These guidelines were implemented at our NICU in January 2017. The purpose of this study was to evaluate if the guidelines were followed and the efficacy of the guidelines in optimising the use ABX for neonates.

Methods used A retrospective chart review study of late pre-term and term infants born to mothers diagnosed with CA from June 1, 2016 through June 14, 2017 was conducted. We collected demographic information, laboratory data, and type and duration of antibiotics given. Data are presented as means±SD and groups compared with t-test.

Summary of results We reviewed 114 charts—66 infants from before the guidelines implementation, and 48 after. Table shows population characteristics. Guidelines were appropriately followed in 60% of cases, 19% had inadequate documentation and 21% did not appropriately follow guideline. During the post-guideline period we saw 12% reduction in ABX initiation (85% vs 97%, $p=0.03$) and the mean duration of antibiotics use was reduced (41 hour vs 52 hour).

Conclusions Implementation of guidelines led to a statistically significant but moderate reduction in the initiation and average duration of antibiotics use. We hope to improve education in the unit to achieve better adherence to the guidelines and decrease unnecessary antibiotic use in neonates.

Abstract 563 Table 1 Neonatal characteristics

	June-Dec 2016	Jan-June 2017
Number of infants	66	48
EGA (wk; mean±SD)	39.07±1.33	39.27±1.4
Birth Weight (gm; mean±SD)	3283±466	3286±522
Male	48.5%	43.75%
Elevated CRP	48.5%	43.75%

Neurology and neurobiology

Concurrent session

2:00 PM

Friday, February 23, 2018

564 SEX DIFFERENCES IN CEREBROVASCULAR SMOOTH MUSCLE CELLS TREATED WITH TNF- α : POSSIBLE IMPLICATIONS IN INTRACRANIAL ANEURYSMS

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10.1136/jim-2017-000697.564

Purpose of study The effect of sex on the pathophysiology of intracranial aneurysms (IA) is not very well understood. Women, especially postmenopausal, are thought to be at a higher risk for formation of IA. Incidence and mortality from subarachnoid haemorrhage (SAH) are also higher in women. This study evaluated the effects of sex on the inflammatory response and phenotypic remodelling processes at the cellular level of the cerebrovasculature in response to TNF- α treatment. TNF- α is a pro-inflammatory cytokine that has been shown to induce phenotypic changes in vascular smooth cells (VSMC) that are similar to those observed in IA.

Methods used VSMC isolated from cerebral blood vessels of both male and female Sprague-Dawley young rats, were treated with TNF- α (10 and 50 ng/ml) for 6, 24, 48 and 72 hours. Gene and protein expression were evaluated using quantitative real-time RT-PCR and a Bio-Plex Pro mouse cytokine 23-plex assay, respectively. Annexin V-FITC apoptosis detection assay was used to detect cell death by flow cytometry. Statistical analyses were performed with SAS version 9.4. We used ANOVA with Tukey's HSD post hoc test to compare means across multiple groups.

Summary of results Results showed the expected phenotypic modulation by TNF- α treatment which is characterised by significant downregulation of VSMC marker genes and upregulation of inflammatory genes in both male and female cells. In addition, the downregulation of the SMC markers SM22 α , SMA α and SM-MHC was significantly higher in female-derived cells than in male-derived cells ($p < 0.0001$). Simultaneously, the upregulation of IL-6, which has been shown to be a reliable early biomarker for predicting vasospasm after SAH, was significantly higher in female-derived cells than in male-derived cells ($p < 0.0001$). At the protein level, females also presented higher concentrations of IL-6 compared to males ($p < 0.01$). Moreover, after 72 hour of TNF- α exposure, cells from male rats underwent apoptosis, whereas the female cells did not ($p < 0.001$).

Conclusions These findings demonstrate a significant difference in the inflammatory response and matrix-remodelling of the cerebrovasculature between males and females, and could potentially shed some light on a mechanism for the sex differences associated with IA that have been observed clinically.

565 UTILISING CRYONEUROLYSIS AS A TREATMENT FOR REFRACTORY OCCIPITAL NEURALGIA

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10.1136/jim-2017-000697.565

Purpose of study Occipital neuralgia is a classification of headache which may present as paroxysmal, shooting or stabbing pain in the posterior part of the scalp in the distribution of the greater, lesser, or third occipital nerves. Occipital neuralgia refractory to medical management may undergo a variety of interventional treatments producing only transient relief of symptoms. No clear guidelines currently exist for minimally invasive management of ON and the intervention of choice is often determined by the preference of the provider. As it has been shown to achieve reliable and long-lasting pain relief in patients with other classifications of headache (i.e., trigeminal neuralgia), usage of cryoneurolysis could be considered as a minimally invasive treatment option for patients seeking symptom relief. Cryoneurolysis is a specialised technique whose mechanism of action results in an insult leading to conduction block of afferent signalling, resulting in lessening or elimination neuropathic pain without significant damage to surrounding tissues.

Methods used Patients diagnosed with occipital neuralgia refractory to medical management underwent an ultrasound guided occipital nerve block, given a pain diary, and instructed to return to clinic in 4–6 weeks. Those who experienced a reduction in headache frequency or cessation of headaches only to have recurrence were eligible for cryoneurolysis. The procedure was performed with ultrasound guidance. Patients returned to clinic for follow up in 6 months and one year.

Summary of results We report on the use of cryoneurolysis of the GON in patients with ON refractory to conventional medical management. Patients presented with 7–9/10 pain and have been refractory to >5 medications along with other treatment options. 90% of patients experienced reduced frequency to no return of headaches to date (greater than 6 months after treatment). Only one patient underwent a second round of cryoneurolysis after a 6 month period.

Conclusions Cryoneurolysis is an underutilised treatment in management of headaches. We show that cryoneurolysis has a 90% reduction in not only the severity of headaches but also frequency in refractory occipital neuralgia. Through future studies, we hope to establish cryoneurolysis as a minimally invasive treatment alternative for refractory occipital neuralgia.

566 BEHAVIORAL CHANGES AFTER TRAUMATIC BRAIN INJURY IN A PAEDIATRIC MOUSE MODEL

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10.1136/jim-2017-000697.566

Purpose of study Traumatic brain injury (TBI) disturbs behaviour of children producing symptoms including increased risk-taking and impulsivity. Few animal studies of TBI have been

done using pediatric-age models of closed head injury (CHI) in both sexes. Prior models also used anaesthesia to restrain animals which confounds analyses of the chemical processes associated with morbidity. This study utilised pediatric-age ePet-EYFP (a marker for serotonin neurons) transgenic mice to determine if TBI in the paediatric age group leads to behavioural abnormalities.

Methods used Unanesthetized, male and female adolescent (PND 35–42) ePET-EYFP transgenic mice were restrained in a plastic cone with slit opening overlying the vertex of the cranium. Cortical injury was performed with a flat, 3-mm-diameter metal tip attached to a Stereotaxic Impactor, driven at 5 m/s, depth of 3 mm and dwell time of 0.2 s. Injuries were centred on left parietal cortex, 2 mm lateral to the midline. Sham mice received same restraint but impact depth set to 0 mm. Mice were evaluated by Rotarod testing on 1 day before CHI and day 1, 5, 9 post injury. Novel object recognition (NOR), open field (OF) and elevated plus maze (EPM) tests were performed at day 5, 7, and 9 post injury, respectively.

Summary of results All CHI mice had lost of consciousness immediately after impact, regaining ability to ambulate by 5 min. Fracture was not seen on skull but tissue damage was obvious on brain surface. CHI and sham mice gained equal weight during study. Male CHI mice displayed motor impairments that did not recover at day 9 after injury, females showed less impairment. Both male and female CHI mice travelled greater distances with less immobile time in OF and EPM tests compared to sham mice, and spent more time in open arms with more entries into open arms in EPM indicating more impulsivity than sham mice. There was no difference between CHI and sham mice in NOR, indicating no cognitive impairments.

Conclusions Our data suggests that CHI in paediatric mice induces motor impairments and increased impulsivity within 9 days of injury. This paediatric CHI model simulates TBI effects observed clinically. Data suggests the utility of this Paediatric CHI model and lends itself to the characterisation of the serotonergic mechanisms implicated in future studies.

567 MODELLING THE EFFECTS OF LEAD EXPOSURE ON FORGETTING IN CHILDREN

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10.1136/jim-2017-000697.567

Purpose of study The detrimental effects of prenatal and early developmental lead exposure have been well documented in multiple species. However, most of this work has been conducted utilising measures that cannot be readily translated across species. This study examined the relationship between lead exposure and forgetting using a cross-species behavioural procedure.

Methods used The participants were 318 children between the ages 6–8 years old that are part of the PROGRESS birth cohort. Blood samples for lead measurement were collected during the 2nd and 3rd trimesters of pregnancy and from children at 4–6 years of age. Forgetting was measured using a Delayed Matching-to-Sample (DMTS) test that was administered using a behavioural test panel similar to those used with

nonhuman primates. The DMTS test required the child to observe a shape on the centre of three buttons, and then press it to extinguish the shape. After a delay, the child then had to choose the button that displayed the same shape that was previously observed. For each correct response the child received a token exchangeable for a prize.

Summary of results The proportion correct at each delay was obtained and a modified power function was fit to the data. A forgetting function model was constructed for each of the three blood lead measurement times which also included maternal IQ, child age and sex as covariates. For each model, the child's age was found to significantly affect the rate of forgetting, with older children exhibiting a slower rate of forgetting (change in rate: $\beta=0.02$ to $\beta=0.03$ per year of age, $p<0.05$). In addition, blood lead level during the 2nd trimester and at 4–6 years of age yielded significant effects on forgetting, with higher concentrations resulting in a steeper rate of forgetting (change in rate: $\beta=-0.06$ per log unit increase in blood lead levels, $p<0.05$).

Conclusions The sensitivity to lead exposure of this cross-species measure of forgetting in humans suggests that it should be a useful cross-species tool for modelling the effects of drugs and toxicants on forgetting.

568 COCAINE-INDUCED QUADRIPLÉGIA

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10.1136/jim-2017-000697.568

Case report A previously healthy 56-year-old male presented with acute quadriplegia. He reported waking up with neck pain and inability to move his arms or legs. Sensation from the lower neck area down was impaired. No history of trauma. He is a cocaine user. His vitals were stable. On exam, there was complete quadriplegia but all CN were intact. He had a sensory level from the lower neck down. Areflexia and poor rectal tone were also noted. CBC and CMP were normal except mild azotemia. Urine drug screen was positive for cocaine. An MRI of spine showed diffuse swelling and oedema in the spinal cord from C2–7 with enhancement of the cord at C2–3 level. CTA and MRI brain were normal. IV methylprednisone was started. The CSF profile was normal with elevated protein level at 278 mg/dL. CSF gram stain, culture, cytology, viral panel PCR, VDRL and oligoclonal band were negative. Serum vitamin B12, folate, ESR, CRP were normal. Angiography did not show evidence of vascular abnormality. He had minimal recovery of motor and sensory function after 5 days of steroids. The hospital course was complicated by respiratory failure, GI bleeding and pneumonia. He remained quadriplegic at the time of discharge.

Our patient presented with acute onset of quadriplegia in the setting of active cocaine use. Sensory level was evident on exam while the cranial nerves were intact, consistent with spinal cord lesion at the cervical level. Acute onset of the deficits and rapid progression at the onset favoured the diagnosis of vascular ischemia. Transverse myelitis is also in the differentials but less likely. Other infectious or inflammatory causes are ruled out. Vascular lesion was not identified by angiography. Therefore, we diagnose cocaine-induced myelopathy in this unfortunate patient.

Cocaine-induced myelopathy is rare with only 12 cases reported in the literature. Most cases involve spinal cord at

the cervical to upper thoracic level. The exact pathophysiology of cocaine-induced ischemia remains unknown but is likely to be multifactorial including vasospasm, platelet activation, vasculitis or embolism due to cardiac arrhythmia induced by cocaine.

Our case demonstrates a rare but catastrophic consequence of recreational cocaine use. Clinicians should also consider cocaine as a cause of acute neurologic symptoms.

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PROSPECTIVE STUDY OF EYEGUIDE FOCUS, A 10-SECOND CONCUSSION MANAGEMENT TOOL, AS AN ADDITIONAL INPUT TO ROUTINE NEUROLOGICAL EXAMINATION TO MEASURE NEUROCOGNITIVE IMPAIRMENT ASSOCIATED WITH MILD TRAUMATIC BRAIN INJURY

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10.1136/jim-2017-000697.569

Purpose of study A concussion or mild traumatic brain injury (mTBI) is from minor trauma to the head, causing an energy deficit to the brain. It is often associated with impairment of consciousness as well as headache, dizziness, abnormal gait, nausea or vomiting.

The purpose of this study is to determine whether there is a correlation between mTBI severity and performance on a smooth pursuit eye test in individuals with mTBI, as well as any prognostic information obtainable from the smooth pursuit eye tests.

Methods used Focus is a 10 s test developed by EyeGuide (Lubbock, Texas, United States), an eye tracking hardware that detects eye movement via the EyeGuide tracking headset. Test subjects will be asked to follow a target stimulus while wearing the headset. The stimulus is a small white circle that moves in a clockwise, figure-eight pattern with a 10degree radius at 0.4 hertz (Hz) for 10 s on a tablet screen. The headset measures the variability of the gaze's position error in the direction parallel to the target. The deviations are totaled to yield a test score. A greater score corresponds to a greater deviation from expected gaze position.

Summary of results Our study will examine patients that present to the Emergency Department of the University Medical Centre, Lubbock, Texas, United States, with direct trauma to the head. We will examine patients from November 2017-January 2018 with follow ups to monitor recovery process.

Conclusions Concussions are a complex and debilitating neurological injury with more than 3 million occurring yearly in the United States. Accumulating evidence suggests that mTBI and concussions are grossly underdiagnosed due to poor understanding of clinical signs and symptoms involved in direct head trauma. Through the use of the Focus tool, this study aims to demonstrate that EyeGuide can augment the current routine neurological examination. By allowing medical providers to monitor patient's daily progress from point of injury back to health, Focus fills a need in concussion detection and treatment to current neurological examination.

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SPINAL INVOLVEMENT OF IGG4 SCLEROSING DISEASE: A DIAGNOSTIC CHALLENGE

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10.1136/jim-2017-000697.570

Introduction IgG4 mediated sclerosing disease is a systemic disorder characterised by multiple organ infiltration by IgG4 positive plasma cells. The usual site of involvement is the pancreas however multiple other organs can be involved like for example the lacrimal, salivary glands, or retroperitoneal involvement.

Case report We present a 59 year old Caucasian female who presented with progressing weakness and numbness of all extremities over the past 4 to 6 weeks. Her complaints started off as neuropathic type pain and progressed to numbness and weakness. MRI revealed C1 to C6 epidural mass causing spinal cord compression. Patient was emergently taken for neurosurgery with successful removal of this mass. Patient clinically improved after the procedure and was eventually discharged to a rehab facility where her neurological deficits continued to improve. Biopsy results showed inflammatory mass, with no evidence of non-Hodgkin's lymphoma or any other malignancy. No clear histological diagnosis was made at that time. Several months later the patient started to develop numbness and weakness again, but this time along with urinary and faecal incontinence. Imaging this time showed similar epidural mass in the T2 to T6 region. Neurosurgical intervention was once again necessary with successful removal. Pathological samples were sent to MD Anderson and results reported IgG4 mediated sclerosing disease. Lab work showed IgG4 level of 207(H) and total IGG of 1765 (H). Patient was started on pulse dose dexamethasone 40 mg weekly and she continued to improve clinically and her IGg4 level trended down to <135. Patient was followed up over the next 3 years, both clinically and with repeat imaging without any relapse.

Dicussion IgG related sclerosing disease is a rare entity which was first recognised as one of the causes of autoimmune pancreatitis. Subsequently extra pancreatic organ involvement was reported, however CNS involvement continues to be exceedingly rare. When the CNS is involved it can present with subacute cord compression which can end up in not only significant morbidity and potentially mortality but can recur if not correctly diagnosed and treated. Once the correct diagnosis has been made the disease can sufficiently be controlled with medical management.

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THE GENETICS OF EPILEPSY

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10.1136/jim-2017-000697.571

Purpose of study Epilepsy affects up to 1% of the population. Identifying a genetic aetiology can help to tailor medical treatment, predict long-term outcome, predict inheritance risk, and clarify the diagnosis. Therefore, genetic testing is an important part of the evaluation of children with epilepsy. Additionally, some of these children also have global developmental delay and/or

autism spectrum disorder, and thus the genetic testing was also done to determine if there was a common genetic aetiology.

Methods used Data will be presented on >250 patients who have undergone genetic testing by epilepsy panels, chromosomal microarrays, and/or whole exome sequencing through GeneDx, Invitae and Hayward Genetics.

Summary of results A variety of mutations have been identified that have impacted treatment, such as: certain anti-epileptic drugs are contraindicated with certain gene mutations such as channelopathies; confirmation of specific epilepsy syndromes; identification of aetiology for familial epilepsies; identification of a common genetic cause for seizures and developmental delay; determination of an alternate diagnosis as the cause of symptoms. Additionally, many of the children with genetic epilepsies have intractable seizures, and the impact of Vagus Nerve Stimulator (VNS) placement in these children will also be presented.

Conclusions Genetic testing can provide valuable information for physicians, patients and families in children with epilepsy. What has become clear is that with continued expansions in available genetic testing options, many children with epilepsy have identifiable genetic causes. A genetic mutation may be even more likely when associated with a developmental disorder, or a family history of epilepsy/seizures. Additionally, as genetic testing expands, it also has become clear that there is significant variability even among family members with the same genetic defect, likely due to a combination of factors such as environmental, incomplete penetrance, and epigenetic or polygenic phenomena.

572 POST-TRAUMATIC STRESS DISORDER IS COMORBID WITH REDUCED MITOCHONDRIAL CAPACITY IN MICE

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10.1136/jim-2017-000697.572

Purpose of study Post-traumatic stress disorder (PTSD) is a debilitating psychiatric condition affecting millions of children worldwide. Childhood traumatic event exposure, including sexual and physical abuse, is associated with increased severity of PTSD psychopathology. Psychopathology is frequently associated with mitochondrial dysfunction, and mitochondrial gene mutations have been identified in post-mortem brains of patients with PTSD. We therefore investigated whether reduced mitochondrial capacity increases PTSD susceptibility.

Methods used We exposed 48 wild-type male mice of the FVB.129P2 background (sighted FVB) to trauma in the form of two decontextualized sessions of inescapable electric foot over two days, previously shown to induce PTSD in ~15% of animals, similar to the PTSD incidence rate in traumatised humans. Behavioural tests for four physical symptoms of PTSD – hyperarousal, hypervigilance, increased risk taking, and disrupted sleep cycle – were used to identify 8 PTSD-vulnerable and 12 PTSD resilient animals based on established scoring and inclusion criteria. Mitochondria from the brains of these animals were isolated, and the activities of electron transport complexes (ETC) I-IV were analysed.

Summary of results PTSD-vulnerable animals showed a statistically distinct behavioural phenotype compared to PTSD-resilient animals. ETC complex activity showed a strong inverse correlation with PTSD-like symptomatology, and ETC complex

activities were significantly reduced in PTSD-vulnerable animals compared to PTSD-resilient animals. We found no significant correlation between ETC enzyme activity and any one behavioural trait, but a significant inverse correlation between average ETC enzyme activity and PTSD-like symptomatology based on the established scoring criterion.

Conclusions Our studies show that mitochondrial capacity may play a role in PTSD vulnerability. In our cohort of 48 WT mice, PTSD-like symptomatology was inversely correlated with ETC capacity, and this correlation was not an artefact of any one behavioural trait's relationship to ETC capacity, but a product of synergy between symptoms. Further studies will focus on transgenic knockdown of mitochondrial ETC capacity to determine if reduced mitochondrial capacity is sufficient to induce PTSD vulnerability.

573 EFFECTIVE TREATMENT OF REFRACTORY SEIZURES WITH DEXAMETHASONE IMPLICATES INFLAMMATION IN DRUG-RESISTANT SEIZURES

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10.1136/jim-2017-000697.573

Purpose of study Even with novel antiepileptic drugs (AEDs), status epilepticus and refractory seizures continue to be a challenge in the inpatient setting. Recent studies have shown a key role of inflammatory mediators in seizure generation and termination. Failure to abort a seizure with standard AEDs may result in aggressive treatment with anaesthetic agents, thereby exposing the patient to significant risks. We describe four patients with refractory seizures that responded to dexamethasone.

Methods used P1, a 61-year-old female with temporal lobe epilepsy, arrived confused and EEG revealed nonconvulsive status epilepticus. P2, a 56-year-old female with an old left frontal haemorrhage, presented with right face and hand epilepsy partialis continua; MRI showed a new left temporo-parietal infarct. P3, a 51-year-old male with a recent right parietal lobe hematoma, presented with left hand epilepsy partialis continua. P4, a 75-year-old female with a history of breast cancer, was admitted with right leg motor seizures; brain MRI was normal and EEG showed left frontocentral ictal discharges even when motor seizures were no longer present.

Summary of results In all patients, standard first-line AED (lorazepam) and at least two second-line AEDs (levetiracetam, lacosamide, valproate, and/or phenytoin) failed to abort the seizures. P4 also received third-line AEDs (propofol and midazolam) which reduced the frequency of subclinical seizures. Dexamethasone 10 mg IV load (except P3) and 4–5 mg IV q6 h (all patients) was administered on day 5 (all patients) resulting in complete cessation of clinical and electrographic seizures 3 days (P1, P2, and P3) or 5 days (P4) after initiation of treatment.

Conclusions In the four cases described, seizures that were refractory to standard AEDs ceased when dexamethasone was administered, suggesting at least a contributory role of inflammation in the pathogenesis of drug-resistant seizures. In rodents, pharmacological studies revealed that inflammatory pathways contribute significantly to the onset or recurrence of acute brief seizures. The role of inflammation in human epilepsy and the efficacy of anti-inflammatory agents in aborting AED-resistant seizures deserves further investigation.

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ADOLESCENT MALE WITH ACADEMIC FAILURE

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10.1136/jim-2017-000697.574

Case report A 13-year-old male presented to clinic for evaluation of a recent episode of status epilepticus and academic decline. He was born term without complications, and his development was normal. He had a past history of 10 febrile seizures between the ages of 3 and 6 years old, and another 'febrile seizure' at 9 years old. Also at 9-years-old he was diagnosed with possible PANDAS due to recurrent strep infections and anxiety, and the following year he had a choking episode and was unable to eat solid foods for 6 months due to anxiety. At 11- years-old he was diagnosed with ADHD due to academic difficulties/worsening behaviour. Over the next two years his academic performance deteriorated, and by the time he presented for evaluation he was failing all of his classes. Over this same time period he was noted to become aggressive and impulsive. On exam he was immature for age, with brisk reflexes including crossed adductors and clonus.

A recent head CT showed nonspecific white matter hypodensities, so a brain MRI was performed, demonstrating symmetrical increased fluid in the bilateral white matter tracts with sparing of the U fibres consistent with a leukodystrophy. Testing of very long chain fatty acid (VLCFAs) found C26:0 and C24:22 and C26:22 ratios were higher than normal, consistent with a defect in peroxisomal fatty acid oxidation. Genetic testing of the ABCD1 gene found a known pathogenic mutation (c1999C>G, pH667D, exon 10, hemizygous).

X-linked Adrenoleukodystrophy is caused by mutations in the adenosine triphosphate binding cassette (ABC), subfamily D, member 1 gene (ABCD1 gene), which helps form the channel through which VLCFAs move into the peroxisome for beta-oxidation and breakdown. Abnormalities primarily affect the CNS (demyelination of white matter tracts), adrenal cortex, and testes. Males often present with learning difficulties and behaviour problems and are initially diagnosed with ADHD. This is then followed by neurologic decline to include increasing cognitive/behavioural abnormalities and then later vision loss and spastic quadriplegia. Treatment is hematopoietic cell transplantation during the early

Abstract 575 Figure 1 Improvement in z-scores change from birth to 36 weeks CGA

stages, while the patient still has mild neurological symptoms. This can both significantly improve five-year survival, as well as slow neurological deterioration/progression.

Nutrition and dietary supplements

Concurrent session

2:00 PM

Friday, February 23, 2018

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NUTRITION REPORT CARD: VALUABLE ASSESSMENT TOOL FOR NUTRITIONAL MANAGEMENT OF HIGH RISK NEONATES

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10.1136/jim-2017-000697.575

Purpose of study Feeding protocols for LBW infants reduce the risk of necrotizing enterocolitis (NEC) and improve growth. However, feeding protocols are often amended to reflect research advances. Altering feeding protocols requires a systematic monitoring process to assess benefits and compliance. We developed a Nutrition Report Card to track process and outcome variables.

Methods used Macronutrients, growth parameters and adverse outcomes are entered in a Nutrition Database. The database includes 437 patients with a BW <1800 g from 2014–2017. Process variables monitored include in part: time to initiate feeds, fortification and goal enteral calories. The 96 outcome variables are monitored including: rate of NEC, growth velocity (GV-gm/kg/d), z-scores for BW, 36 weeks corrected gestation age (CGA) and %SGA at 36 weeks CGA.

Summary of results For the 4 year monitoring period, even with changes in the feeding protocol, NEC rate decreased from 9.8% in 2014 to 2.8% in 2017. GV has steadily increased for all weight groups. There was a year over year improvement in feeding advancement to full calorie feeds at day 21. The figure shows the improvement in z-scores change from birth to 36 weeks CGA.

Conclusions By utilising the Nutrition Report Card one can assess the impact of feeding protocols and make pertinent adjustments to ensure optimal growth for LBW infants.

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HUMAN MILK FORTIFICATION FOR PRETERM INFANTS: OPTIMISING OSMOLALITY AND NUTRITION

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10.1136/jim-2017-000697.576

Purpose of study To report the unknown osmolality and protein/energy (P/E) of fortified human milk (HM) using locally derived recipes.

Methods used Thawed HM was pooled and mixed in small volume recipes. Osmolality was measured by freezing point depression (Advanced Instruments Model 3320, Norwood, MA) in triplicate. The osmolality of individual ingredients

were measured and used to calculate predicted osmolality. P/E was calculated from HM norms and product information.

Abstract 576 Table 1 Recipe comparisons

Calories per ounce	% HM	Protein/energy	Recipe	Measured osmolality mOsm/kg	Predicted osmolality mOsm/kg	Reported osmolality mOsm/kg
24	83%	3.3	EHMF	356±10	351	326
	83%	3.0	SHMF	514±4#	540	450
25	80%	3.5**	EHMF^	365±6	359	—
	80%	3.2	SHMF^	564±6#	586	—
26	75%	3.9**	EHMF^	374±2	372	—
	75%	3.7**	SHMF^	631±5#	656	—
27	66%	3.2	EHMF	427±3	422	—
			+Nt40^			
	66%	3.0	SHMF	558±7#	572	—
			+Nt40^			
	45%*	3.2	EHMF	343±5	333	—
			+EP30			
	45%*	3.0	SHMF	444±9	450	—
			+SSC30			
28	100%	3.1	PL+8	405±5	407	<380
30	100%	3.5**	PL+8^	439±6	432	—
	50%	3.0	EHMF	487±5	487	—
			+Nt40^			
	50%	2.9	SHMF	594±9#	600	—
			+Nt40^			

*HM 3.3, ^Locally derived recipe, #Measured Osmolality >450 mOsm/kg

Summary of results Osmolality of the thawed HM was slightly higher (308 mOsm/kg) but within 10% of accepted human milk norms (290 mOsm/kg). Osmolality of additives is not reported by manufacturers and varied widely: Enfamil Human Milk Fortifier Acidified Liquid (EHMF; 563 mOsm/kg), Similac Human Milk Fortifier Hydrolyzed Protein Concentrated Liquid (SHMF; 1700 mOsm/kg), Nutramigen 40 kcal/oz Concentrate (Nt40; 691 mOsm/kg), and Prolacta+8 Human Milk Fortifier (PL +8; 555 mOsm/kg). Predicted osmolality for recipes was within 10% of the measured osmolality. Locally derived recipes provide more HM, but are often higher than recommended in osmolality (5/9) or P/E (4/9).

Conclusions Practitioners need full product information to compare HM fortification options. When the osmolality of individual additives is known, calculated osmolality appears to be a reliable estimate of final osmolality. Optimising osmolality, % HM, and P/E is a challenge with commonly used HM fortification products.

577 VERY LOW BIRTH WEIGHT FEMALE INFANTS NEED HIGHER PROTEIN AND CALORIES FOR NORMAL GROWTH

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10.1136/jim-2017-000697.577

Purpose of study

Purpose To study, if the protein (P), and calorie (C) requirements for preterm infants of ≤1 kg (ELBW) BW to maintain

appropriate for gestational age (AGA) status for weight (WT) and head circumference (HC) at discharge (d/c) are different between sexes while on full enteral nutrition.

Methods used A retrospective data were collected for all ELBW infants born between 2013–2015 on gestational age (GA), WT and HC centiles at birth, and at d/c, mean daily P and C/kg/d while on full enteral feeds, BPD, NEC, IVH. All received 4 g/kg/d of P from birth while on TPN with varying amounts of dextrose, and a max 3 g/kg/day lipids. All ELBW infants received breast milk mother's or donor, fortified to 24 cal/oz after enteral feeds were >60 ml/kg/d. Target daily weight gain was 15–20 g/kg/day. Infants were excluded if they died before reaching 36 weeks of corrected GA or never reached full enteral feedings. We compared the P and C during enteral nutrition, and morbidities between male and female ELBW infants who maintained AGA status from birth to d/c. We used independent t-test and factorial ANOVA to test significance.

Summary of results There were no differences in morbidities between both the genders. To maintain AGA status for both HC and WT, mean P and C requirements for males were significantly lower than for females (P(g/kg/day) (table). P requirement was significantly lower in males <25 weeks (3.43 ±0.29 vs 3.78±0.13; p=0.008).

Conclusions P and C requirements for females were significantly higher to maintain AGA status from birth to d/c in ELBW infants. Protein requirements at <25 weeks GA, and calorie requirements at <25 and 25–27 weeks were significantly higher for females respectively on enteral nutrition. Larger studies may help to confirm and explore the physiological basis for such differences.

Abstract 577 Table 1 Demographics

Parameter	Males(n=25)	Females(n=31)	P value
GA(wks)	25±1	26±1	0.19
BW(gms)	851±122	816±121	0.29
DOL BW regained	8±5	7±4	0.50
CLD	24%	32%	0.35
Severe IVH	8%	6.5%	0.60
NEC	4%	0%	0.44
Duration of ventilation	17±16	15±19	0.71
Calories (kg/d)	118.7±6.6	123.5±4.4	0.002
Protein (g/kg/d)	3.53±0.3	3.71±0.16	0.003

578 OVER THE COUNTER CAN BE OVERLY DANGEROUS: A CASE OF EXCESSIVE VITAMIN D SUPPLEMENTATION IN A 6 YEAR-OLD MALE

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10.1136/jim-2017-000697.578

Case report A 6 year-old male with autism presented to the hospital with intermittent fevers for the past month. He was also noted to have bilateral leg pain and was limping. He had a visit to his primary care physician one week prior where complete metabolic panel showed calcium at upper limit of normal (10.8 mg/dL). Leg pain was thought to be due to toxic synovitis following an upper respiratory infection and no further workup was obtained. After PCP appointment, leg pain persisted and he began having decreased oral intake, nausea, emesis, and refusal to walk. At presentation to the hospital, his serum calcium was 17.8 mg/dL and ionised calcium

8.9 mg/dL. Mother noted that she gave the patient a strict dairy-free, gluten-free diet. He took both calcium and vitamin D but mother was not concerned that he accidentally ingested these medications, and reported giving these as prescribed.

The patient was admitted to the PICU and hydrated with IV normal saline. He was given one dose of IV pamidronate 0.05 mg/kg. Mother brought in medications to the hospital and vitamin D drops were noted to be 1,000 IU per drop. Mother explained that she had been giving an entire dropperful of medication each day for the past year, a dosage of 30 000 to 40 000 units, and explained that she was uncertain if she should have been giving a drop vs an entire dropper of medication each day. 25-OH vitamin D returned elevated at 97 ng/mL. The patient had likely been receiving an excessive dose of vitamin-D for roughly a year. Calcium normalised with adequate hydration, one dose of pamidronate, and cessation of vitamin-D and calcium supplements. Fever was found to be due to bilateral acute otitis media. After calcium level normalised and symptoms resolved, patient was able to be discharged home.

579 THE HISTORY OF PARENTERAL NUTRITION

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10.1136/jim-2017-000697.579

Case report Parenteral nutrition (PN) is one of the greatest medical inventions which has made conditions previously known to be incompatible with life, now survivable. The idea of infusing energy and vigour to prolong and enrich life has always fascinated human beings. In 1656, Sir Christopher Wren, injected wine and opium into a dog's vein using a goose quill attached to a pig's bladder. Jean-Baptiste Denys, is reported to have transfused sheep's blood to humans in 1667. In 1831, Thomas Latta, formulated a solution of water and 'oxygenating salts' to treat cholera patients. The idea of PN was first attempted by Claude Bernard in 1843, when he administered sugar solution, milk, and egg white to rabbits.

The first successful report of modern day PN in human beings was published by Clark, Brunschwig and Corbin in 1942, when they corrected the negative nitrogen balance in postsurgical patients by infusing casein digest. In 1944, Helfrick and Abelson applied this practice in paediatrics by providing PN to a 5 month child. In 1967, Stanley Dudrick and Douglas Wilmore, by introducing central venous access were able to provide PN over long term. They were able to provide PN to infants up to 400 days. PN made its entry into the NICU when Benda and Babson in 1971, provided PN to preterm infants for up to 3 weeks.

Though, Yamakawa injected emulsified fat in 1920, attempts to introduce fat emulsions were met with serious side effects. Lipomul made of cottonseed oil was the first intravenous lipid emulsion (IVLE) to be used in the US in 1957, only to be withdrawn due to adverse events. Intralipid, a soybean oil-based lipid emulsion (SOLE) was released in Sweden in 1962 and was approved by the FDA in 1972 for use in the US. In the 2000s with parenteral nutrition

associated liver disease (PNALD) linked to SOLE, Omegaven, a fish oil-based lipid emulsion (FOLE) became popular in its treatment. Omegaven though used in the Europe and Asia, is not yet approved by the FDA for use in the US. In 2016, a multicomponent oil-based lipid emulsion, SMOFlipid was approved by the FDA for use in the adults, thus opening the options for off-label use in children. However even with these new generation IVLEs, the concern for PNALD continues. Even though great progress has been made since the first attempt to provide PN 170 years ago, the search for safe and effective PN continues.

580 MINERAL DEFICIENCY MASQUERADING AS STAPHYLOCCAL SCALDED SKIN SYNDROME

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10.1136/jim-2017-000697.580

Case report Acrodermatitis enteropathica (AE) is an autosomal recessive defect involving intestinal zinc transport. Infants with zinc deficiency can develop symptoms of chronic diarrhoea, nail and hair changes, and perioral and perianal dermatitis. This dermatitis can mimic other skin findings in infants, such as staphylococcal scalded skin syndrome (SSSS), atopic dermatitis, fungal dermatitis, and seborrheic dermatitis. We present an infant initially treated for SSSS but was ultimately diagnosed with zinc deficiency.

An 8 week old male was admitted with an 11 day history of worsening facial and genitourinary rash. The patient had been to both paediatric and dermatology visits and was treated with nystatin, cephalexin, and prednisone with no improvement. On exam he had erythematous patches with erosions and scabbed areas on his face periorally, and on his ears, neck, and anterior scalp. He also had scaly, hypopigmented patches of the perianal skin and axilla. Initial lab work revealed mild thrombocytosis, a normal CMP and a negative blood culture. Due to the severity and distribution of the rash, he was placed on IV clindamycin and vancomycin for treatment of SSSS. Infectious disease and dermatology were consulted, and skin swabs showed a polymicrobial infection with MSSA, *Acinetobacter*, *Klebsiella*, and yeast. Antimicrobial therapy was adjusted and zinc levels were sent due to inadequate improvement of his rash. On hospital day 5, the serum zinc level returned at 0.10 mcg/mL (0.70 to 1.20 mcg/mL) indicating severe zinc deficiency. Oral zinc supplementation was initiated, and significant improvement was seen within 3 days.

AE is a rare condition characterised by zinc deficiency which can lead to poor immune function, frequent infections, dermatitis, alopecia, ophthalmic disorders, diarrhoea, and growth retardation. The incidence of the congenital form of AE is about 1 in 5 00 000 births. Treatment involves lifelong oral replacement of zinc and yields a highly effective response. Paediatricians must have a high index of suspicion for zinc deficiency in infants presenting with severe skin infections. Measurement of the plasma zinc level is a simple and readily available test that can prevent delayed diagnosis of this easily treated condition.

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VITAMIN D SUPPLEMENTATION FOR URGENCY URINARY INCONTINENCE IN POST-MENOPAUSAL WOMEN: A PILOT RANDOMISED CLINICAL TRIAL

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10.1136/jim-2017-000697.581

Purpose of study Urgency urinary incontinence (UUI) is a very common, distressing condition. The primary aim of this study was to evaluate the efficacy of vitamin D supplementation compared to placebo to improve UUI in postmenopausal women with vitamin D insufficiency.

Methods used This was a single-site pilot randomised trial conducted 2013–2017. Participants were community-dwelling postmenopausal women, 50 years of age or older, with at least 3 UUI episodes on 7 day bladder diary and 25(OH)D ≤ 30 ng/mL (insufficiency). They were randomised to 12 weeks of weekly 50,000 IU vitamin D₃ or placebo. Using Wilcoxon tests, we calculated the percent reduction in 24 hour UUI episodes (primary outcome), along with urinary frequency and nocturia episodes from the diaries for the overall group and for African American (AA) and obese women. Secondary outcomes included scores on validated bladder symptom questionnaires.

Summary of results We randomised 56 women (50 to 84 years of age; mean age = 60.5 ± 8.2 ; 70% AA; 64% obese), 28 to vitamin D and 28 to placebo; 51 completed treatment. For the completer analysis, mean 25(OH)D at baseline (21.2 ± 5.2 and 18.2 ± 5.6 , $p = 0.30$) improved to 57.9 ± 16.3 with vitamin D₃ and to 21.9 ± 8.2 with placebo ($p < 0.001$). UUI episodes per 24 hour day decreased 52.4% with vitamin D₃ compared to 30.9% with placebo ($p = 0.09$). Among Black women, changes in UUI episodes decreased 63.2% with vitamin D₃ compared to 23.0% with placebo ($p = 0.03$). There were no group differences among obese women ($p = 0.29$). For all women, no differences between D₃ and placebo were found for improvements in voiding frequency ($p = 0.40$), nocturia ($p = 0.40$), incontinence severity ($p = 0.80$), or overactive bladder severity ($p = 0.47$).

Conclusions Post-menopausal women with UUI and vitamin D insufficiency recorded a $>50\%$ decrease in UUI episodes that did not reach statistical significance compared to placebo, except in the subset of AA women. Based on these pilot study estimates for efficacy, further investigation of vitamin D₃ alone or in combination with other treatments for UUI is warranted, particularly for women in higher-risk subgroups.

Perinatal medicine I

Concurrent session

2:00 PM

Friday, February 23, 2018

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HYALURONANS EFFECT ON TIGHT JUNCTION IN EXPERIMENTAL NEC

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10.1136/jim-2017-000697.582

Purpose of study Intestinal permeability of small intestine is primarily regulated by complex paracellular tight junction (TJ) proteins (such as Claudins, Occludins, ZO-1). Disruption of intestinal permeability predisposes to translocation of microbial organisms, intestinal inflammation and necrotizing enterocolitis (NEC). Results from our previous experiments in a murine NEC model has shown that oral administration of hyaluronan (HA) ~ 35 Kda, a glycosaminoglycan, is protective in NEC by reducing bacterial translocation and maintaining intestinal permeability. The purpose of this study was to determine the effect of HA on small intestinal TJ protein and RNA expression in experimental NEC

Methods used We used paneth cell ablation and klebsiella infection model for inducing NEC. CD1 pups were divided into three groups sham, NEC, and NEC+HA. HA 35 kDa administered orally to the NEC+HA group at 72, 48, 24 and 1 hour prior to NEC. At the end of the experiment, pups were euthanized and small intestinal tissues harvested. Immunohistochemistry (IHC) was performed for Claudin-3 and Occludin protein from each group. Intensity of the staining was graded by a blinded pathologist based on the location (apical, lateral and cytoplasmic). Quantitative assay was also performed by RT-RNA PCR. RNA was isolated with an RNeasy Kit from Qiagen and reverse transcribed with a high capacity cDNA kit. Statistical analysis was performed using student t-test as appropriate.

Summary of results Occludin staining intensity was increased in the cytoplasmic region in the NEC+HA group compared to NEC alone. However, Claudin -3 staining intensity was noted to be higher in the lateral walls of the cells in the NEC group compared to the NEC+HA group. Quantitative RNA PCR revealed a 1.4 fold increase in Occludin expression in the NEC+HA group compared to NEC alone ($n = 5$; $p < 0.002$).

Conclusions HA treatment in NEC was associated with increased occludin expression at the protein and RNA level. This could partially explain the protective mechanism of HA on maintaining intestinal permeability and reducing bacterial translocation in NEC. Further experiments are undergoing to determine changes in other NEC relevant TJ proteins (ZO-1, Claudins 3, 4, 7).

583

ORAL MICROBIOTA ATTENUATE NITRATE REDUCTASE ACTIVITY IN EXTREMELY PRETERM INFANTS

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10.1136/jim-2017-000697.583

Purpose of study Necrotizing enterocolitis (NEC) is a major morbidity in extremely low birth weight (ELBW) infants. NEC pathogenesis is associated with increased intestinal vascular resistance and impaired perfusion, possibly modulated by abnormal nitric oxide and nitrate metabolism. Nitrate from the blood is actively concentrated in saliva, converted to nitrite by bacterial nitrate reductase (NR) on the tongue dorsum, and reduced to nitric oxide in the GI tract. Increased nitrite has been observed in infants that develop NEC; however, NR activity and the oral microbiota responsible for NR production have never been assessed in ELBW infants.

Methods used This was a single centre prospective cohort study in ELBW infants < 29 weeks gestation ($n = 29$). A cohort of full term infants ($n = 8$) were used as controls for early

sample comparisons. Informed consent was obtained prior to sample collection. Samples for NR analysis and 16 s rRNA sequencing were first collected within 72 hours of birth and then weekly until infants reached 32 w PMA. For NR activity determination, samples were taken from infants' posterior oropharynx and exposed to nitrate to measure nitrite production. The influence of various clinical factors including intrapartum and postnatal antibiotic use, mode of delivery, and type of enteral feeds were analysed.

Summary of results NR activity was assessed in 190 samples over an 8 month period from infants with a mean gestational age of 25 w 5/7±1.6 and mean birth weight of 733 g±233 g.

- ELBW infants had significantly higher NR activity at birth than full term infants ($p<0.05$).
- Nitrate reducing bacteria were present on the tongue dorsum of ELBW infants at birth.
- NR activity spiked near the peak post-menstrual age of NEC onset ($p<0.05$).
- The alpha and beta biodiversity of oral microbiota were higher at birth compared to the time of peak NR activity ($p<0.05$).
- At the time of peak NR activity, samples with low NR activity had fewer nitrate reducing bacteria compared to samples with higher NR activity ($p<0.05$).

Conclusions Oral microbiota dysbiosis mediated increases in NR activity may play a role in the pathogenesis of NEC as changes in oral microbiome composition were noted during the 'NEC Window.' Microbiota induced NR activity could be targeted for prevention or therapeutic development for NEC.

584

MICROBIOME ANALYSIS OF PLACENTA AND ITS RELATIONSHIP WITH THE MICROBIOME OF THE CORD BLOOD AND FIRST MECONIUM

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10.1136/jim-2017-000697.584

Purpose of study Recent studies confirm the presence of a placental microbiome (PMB) and have refuted the notion that the fetus develops in a sterile environment. Mutual interaction between microbiota and immune system of the newborn can define the lifelong health status of the newborn. Studies using metagenomic analysis of randomly selected snap frozen placental tissue samples from term uncomplicated deliveries revealed a unique, low abundance community of bacteria with limited diversity that most closely resembled the nonpregnant oral microbiome. Our objectives were to test the hypotheses that 1. The amnion, parenchyma, and basal plate have similar MBs; and 2. Cord blood (CB) and meconium have distinct microbiome (MB)

Methods used Amniotic, parenchymal, and basal plate samples were taken from 24 term placentas in the operating room immediately after delivery to reduce risks of sample contamination. CB and infant first meconium samples were also collected from the same infants. All samples were snap frozen, microbial DNA was isolated, a 16 S V4 amplicon library was created, and DNA sequencing was performed. Sequences were

grouped into OTUs to Genera levels. Only samples with >1000 reads were included. Shannon diversity index (SDI) was calculated for each group

Summary of results Phyla are listed in order of abundance ($p<0.05$) for each specimen with p-values for SDI:

- Placenta: Proteobacteria [Subphylum γ (Genus *Escherichia*) >>Subphylum β], Firmicutes, Bacteroides, Fusobacteria, and Tenericutes; among the 3 placental sample types (p -values for SDI=0.33 – 0.64)
- CB: Firmicutes, Proteobacteria (Subphylum β >> Subphylum α), Bacteroides, and Fusobacteria
- Meconium: Proteobacteria (Subphylum γ) >> Fusobacteria >> Bacteroides
- Placental sample types: CB p -values of SDI=2.16e08 – 0.00017. Basal plate: Meconium SDI=5.47e-08.

Conclusions Our preliminary findings confirm the existence of a unique PMB; however,our data revealed greater Firmicutes and lower Actinobacteria abundance than previously reported by Aagard *et al.* These variances may be influenced by the proportion of African-American patients in our cohort, our sample size, and/or our method of sample collection.

585

ASSOCIATION OF INTRAVENTRICULAR HAEMORRHAGE AND ACUTE KIDNEY INJURY IN PREMATURE INFANTS FROM THE ASSESSMENT OF WORLDWIDE ACUTE KIDNEY INJURY EPIDEMIOLOGY IN NEONATES (AWAKEN) STUDY

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10.1136/jim-2017-000697.585

Purpose of study Utilising the AWAKEN trial (a 24-centre cohort) we hypothesised that infants with acute kidney injury (AKI) have an increased risk of intraventricular hemorrhage (IVH) independent of variables associated with both AKI and IVH.

Methods used This investigation consisted of 825 infants from the AWAKEN study with a gestational age of ≤ 33 weeks. A modified KDIGO definition of AKI was used based on serum creatinine (sCr) and/or urine output, with baseline sCr defined as the lowest previous value. IVH status was obtained from discharge diagnoses based on head ultrasounds.

Summary of results AKI was documented in 183/825 (22.2%) infants and IVH in 118/825 (14.3%). Those with AKI were more likely to have IVH than those without [49/118 (41.5%) vs 134/707 (19.0%) $p<0.0001$]. Infants with AKI had a higher odds to develop IVH (OR 1.8, 95% CI: 1.14 to 2.85) when controlling for confounders. Infants with AKI had 2.3 times increased odds ratio to develop IVH ≥ 2 grade and 3 times higher odds to develop IVH ≥ 3 grade when controlling for confounders (table 1).

Conclusions We present the first multicenter study of the association between AKI and IVH in premature infants. An overall association does exist showing infants with AKI had a 1.8 times greater odds ratio of developing IVH, with increased odds ratios with higher grades of IVH when controlling for confounders. Further studies are indicated to increase sample size and examine temporality between AKI and IVH.

Abstract 585 Table 1 Crude and adjusted odds ratios (ORs) and associated confidence intervals (CIs) for the association between acute kidney injury (AKI) and intraventricular haemorrhage (IVH) grades

IVH grade	No AKI (n=642)	AKI (n=183)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
No IVH	573 (89.3%)	134 (73.2%)	REF	REF	N/A
≥1 [^]	69 (10.7%)	49 (26.8%)	3.021 (2.00–4.56)	1.799 (1.14–2.85)	0.01*
≥2	35 (5.5%)	34 (18.6%)	4.154 (2.50–6.90)	2.26 (1.28–4.00)	0.005*
≥3	24 (3.7%)	24 (13.1%)	6.414 (3.31–12.41)	3.07 (1.47–6.45)	0.003*

*Odds ratios (ORs) were obtained from a logistic regression and IVH grade adjusted for 1 min Apgar, 5 min Apgar, Vasopressor support within 1 st week of life, and AKI. [^]Reference all to zero (no IVH)

586 EXTREME PREMATURITY AND MICROALBUMINURIA LEVELS IN EARLY CHILDHOOD

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10.1136/jim-2017-000697.586

Purpose of study Microalbuminuria is a well-established marker of renal dysfunction, early chronic kidney disease (CKD), and metabolic syndrome. Very low birth weight (VLBW, <1500 g) infants are at increased risk of developing microalbuminuria later in life and recent evidence suggests that screening of premature infants will help identify children at higher risk for CKD. This study aim was to investigate the prevalence of microalbuminuria at 1–3 years after VLBW birth and investigate associated perinatal factors.

Methods used We conducted a retrospective review of 360 VLBW patients admitted to the Neonatal Intensive Care Unit at the University of Kentucky between 2013–2016. Inclusion criteria were at least 1 measured urinary albumin and creatinine documented at 1, 2 or 3 years follow up visit at NICU graduate clinic. Urinary albumin of >1.9 mg/dl and/or albumin/creatinine ratio (ACR) of ≥30 was defined as abnormal. Antenatal and postnatal attributes and patient demographics were analysed. Spearman nonparametric correlation analyses was used for analysis.

Summary of results A total of 290 VLBW infants had urinary albumin and creatinine levels recorded at 1, 2 and/or 3 years of age; 38 of these patients (13%) had abnormal urinary values. 35% of these infants (35%) had recorded blood pressure of >85 th percentile and 73% had below average score (<85) in 1 or more domains of cognitive, motor or language development on Bayley Scales of Infant and Toddler Development III. The majority of these 38 patients (70%) were extremely low birthweight (<1000 g), had <5% wt loss in the first week of life (77%) and/or hypernatremia in first week of life (77%).

Conclusions More than 10% of VLBW patients in our cohort had elevated ACR value at 1–3 years of age, suggesting a protracted postnatal renal injury/dysfunction. Initiating mechanisms are not well defined but very early events may be key contributors to abnormalities observed at 1–3 years. These

patients are at increased risk of developing hypertension and developmental delay. Routine urinary screening for microalbuminuria and close follow up for early recognition of HTN and CKD might be warranted in this specific population. Further studies of early mechanisms and strategies for prevention of renal injury are clearly needed.

587 PREDICTIVE VALIDITY OF THE AGES AND STAGES QUESTIONNAIRE IN TODDLERS BORN LESS THAN 28 WEEKS GESTATION

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10.1136/jim-2017-000697.587

Purpose of study The Bayley Scales of Infant Development (BSID) is the gold standard developmental assessment tool from 0–42 months, but is costly, time-consuming and requires specialised personnel. Screening can assist with determining who to refer for full evaluation. Texas Medicaid mandates the use of 1 of 2 parent report measures for early childhood screening, but their predictive validity among extremely pre-term (EP) infants is not well known. The Ages and Stages Questionnaire (ASQ) is the more sensitive and specific of the 2, thus we aim to investigate how ASQ scores predict BSID scores to provide a more cost-effective and feasible method of assessing at EP infants.

Methods used Retrospective study of EP infants given BSID at 22–26 months corrected age (CGA) and ASQ at 9 and/or 18 months chronological age (CA). Statistical analyses calculated to determine if failure on ASQ predicted failure on BSID.

Summary of results (See table 1) 73 subjects met inclusion criteria to date. 9 month ASQ: Communication scale had excellent specificity and PPV but poor sensitivity and NPV; Problem Solving scale had high specificity and NPV but low sensitivity and PPV; Gross and Fine Motor scales had high specificities and NPVs, but poor sensitivities and PPVs. 18 month ASQ: Communication scale had poor sensitivity, specificity, PPV and NPV; Problem Solving scale had excellent sensitivity and NPV, but poor specificity and PPV; Gross and Fine Motor scales had high sensitivities and NPVs, but poor specificities and PPVs.

Conclusions Failure on ASQ at 9 and/or 18 months CA does not strongly predict failure on BSID at 22–26 months CGA in EP infants. At 9 months, sensitivity is low but improves at 18 months. The high sensitivity at 18 months indicates that the ASQ may be a useful screening tool to identify developmental delay earlier but cannot replace BSID since low PPV indicates that few children with failing ASQ will have poor BSID scores.

Abstract 587 Table 1

ASQ	BSID	Sensitivity	Specificity	PPV	NPV
9 months (n=60)					
Problem Solving	Cognitive	0.37	0.90	0.38	0.90
Communication	Language	0.10	1.00	1.00	0.69
Gross Motor	Gross Motor	0.25	0.91	0.17	0.94
Fine Motor	Fine Motor	0.50	0.93	0.33	0.96
18 months (n=31)					
Problem Solving	Cognitive	1.00	0.46	0.17	1.00
Communication	Language	0.42	0.79	0.56	0.68
Gross Motor	Gross Motor	1.00	0.68	0.25	1.00
Fine Motor	Fine Motor	1.00	0.66	0.17	1.00

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FIRST TRIMESTER PREDICTION OF PRE-ECLAMPSIA IN WOMEN WITH TYPE 1 DIABETES

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10.1136/jim-2017-000697.588

Purpose of study Pre-eclampsia (PE) occurs ~4 x more frequently in diabetic than non-diabetic women (~20% vs ~5%). Early identification of women at highest risk is urgently needed. We investigated the predictive ability of plasma leptin, a marker of insulin resistance, and creatinine-corrected urinary neutrophil gelatinase-associated lipocalin (uNGALcc), a marker of kidney dysfunction. We used a subset of samples and clinical data from an established, prospective cohort of type 1 diabetic (T1DM) women and non-diabetic women.

Methods used The subset comprised 23 T1DM women who developed PE, 24 who remained normotensive, and 19 non-diabetic women. Biomarkers were measured by ELISA (R and D Systems) in samples collected at three study visits (12.3 ±1.8, 21.7±1.4, and 31.4±1.5 wks gestation; mean ±SD). All subjects were free of microalbuminuria and hypertension at enrolment. All study visits preceded clinical onset of PE.

Summary of results At first trimester, in T1DM women with vs without PE (primary analysis), leptin ($p<0.01$) and uNGALcc ($p<0.05$) were elevated. In normotensive T1DM vs non-diabetic women (secondary analysis), there were no differences. At the second and third trimesters, findings for leptin persisted and there was no longer a difference in uNGALcc; secondary analyses again showed no differences. After adjustment for established maternal risk factors (HbA1c, BMI, insulin dose/kg/day, gestational age (weeks)), first trimester leptin and uNGALcc remained independently associated with PE outcome. Adding both to a model comprised of four simple maternal clinical risk factors improved the area under the ROC curve 0.78 to 0.95 ($p=0.03$).

Conclusions As early as the first trimester, plasma leptin and urinary NGAL may have utility as effective predictors of PE in women with T1DM. Maternal insulin resistance and sub-clinical renal dysfunction may underlie these associations, and may predispose women with T1DM to PE.

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ASSOCIATION BETWEEN PLACENTAL PATHOLOGY, CEREBRAL BLOOD FLOW AND BRAIN INJURY OF PRETERM INFANTS <32 WEEKS

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10.1136/jim-2017-000697.589

Purpose of study To evaluate the relationship of pathologically confirmed placental inflammation on Doppler ultrasound peak systolic velocities (PSV) and resistive indices (RI) in the anterior cerebral artery (ACA) and right middle cerebral artery (RMCA) in relation to the presence of IVH in premature neonates thus providing an explanation of how placental lesions may relate to neurological outcomes.

Methods used A retrospective cohort study of preterm infants born between 23 0/7–32 6/7 weeks gestation at Parkland Hospital between 1/1/13 – 6/31/15. For each of the infants

included in the study, placental pathology reports and ultrasound data were reviewed.

Summary of results A total of 255 infants (mean gestational age 28 4/7±2 weeks, birth weight 1.2±0.33 kg) were included in this study. Of the 255 infants in the study, 165 (65%) had significant placental pathology and 55 (22%) had >1 significant placental pathology. Infants with abnormal placental pathology were found to have decreased PSV's and RI's in the ACA and RMCA. Neonates with IVH (grades 2, 3 or 4) were found to have decreased PSV's, but no difference in the RI's of the ACA or RMCA. Therefore, infants with placental pathology were not more likely to have IVH.

Conclusions We present the first data to evaluate the relationship between placenta pathology, blood flow and IVH. The infants with abnormal placental pathology did have significantly decreased PSV of the ACA and RI's of the ACA and RMCA; however, our data suggest that this did not directly translate to worse IVH in these infants.

Abstract 589 Table 1 Comparison of Blood Flow Velocity and RI between Abnormal and Normal Placental Pathology at time of Worst IVH (right or left)

PSV and RI	Abnormal placental pathology n=166	Normal placental pathology n=89	P-value
ACA PSV	43.3	48.3	0.02
ACA RI	0.78	0.80	0.006
Right MCA PSV	28.9	31.0	0.23
Right MCA RI	0.76	0.78	0.05

P-value determined by T-test; Mean ±standard deviation

Abstract 589 Table 2 Comparison of Blood Flow Velocity and RI between Presence and Absence of Significant IVH (right or left)

PSV and RI	IVH (grades 2, 3 or 4) n=42	No IVH (grades 0 or 1) n=213	P-value
ACA PSV	39.0	46.2	0.01
ACA RI	0.78	0.78	0.89
Right MCA PSV	25.2	30.4	0.02
Right MCA RI	0.76	0.77	0.622

590

NEUROPROTECTIVE EFFECTS OF LUTEIN IN PERINATAL BRAIN INJURY

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10.1136/jim-2017-000697.590

Purpose of study To determine the neuroprotective effects of lutein using a validated neonatal rat model of hypoxic-ischaemic injury.

Methods used Dams were fed a lutein-rich or control chow diet throughout pregnancy and lactation. From P7 (HI) to P10 (sacrifice), nursing pups also received lutein or vehicle by i.p. injection. Brain sections were examined with immunohistochemical stains, and apoptotic assays. Protein expression,

targeted gene expression involved in hypoxic, apoptotic, and neuroinflammatory pathways were analysed.

Summary of results Lutein treatment reduced histological brain injury scores and suppressed RNA and protein expression of key neuroinflammatory mediators, expression of hypoxia-inducible proteins, and microglial activation.

Conclusions Pre and perinatal lutein supplementation suppresses hypoxic/ischaemic brain injury. Lutein is transferred via placenta and breast milk to the developing brain.

Abstract 590 Table 1 Lutein concentration

Lutein concentration (pmol/gm)	Control	Lutein+no HI	Lutein+HI
Brain	ND	175±00	208.2 ±6.79
Breast milk	ND	14.4±00	12.45±0.5

Lutein is transferred via placenta and breast milk to the developing brain.

Abstract 590 Figure 1 P10 brain sections were stained for astrocytes using an anti-GFAP antibody

Abstract 590 Figure 2

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MATERNAL NUTRITION, OBESITY, AND DIABETES: EFFECTS ON INFANT GROWTH AND BODY COMPOSITION

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10.1136/jim-2017-000697.591

Purpose of study In 2014, up to 70% of adults and 29% of children and adolescents were overweight or obese in the United States. The purpose of this study was to determine the effects of maternal obesity/diabetes and maternal nutrient intake on infantile body composition.

Methods used A cohort of 24 term infants born to normal healthy (NT), obese (OB), or diabetic (DM) mothers were enrolled in this prospective, longitudinal study. Infant body composition was measured by anthropometric and skin fold measurements (SF), air displacement plethysmography (PeaPod), and/or dual-energy x-ray absorptiometry (DXA) at birth and 3 months. Maternal nutritional intake was collected utilising a validated diet survey. Statistical analyses were performed using SPSS 22.0.

Summary of results All mothers were of similar age and infants of similar gestation at birth. The DM group had a higher rate of c-section and lower educational level. As expected, pre-pregnancy BMI ($p=0.02$) and infant BW ($p<0.01$) was greatest in the OB group. At birth, anthropometrics and SF were similar between all groups, with no differences in percent body fat (%BF) or percent fat free mass (%FFM). At three months, abdominal circumference tended to be smaller and %BF tended to be greater in the OB group ($p=0.06$). In contrast, %FFM tended to be greater in the DM group ($p=0.06$). A total of 392 maternal nutritional variables were collected. The total caloric intake was similar between the NT, OB, and DM groups (1952 ± 584 , 2209 ± 668 , and 2047 ± 880 kcal/day, respectively). The total fat intake was 17% higher in OB and DM mothers, although not statistically significant, it is clinically relevant. OB mothers had a four-fold greater intake of total grams of soft drinks ($p=0.04$) and tended to have higher intake of non-fibre cereals, fried fish, and salty snacks ($p=0.1$).

Conclusions Infants of obese mothers had higher birth weight and %BF at three months of age while infants of diabetic mothers had a higher %FFM. Additionally, obese mothers showed a significantly higher intake of soft drinks which may translate into additional metabolic derangements in the offspring. Analyses are still ongoing.

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MATERNAL TOBACCO EXPOSURE LEADS TO CYTOKINE DYSREGULATION IN PLACENTAL MEMBRANES EXPOSED TO LIPOPOLYSACCHARIDE

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10.1136/jim-2017-000697.592

Purpose of study Despite widespread knowledge of maternal and neonatal consequences, 10%–23% of pregnant women self-report smoking. Previous studies on placental membranes

exposed to cigarette smoke extract demonstrate alteration of cytokines *in vitro* that may be linked to premature rupture of membranes and preterm birth. Our goal was to further those observations by associating tobacco exposure in pregnancy to placental inflammatory response. We hypothesise physiologic maternal smoking will alter placental membrane pro-inflammatory cytokine expression compared to non-smokers.

Methods used We conducted a prospective, pilot study on a convenience sample of pregnant women undergoing scheduled c-sections from Dec 2016 to July 2017 at University of Oklahoma Health Sciences Centre. We excluded mothers with labour, suspected chorioamnionitis, recent infection, and known major fetal anomalies. Mothers completed a short Maternal Tobacco Exposure Questionnaire and were classified as smoker or non-smoker based on response. Following placental delivery, sections of amniochorionic membrane were placed in an organ explant system and cultured in media±LPS (100 ng/ml) for 24 hours. IL1β and IL10 were measured from media using ELISA. Data was analysed using student t-test or Wilcoxon-Mann-Whitney.

Summary of results We included 41 mothers of which 21 (51.2%) reported active or passive tobacco exposure (smokers) during the current pregnancy. There were no significant differences in demographics between groups with exception of marital status ($p=0.015$). Interestingly, smokers had significantly higher IL1β in control media (–LPS), but not after exposure to LPS when compared to non-smokers. In contrast, IL10 in control media was not statistically different between groups, but was elevated in smokers after exposure to LPS (table 1).

Conclusions Tobacco exposure during pregnancy can lead to dysregulated expression of placental membrane IL1β and IL10 in response to simulated infection with LPS. Further studies are needed to determine the clinical significance of these findings.

Abstract 592 Table 1

Placental membrane cytokines (pg/ml)	Non-smokers (mean ±SD, n=20*)	Smokers (mean ±SD, n=21*)	P value
IL1β Control	137±89.3	235±60.5	<0.001
IL1β+LPS	246±90.8	255±80.4	0.75
IL10 Control	65.3±78.4	75.3±96.4	0.86
IL10+LPS	184±119	286±83.1	0.0024

Pulmonary and critical care

Concurrent session

2:00 PM

Friday, February 23, 2018

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HIV TRANSGENE EXPRESSION INCREASES MATRIX METALLOPROTEINASE 9 IN RAT ALVEOLAR MACROPHAGES

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10.1136/jim-2017-000697.593

Purpose of study Persons living with HIV (PLWH) often develop emphysema, but little is known about the mechanism behind this association. Several hypotheses have been proposed, including the presence of co-infections and increases in oxidative stress levels in the alveolar space. One intriguing possibility is the presence of elevated matrix metalloproteinase 9 (MMP-9) levels previously found in the bronchoalveolar lavage fluid of persons living with HIV. MMP-9 is a known cause of emphysema in patients without HIV, and elevated levels in PLWH may well predispose them to early development of this debilitating chronic lung disease. In this study, we sought to determine how HIV-related viral proteins modulate MMP-9 expression in the alveolar macrophage (AM).

Methods used We modelled the alveolar space of PLWH using an HIV-1 transgenic rat model that expresses the same viral proteins in the alveolar space that can be found in human subjects. AMs isolated from whole-lung lavage of both HIV-1 transgenic rats and their wild-type littermates were cultured for 24 hours±10 ug/mL of tuberculosis cell wall antigen prior to analysis of gene expression by qRT-PCR. NR8383 cells (a rat alveolar macrophage cell line) were treated ±50 ng/mL gp-120 and Tat (two HIV-related viral proteins) for 48 hours and MMP-9 gene and protein expression were assessed by qRT-PCR and Western blotting, respectively.

Summary of results AMs from HIV-1 transgenic rats demonstrated over-exuberant MMP-9 gene expression in response to tuberculosis cell wall antigen. Tat and gp-120 had no effect on MMP-9 gene expression, but increased MMP-9 protein expression in NR8383 cells.

Conclusions Enhanced expression of MMP-9 gene after the addition of TB cell wall antigen supports existing clinical evidence of co-infections as a possible cause of emphysema in PLWH. Although baseline MMP-9 gene expression was not altered by two key HIV-related viral proteins, protein expression was enhanced, suggesting that HIV-related viral proteins may cause an over-exuberant response to pulmonary insults and also increase baseline translation of MMP-9 mRNA. Further studies are needed to clarify the relationship between MMP-9 expression and MMP-9 activity in the setting of HIV infection and whether MMP-9 contributes directly to development of emphysema in HIV.

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FGF23 REGULATES INFLAMMATION AND OXIDATIVE STRESS THROUGH O-LINKED N-ACETYL-GLUCOSAMINE MODIFICATION IN THE AIRWAY EPITHELIUM

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10.1136/jim-2017-000697.594

Purpose of study Chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality in the U.S. and most cases are caused by cigarette smoke. Inflammation and oxidative stress are critical underlying mechanisms in COPD pathogenesis. Past reports show that dysregulation of the fibroblast growth factor (FGF) 23/α-klotho (Kl) axis promotes inflammation and oxidative stress in disease. Also, the activation of the hexosamine biosynthetic pathway (HBP), a stress sensor, induces these disease processes. However, the link between the FGF23/Kl axis, the HBP, and the mechanisms involved in these stress responses have not been defined.

Methods used Adult wild-type (WT) and KI deficient (KI^{-/-}) mice were assessed for spontaneous emphysema and FGF23 expression in lung and serum. FGF23, HBP activation, and inflammatory and oxidative stress markers were also analysed from human bronchial epithelial cells (HBECs) and mouse tracheal epithelial cells (MTECs) at the air liquid interface.

Summary of results KI^{-/-} mice show emphysematous lung changes and elevated FGF23 serum levels compared to WT mice. Additionally, FGF23 expression was upregulated in lung tissue from KI^{-/-} vs WT mice, and immunohistochemical staining of FGF23 was increased in the airway epithelium. Stimulation of primary HBECs or MTECs with FGF23 led to increased HBP activation, determined by OGT/O-linked N-Acetyl-Glucosamine (O-GlcNAc) assessment, as well as oxidative stress and inflammation. Conversely, inhibition of FGF23 signalling or OGT/O-GlcNAc reversed these pathological effects.

Conclusions Collectively, these data suggest that FGF23 is increased in the serum and airway epithelium of KI^{-/-} mice and is associated with emphysema when compared to WT. Furthermore, dysregulation of the FGF23/KI axis leads to increased oxidative stress and inflammation that is mediated by activation of the HBP and O-GlcNAc changes in epithelial cells. These findings are novel and link the FGF23/KI axis and glycosylation as mediators of inflammation and oxidative stress in disease pathology.

595 PLASMA PROLINE-GLYCINE-PROLINE AND COPD EXACERBATION RISK IN CHRONIC AZITHROMYCIN USE

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10.1136/jim-2017-000697.595

Purpose of study Acute exacerbations of COPD (AECOPD) contribute to disease progression. Proline-glycine-proline (PGP) and its acetylated form (AcPGP) are collagen breakdown products involved in neutrophilic inflammation seen in COPD. We have previously shown that sputum PGP is increased in AECOPD and that daily azithromycin use for 12 months was associated with reduced sputum PGP. However, it is unknown if these findings are reflected in the plasma. Therefore, we aimed to identify if daily azithromycin use affected plasma PGP/AcPGP and if these levels correlated with exacerbation frequency.

Methods used We used solid phase extraction on plasma collected at baseline and at 12 months from randomly selected MACRO trial participants, matched 1:1 by treatment allocation (azithromycin/placebo). PGP/AcPGP were measured by tandem mass spectrometry. Regression models were used to measure associations with azithromycin use and exacerbations.

Summary of results The 80 participants analysed were 66±7 years old, 60% male, 95% white, had a 58±35 pack-year smoking history, FEV₁40%±15%, and AcPGP 0.59±0.32 ng/ml. There were no baseline differences in characteristics or AcPGP levels based on treatment allocation. Within-subject AcPGP was not significantly decreased by azithromycin at 12 months and was not different compared to placebo at study end (0.61±0.31 vs 0.60±0.25 ng/ml, p=0.964). However, change in AcPGP between 1 year and baseline was associated with an increased exacerbation frequency when adjusted for FEV₁ and treatment allocation (table 1).

Conclusions While there was no direct association between daily azithromycin use and plasma AcPGP, there was a significant association between AcPGP and exacerbation frequency.

Abstract 595 Table 1 Plasma AcPGP and exacerbation frequency

	Unadjusted		Adjusted	
	IRR (95% CI)	P-value	IRR (95% CI)	P-value
AcPGP change	1.94 (1.10–3.41)	0.022	1.85 (1.06–3.25)	0.032
FEV1, percent predicted	0.98 (0.97–0.99)	0.003	0.98 (0.97–0.99)	0.005
Azithromycin use	1.12 (0.81–1.55)	0.505	1.04 (0.75–1.45)	0.803

IRR, incident rate ratio; CI, confidence interval; AcPGP, acetylated proline-glycine-proline; FEV1, forced expiratory volume in one second

596 TH17 CYTOKINE PRODUCTION INDUCED BY ALCOHOL EXPOSURE CONTRIBUTES TO MYOFIBROBLAST DEVELOPMENT

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10.1136/jim-2017-000697.596

Purpose of study The lung is a complex organ and following an injury multiple cell types are involved in tissue repair. We previously showed that alcohol induces TGFβ1 and primes the lung for fibroproliferative disrepair following acute lung injury. We and others have shown that TGFβ1 can induce a pro-fibrotic phenotype in a variety of cells including lung fibroblasts and CD4 T-cells. Further, cytokine secretion by adaptive immune cells can influence fibroblast phenotype. IL-17 and IL-22 secreted by Th17 cells have been shown to influence tissue remodelling by contributing to myofibroblast development in liver fibrosis. Accordingly, we hypothesised that alcohol-induced TGFβ1 promotes Th17 development and that IL-17 and IL-22 secreted by these cells lead to pro-fibrotic lung fibroblasts by increasing the Thy-1 negative cell population.

Methods used C57Bl/6J mice were fed standard chow +alcohol in drinking water (20% v/v) for 8 weeks. CD4 cells were harvested and stimulated *ex vivo* and assessed for IL-17 and IL-22 secretion. To assess the effects of IL-17, fibroblasts were treated with IL-17 *in vitro* and assessed for Thy-1, α-SMA, and RORγt expression.

Summary of results Alcohol exposure induced the Th17 CD4 phenotype as demonstrated by a significant induction of IL-17 and IL-22 expression. We further showed an increased trend toward RORγt gene expression. Further, treatment of fibroblasts with IL-17 significantly attenuated Thy-1 protein expression but had no effect on α-SMA expression.

Conclusions Chronic alcohol exposure polarises CD4 T cells toward the Th17 phenotype, possibly through the induction of RORγt. A key cytokine produced by Th17 cells, IL-17, attenuates fibroblast Thy-1 expression leading to a pro-fibrotic phenotype. However, direct exposure to IL-17 does not fully induce fibroblast-to-myofibroblast transdifferentiation, suggesting other cytokines and growth factors are necessary for this transformation. Taken together, our results suggest that Th17 signalling may play an indirect role in aberrant tissue remodelling in the alcoholic lung. The mechanism by which IL-17 affects fibroblast phenotype and the factors it interacts with to drive myofibroblast development warrant further investigation since it has the potential to be a future therapeutic target in lung fibrosis.

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HDAC8 INHIBITION AMELIORATES PULMONARY FIBROSIS

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10.1136/jim-2017-000697.597

Purpose of study Idiopathic pulmonary fibrosis (IPF) is a deadly lung disease. Histone deacetylase 8 (HDAC8) associates with α -smooth muscle actin (α -SMA) and regulates cell contractility in vascular smooth muscle cells. This study investigates a role for HDAC8 in pulmonary fibrosis, with a particular focus on FMD (fibroblast-myofibroblast differentiation; a key event in the pathogenesis of IPF).

Methods used HDAC8 expression in IPF lung tissue was assessed using immunoblots. Localization of α -SMA and HDAC8 in TGF- β 1-treated normal human lung fibroblasts (NHLFs) was assessed using immunofluorescent staining. To determine whether HDAC8 regulates TGF- β 1-induced contraction, NHLFs were cultured in collagen gel, with or without TGF- β 1 $\pm$ NCC170 (an HDAC8 selective inhibitor). To assess whether HDAC8 inhibition represses FMD, NHLFs were treated with HDAC8 siRNA or NCC-170 $\pm$ TGF- β 1; protein and mRNA expression were assessed using immunoblots and qRT-PCR. Chromatin immunoprecipitation (ChIP)-PCR was performed using an antibody against H3K27ac (acetylated H3K27; a known HDAC8 substrate and a marker for active enhancers) on NHLFs treated with or without TGF- β 1 $\pm$ NCC170. To investigate the effects of HDAC8 inhibition in pulmonary fibrosis *in vivo*, mice were treated with bleomycin $\pm$ NCC170, and lung collagen expression was measured using qRT-PCR, and immunoblots.

Summary of results In IPF lungs, HDAC8 expression was increased and correlated with the disease severity as measured by forced vital capacity. HDAC8 associated with α -SMA in TGF- β 1-treated NHLFs. Inhibition of HDAC8 repressed TGF- β 1-induced fibroblast contraction and α -SMA protein expression. HDAC8 inhibition also repressed TGF- β 1-induced mRNA/protein expression of CTGF and PAI-1, and increased PPAR- γ mRNA/protein expression. ChIP-PCR suggested that TGF- β 1-induced loss of H3K27ac at PPAR- γ gene enhancer was ameliorated by HDAC8 inhibition. NCC170 treatment significantly decreased type-1 collagen expression in bleomycin-treated mouse lungs.

Conclusions HDAC8 expression is altered during lung fibrogenesis. HDAC8 inhibition represses some features of TGF- β 1-induced FMD, and increases PPAR- γ mRNA transcription by increasing H3K27 acetylation at enhancer region. The data that an HDAC8 inhibitor ameliorates bleomycin-induced pulmonary fibrosis in mice suggest a therapeutic potential for HDAC8 inhibitors to treat IPF and possibly other fibrotic lung diseases.

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O-GLCNAC TRANSFERASE REGULATES GLUCOSE UTILISATION AND SPROUTING ANGIOGENESIS IN PULMONARY ARTERIAL HYPERTENSION

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10.1136/jim-2017-000697.598

Purpose of study We recently published that the serine/threonine hydroxyl-linked N-Acetylglucosamine (O-GlcNAc) transferase (OGT) drives pulmonary arterial smooth muscle cell (PASMC) proliferation and associates with idiopathic

pulmonary arterial hypertension (IPAH) clinical worsening. OGT, a known nutrient sensor, is involved in cell cycle/proliferation and metabolism. Balance of the OGT/O-GlcNAc axis is required for proper cell function and an imbalance can impact disease progression.

Methods used Human IPAH and control PASMCs were subjected to bioenergetic analyses with and without OGT inhibition. Several metabolic pathway intermediates were also examined by LC/MS/MS after knockdown of OGT in PASMCs. Finally, PASMCs and PAECs (pulmonary arterial endothelial cells) from control and PAH patients were subjected to spheroid co-culture and vascular sprouting was assessed.

Summary of results Glycolytic capacity and reserve rates were increased in IPAH PASMCs compared to controls, while oxygen consumption rates (OCR) were reduced in IPAH. Upon inhibition of OGT, glycolytic capacity and reserve rates as well as OCR in IPAH PASMCs were reduced similar to control PASMCs levels. Interestingly, metabolomics analysis showed that key metabolic intermediates (i.e., lactate production) trended in a similar manner to the bioenergetics data. Furthermore, assessment of vascular sprouting from IPAH and control PAEC/PASMC spheroid co-cultures showed increased sprouting from IPAH spheroids compared to controls. The increased vascularisation was blocked by inhibition of OGT.

Conclusions Our data demonstrate that regulation of OGT lead to changes in glucose utilisation and mitochondrial oxygen consumption rates in IPAH PASMCs. These metabolic alterations, which are regulated by the OGT/O-GlcNAc axis, may result in augmentation of angiogenesis and vascular sprouting in IPAH. Collectively, these data suggest that the OGT/O-GlcNAc axis is involved in metabolic and angiogenic dysregulation in IPAH, and may be a therapeutic target to regulate these dysfunctional processes in the IPAH lung vasculature.

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HIV-1 ENVELOPE PROTEIN GP120 AUGMENTS MARKERS OF MYOFIBROBLASTIC DIFFERENTIATION IN MOUSE LUNG FIBROBLASTS

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10.1136/jim-2017-000697.599

Purpose of study Individuals living with HIV have ~2 fold risk of developing pulmonary fibrosis; however, the mechanism(s) by which HIV promotes pulmonary fibrosis is not yet determined. HIV gains cell entry by binding of the envelope protein gp120 to the host cell surface receptors CD4 and CXCR4 or CCR5. Activation of CXCR4 by its natural ligand SDF-1 induces ERK and PI3K/Akt signalling pathways. ERK and PI3K/Akt pathway activation can also be mediated by TGF β 1, and promotes fibroblast to myofibroblast transdifferentiation, a key step in the development of pulmonary fibrosis. Finally, gp120 increases α -smooth muscle actin (α -SMA), a marker of myofibroblastic differentiation, in the human hepatic stellate cell via ERK signalling; however, to date it is unknown if gp120 has any pro-fibrotic effects in the lung. With this background, we hypothesised that gp120 induces murine lung fibroblast-to-myofibroblastic transdifferentiation.

Methods used Lungs from 4 month-old wildtype and HIV-1 transgenic mice (both in C57BL/6 background) were analysed for α -SMA protein expression as a marker of fibroblast-to-

myofibroblastic transdifferentiation. In parallel, mouse primary lung fibroblasts were cultured $\pm$ gp120 (10 ng/mL) for 72 hours and we then quantified gene and protein expression of α -SMA and fibronectin extra domain A (FnEDA; another marker of fibroblast-to-myofibroblastic transdifferentiation).

Summary of results There was a trend toward increased α -SMA protein expression in the lungs of HIV-1 transgenic mice, and gp120 treatment increased α -SMA gene and protein expression with a trend toward increased FnEDA gene and protein expression in the primary lung fibroblasts.

Conclusions HIV-1 transgene expression appears to increase α -SMA protein expression in the lung. In parallel, direct exposure to gp120 was associated with increased gene and protein expression of markers of myofibroblastic transdifferentiation in primary lung fibroblasts. These are novel insights that may help define the mechanisms by which chronic HIV infection promotes pulmonary fibrosis, and additional studies are underway to elucidate the mechanism(s) by which gp120 mediates lung fibroblast differentiation.

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PSEUDOMONAS AERUGINOSA QUORUM SENSING MOLECULE-INDUCED MITOCHONDRIAL DAMAGE, OXIDATIVE STRESS AND EPITHELIAL BARRIER DYSFUNCTION IS RESCUED BY PHARMACOLOGIC ACTIVATION OF PPAR γ COACTIVATOR 1-ALPHA (PGC1- α)

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10.1136/jim-2017-000697.600

Purpose of study *P. aeruginosa* is a significant health threat responsible for recalcitrant infections. The pathogenicity of *P. aeruginosa* is dependent on quorum sensing (QS), an inter-bacterial communication system critical for virulence. QS molecules, such as N-3-oxododecanoyl homoserine lactone (3O-C12-HSL) also modulate host biology. We have previously demonstrated that 3O-C12-HSL disrupts bronchial epithelial cell mitochondrial bioenergetics and attenuates expression of PGC1- α , a master regulator of mitochondrial biogenesis, antioxidant defense, and cellular respiration. The purpose of this study was to further characterise the mitochondrial damage and epithelial barrier dysfunction induced by 3O-C12-HSL and to determine if pharmacologic activation of PGC1- α could restore barrier integrity.

Methods used BEAS-2B bronchial epithelial cells were treated for 6 hours with 100 μ M 3O-C12-HSL. Mitochondrial morphology was analysed using electron microscopy. Reactive oxygen species (ROS) were detected with MitoSOX Red using flow cytometry. Mitochondrial DNA (mtDNA) integrity was assessed as the ratio of a 79 bp mtDNA fragment to a 230 bp mtDNA fragment. Calu-3 cell monolayers grown on transwell inserts were pretreated with 50 μ M metformin or 20 μ M resveratrol for 24 hours prior to 3O-C12-HSL treatment, and transepithelial electrical resistance (TER) was serially measured.

Summary of results Treatment with 3O-C12-HSL decreased mitochondrial number, area, and length/width ratio. 3O-C12-HSL also increased ROS and mtDNA damage and decreased TER. Pretreatment with metformin or resveratrol attenuated reductions in TER at 24 and 48 hours as compared to cells treated with 3O-C12-HSL alone.

Conclusions The *P. aeruginosa* QS molecule, 3O-C12-HSL alters mitochondrial morphology, induces ROS production, decreases mtDNA integrity, and disrupts epithelial barrier function in bronchial cells. Pre-treatment with agents that induce PGC1- α activity partially restore barrier integrity. Therapies aimed at rescuing PGC1- α function may provide a complementary approach in the treatment of *P. aeruginosa* infection.

Renal, electrolyte and hypertension I

Concurrent session

2:00 PM

Friday, February 23, 2018

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GUT MICROBIOTA BIODIVERSITY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ADVANCED CHRONIC KIDNEY DISEASE

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10.1136/jim-2017-000697.601

Purpose of study Type 2 diabetes mellitus (T2DM) is the leading cause of chronic kidney disease (CKD) in the United States and linked to gut microbiome imbalance. The aim of our research was to evaluate the imbalance of gut microbiome composition in T2DM-CKD patients and the impact of impaired gut permeability on elevated levels lipopolysaccharide (LPS) in blood and chronic inflammation.

Methods used Forty adult (18 years or older) subjects, 20 healthy subjects (HS) and 20 T2DM-CKD patients with CKD 4 and 5 not in dialysis, were recruited from the outpatient clinic. The healthy subjects were referred by primary care physicians and were not on any medications and had no significant medical problems. The T2DM-CKD patients with eMERGE phenotype definition for diabetes and for CKD, the EPI GFR <30 ml/min/1.72 m². The composition of gut microbiota was analysed by amplification of V3-V4 regions of the 16S ribosomal RNA genes and DNA sequencing. The serum biomarkers LPS, zonulin (Zo) – a gut permeability marker, and serum inflammatory (IL-6, TNF α and CRP) and endothelial dysfunction (ET-1) biomarkers were assayed by ELISA.

Summary of results The dominant phyla in both groups were Bacteroidetes and Firmicutes. At the level of phyla there were no significant changes in the composition of gut microbiota between the patient and HS groups. Significant differences were observed in the abundance of LPS producers of four bacterial families (Micrococcaceae, Clostridiaceae, Enterobacteriaceae and Prevotellaceae). A positive correlation was observed between elevated levels of serum LPS and Zo. LPS also showed positive correlation with studied inflammatory biomarkers in T2DM-CKD patients.

Conclusions The study showed for the first time, the gut microbiota diversity in patients with T2DM-CKD. The significantly higher abundance of LPS producing bacteria and the increased gut permeability, substantially impact levels of chronic inflammation, which is known to play a role in CKD progression and cardio-vascular health.

602 LITERACY LEVEL, COGNITIVE FUNCTION, AND CLINICAL OUTCOMES IN KIDNEY TRANSPLANT PATIENTS

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10.1136/jim-2017-000697.602

Purpose of study Kidney transplantation (KT) is a precious resource requiring lifelong self-care and management to prevent poor clinical outcomes. Limited literacy has been associated with medication non-adherence in KT recipients, and mild cognitive impairment has been related with lower treatment knowledge. This study aims to assess kidney transplant recipients' literacy and cognitive function levels as risk factors for post-transplant complications.

Methods used Personal interviews were conducted utilising the Rapid Estimate of Adult Literacy in Medicine-Revised test and the Montreal Cognitive Assessment with 100 adult KT recipients from May 2017 to July 2017 at the Augusta University Transplant Centre in Augusta, GA. Clinical outcomes were extracted from EMR. All analyses were performed using SAS University Edition (Cary, NC).

Summary of results Two-fifths (41%) of the participants had limited literacy, and two-thirds (67%) of the participants had mild cognitive impairment. Limited literacy and mild cognitive impairment were both significantly associated with race, education, and unemployment. Limited literacy was associated with having a deceased donor, more than one hospitalisation due to renal complications over 5 years, and more than one infection over 4 years. Mild cognitive impairment was associated with older age, number of medications, and having two or more total urinary tract infections since KT (all $p \leq 0.05$). Those who had limited literacy had eight times the odds of having more than one infection over 4 years than those who had adequate literacy (OR 8.331, 95% CI: 2.13 to 32.54), $p=0.002$, after adjusting for cognitive impairment, sex, race, age, education, employment, comorbidities, and medications.

Conclusions Based on the adjusted logistic regression model, there was a large effect of literacy level on the number of infections over 4 years that was positive and significant. The findings suggest that limited literacy and mild cognitive impairment have a long-term impact on post-operative medical complications in KT recipients. Identification of literacy and cognitive levels in patients early in the transplantation process could help physicians intervene with at-risk patients to ensure more successful clinical outcomes.

603 CRISPR/CAS9-MEDIATED KNOCKOUT OF SODIUM DICARBOXYLATE COTRANSPORTER 1 IN A PROXIMAL TUBULE CELL LINE

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10.1136/jim-2017-000697.603

Purpose of study Renal citrate excretion depends on the proximal tubule reabsorption of citrate via the dicarboxylate transporter NaDC1. Urinary citrate is the most important endogenous inhibitor of calcium stone formation by complexation of Ca^{2+} ions. Here we demonstrate CRISPR-Cas9 gene-editing knockdown of NaDC1 resulting in the first established proximal tubule NaDC1^{-/-} OK cell line.

Methods used For gRNA/Cas9 based strategy we selected three different gRNAs target sequences consisting of G(N)19NGG

near the desired target sites. The gRNA targeted Cas9 machinery immediately downstream of the NaDC1 start codon. CRISPR mediated knockdown was achieved by cotransfecting OK cells in the presence of turbofectin. Post-transfected GFP sorted OK NaDC1^{-/-} single cell clones were grown in the presence of puromycin and expanded for validation studies. OK NaDC1^{-/-} cell line characterisation by qPCR yielded 80% and 62% lower mRNA for NaDC1. These results indicate that the genomic edit may interfere with either expression or stability of the edited transcripts.

Summary of results Western analysis determined no detectable NaDC1 protein expression in OK NaDC1^{-/-} in contrast to OK cell line.

PCR was used to confirm that the genome of OK cells was edited. By designing primers for genomic PCR, one primer outside of the homologous arm region in donor DNA and one primer in the functional cassette (PKG-Puro), we obtained PCR product at the size of 1052 bp as expected.

¹⁴C labelled citrate, succinate, and α -ketoglutarate were used to measure transport in both OK and OK NaDC1^{-/-} cells. Despite the absence of NaDC1, transport of each of these dicarboxylates continued, essentially unchanged, with the exception that calcium sensitivity varied with dicarboxylate.

Conclusions Using CRISPR-Cas9 we successfully achieved 100% knockdown of NaDC1 in the highly studied OK proximal tubule cell line. Thus NaDC1 does not account for much of the dicarboxylate transport previously determined in the OK cell line.

604 GENOMIC OCCUPANCY OF TRANSCRIPTION FACTOR P63 IN THE DEVELOPING URETERIC BUD TIP CELLS

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10.1136/jim-2017-000697.604

Purpose of study P63 is a member of the p53 family of transcription factors. Previous studies showed that p63 is spatially restricted to ureteric bud tip cells (UBTC) in humans and mice, and that UBTC-p63⁺ cells give rise to cortical intercalated cells during kidney morphogenesis. However, the regulatory mechanism remains unclear. This study aims to identify the putative downstream transcriptional targets of p63 during the ureteric bud branching morphogenesis.

Methods used Chromatin Immunoprecipitation followed by the next generation sequencing (ChIP-Seq) was utilised to reveal the distribution of p63 genomic binding loci in mouse kidneys (i.e., p63-target genes).

Summary of results We identified 5625 peaks ($p\text{-value} < 10^{-5}$), with which 4600 genes were found to be associated. The distribution of peaks is concentrated around the transcription start sites and the proximal promoter regions. There also is a tendency of positive correlation between peak value and both CG% and number of CpG islands, highlighting the p63 binding in epigenetic regulatory domains. In addition to a putative p63-binding motif identified by Genomatix, the functional analysis (IPA) resulted in the Top Networks from the p63 binding sequences, which involves cellular organisation, inter-cellular signalling, cell fate and gene expression. Network analysis revealed 105 functionally inter-connected genes involved in cellular morphology, cellular movement, cell-to-cell signalling and interaction.

Conclusions Our ChIP-seq results indicate that p63 targets key developmental networks responsible for the differentiation and functional patterning of UBTC. Our findings may have important implications in regenerative renal medicine.

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POTENTIAL COST SAVING OF A COMPREHENSIVE DISEASE MANAGEMENT PROGRAM FOR RELEASED INMATES ON HEMODIALYSIS

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10.1136/jim-2017-000697.605

Purpose of study Upon reentry into society (reentry), newly released inmates with end stage renal disease (ESRD) face significant barriers in the continuation of hemodialysis (HD) due to the lack of Medicare coverage, ineffective navigation of the health care system, and the general lack of a comprehensive disease management program (CDMP). HD may be planned (outpatient, center-based) or unplanned (emergency department (ED) – based). The specific goal of this performance improvement project was to focus on the cost saving aspect of the CDMP when inmates receive planned rather than unplanned hemodialysis upon reentry into society.

Methods used The records of ESRD patients at the Augusta State Medical Prison (ASMP) for 2014–2016 were reviewed for demographics and anticipated reentry date (ASMP provides lodging and dialysis services to all Georgia prisoners with ESRD). In addition, reentry protocols, and costs of center-based and ED-based dialysis treatment sessions were documented.

Summary of results In June 2016, there were 48 patients of mean $\pm$ SD age of 48.8 ± 11.3 years with a mean release date of 2025 ± 8 years on HD at ASMP. From 2014–2016, the ASMP discharged 73/180 (41%) patients (mean $\sim$ 24/year, range: 20–29) from prison. These rates are comparable to the 2015 data from 4 state prison units outside of GA (133 patients, 42% discharge rate). The estimated cost of planned HD is \$89,000/year/person. Medicare takes 12 weeks to be approved, necessitating 36 ED dialysis sessions (\$25,000/treatment) for an estimated cost of \$900,000/patient prior to approval. As a result, it is estimated that over \$21 million could be saved annually if 24 reentry inmates were managed by an effective CDMP.

Conclusions The findings support the need to develop an effective CDMP for reentry inmates receiving HD. A first step is to initiate the Medicare application process in the six months prior to the reentry date.

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RISK FACTORS FOR MORTALITY IN PATIENTS WITH SCHIZOPHRENIA AND END-STAGE RENAL DISEASE

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10.1136/jim-2017-000697.606

Purpose of study End-stage renal disease (ESRD) patients with schizophrenia in the US show higher mortality rates than their non-schizophrenic counterparts. The specific risk factors for this observed increase in mortality remain unclear. To address this problem, we queried the United States Renal Data System

(USRDS) and assessed mortality and relevant comorbidities in ESRD schizophrenic patients.

Methods used Incident dialysis patients from 2005–2010 were investigated. Schizophrenia was defined using ICD-9 codes as disorganised (295.1), catatonic type (295.2), paranoid type (295.3), schizophreniform (295.4), latent (295.5), and schizoaffective (295.7). Mortality, demographic variables, and relevant clinical diagnoses were extracted from the CMS Form-2728, physician/supplier, or hospital claims using ICD-9 codes. To examine the association of different diagnoses and mortality, Cox proportional hazards (CPH) modelling was used. The adjusted HR (aHR) for schizophrenia and other demographic and clinical diagnostic risk factors were determined.

Summary of results 2451 schizophrenic patients were identified from a total population of 265,119, and had a mean $\pm$ SD age of 52 ± 9 years, 50% white, and 47% black. In the final CPH model, patients showed a significantly increased aHR for death with age >35 (1.48 for 36–50 years, 1.87 for 51–65 years), catheter access vs AVF (1.34), and heart failure (1.17). Patients showed a significantly decreased aHR with hypertension (0.33), suicidal ideation (0.72), drug dependence (0.84), ischaemic cardiovascular (CV) disease (0.86), and non-compliance with treatment (0.77).

Conclusions Among ESRD schizophrenic patients, older age, catheter access, and heart failure are associated with an increased risk for death. Suicidal ideation, drug dependence, and non-compliance with treatment are associated with a decreased risk for death. We speculate that the above commonly warrant hospitalisation and an escalation of care and follow-up, thus contributing to prolonged survival. These data suggest that schizophrenic dialysis patients suffer from common risk factors for mortality, but some also have an unexpected survival advantage by virtue other factors triggering more intense monitoring and follow-up.

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OCTREOTIDE: A SOLUTION FOR EXCESS PERCUTANEOUS BILIARY CHOLERESIS

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10.1136/jim-2017-000697.607

Case summary A 95 year-old African-American female with past medical history of pancreatic head mass diagnosed 2015 with percutaneous biliary drain placement April 2017, diabetes mellitus and breast cancer presented with lethargy and dehydration. The patient had frequent admissions for dehydration and hyponatremia related to high biliary drain output after initial placement. She complained of one day of fatigue, weakness and leakage around her biliary tube. Physical signs of hypovolemia were present with dry oral mucosa and skin tenting. Initial labs were significant for Na=125 mEq/L, HCO₃=17 mEq/L, anion gap=15 and serum creatinine=1.39 mg/dL (baseline 0.7). Urine chemistry revealed urine creatinine=136.6 mg/dL, urine Na=10 mEq/L, urine K=30.3 mEq/L, and urine Cl=10 mEq/L. Interventional radiology was consulted for biliary tube exchange, which resolved surrounding leakage. Intake and output measurements showed prolific bile output of 1.975 litres during first day of admission and greater than 1.5 litres thereafter. Acute kidney injury and hypovolemic hyponatremia were initially managed with IV normal saline at 100 cc/hour, HCO₃ losses with oral NaHCO₃ 650 mg tid. Continued heavy biliary output made

sodium and bicarbonate losses challenging to match. Gastroenterology was consulted for biliary diversion, but given her age and frailty were concerned about risk of surgical intervention. Octreotide 50 mcg bid was administered subcutaneously in an attempt to reduce biliary output. After administration bile output reduced to 275 mL.

Discussion Our patient presented with high biliary output from a percutaneous drain and comorbidities precluding biliary diversion. Resultant hyponatremia, pre-renal azotemia ($\text{FeNa}=0.08\%$), and bicarbonate losses (urine anion gap= -30) ensued due to bile loss. Per literature, bile $\text{Na}=140$ meq/L, bile $\text{HCO}_3=40$ meq/L, thus external cholerisis contributes significantly to hyponatremia and acidemia. Octreotide inhibits bile secretion and has useful cholestatic properties. It has off-label uses in refractory diarrhoea, post-gastrectomy dumping syndrome, bowel obstruction, and as in this case, has clinical utility in percutaneous biliary cholerisis not amenable to surgery.

Conclusions Octreotide may be a viable salvage therapy for high biliary output not amenable to surgery in select patients.

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RISK FACTORS FOR HUMAN PAPILLOMAVIRUS-ASSOCIATED MALIGNANCIES IN WOMEN WITH END-STAGE RENAL DISEASE

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10.1136/jim-2017-000697.608

Purpose of study Human papilloma virus (HPV) is the most common sexually transmitted infection in the U.S. and is a leading cause of oropharyngeal, anal, and cervical cancer. End stage renal disease (ESRD) is linked to higher risk of developing HPV-associated cancers, most frequently cervical. These cancers may be asymptomatic prior to development of advanced disease. Defining risk factors for these malignancies in women with ESRD may encourage earlier cancer detection, which is associated with better prognosis.

Methods used This retrospective cohort study examined demographic and clinical risk factors for HPV-related cancers, grouped into cervical, head/neck, and anal/rectal cancer. All incident ESRD female patients from 2005–2010 in the U.S. Renal Data System were queried using ICD-9 codes. A 5% random sample of subjects without HPV-related cancer was used for statistical analysis. Generalised linear models were used to calculate the adjusted relative risk (aRR) for each cancer type.

Summary of results In the study population ($n=224,023$), we identified 1032 subjects with an HPV-associated cancer diagnosis. Adding the 5% control sample, the total sample size was 11 457. Major risk factors for cervical cancer included HIV ($\text{aRR}=2.65$, 95% confidence interval (CI: 1.72 to 4.10)), herpes simplex virus ($\text{aRR}=2.58$, CI: 1.38 to 4.81), catheter access type compared to AVF (arteriovenous fistula) for dialysis ($\text{aRR}=1.87$, CI: 1.33 to 2.61), and tobacco use ($\text{aRR}=1.84$, CI: 1.48 to 2.29). Notable risk factors for anal/rectal cancer included ulcerative colitis ($\text{aRR}=5.11$, CI: 2.07 to 12.61), Crohn's disease ($\text{aRR}=3.26$, CI: 1.42 to 7.45), and tobacco use ($\text{aRR}=1.85$, CI: 1.38 to 2.48). Risk factors for

head/neck cancers included alcohol use ($\text{aRR}=9.09$, CI: 4.89 to 16.91), organ transplant ($\text{aRR}=2.74$, CI: 1.37 to 5.49), and tobacco use ($\text{aRR}=2.42$, CI: 1.56 to 3.74).

Conclusions HPV-associated cancers may be asymptomatic; thus, early detection is unlikely without intentional screening. This study in women on dialysis reveals tobacco use, HIV, herpes simplex, alcohol use, inflammatory bowel disease and transplant history to be associated with increased risk of these malignancies. These comorbidities may indicate the need for closer monitoring to prevent HPV-associated cancer progression.

Cardiovascular II

10:30 AM

Saturday February 24, 2018

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TAKOTSUBO CARDIOMYOPATHY IN SETTING OF ACUTE CORONARY SYNDROME

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10.1136/jim-2017-000697.609

Background Takotsubo cardiomyopathy is usually a diagnosis of exclusion with angiographically normal coronary arteries. Stress induced cardiomyopathy with concomitant acute coronary syndrome (ACS) is uncommon.

Case 57 years old male with history of hypertension presented with complaint of atypical chest pain after argument with his landlord. Nuclear stress test one month prior to presentation showed no inducible ischemia with preserved ejection fraction. In ED, his Troponin I was 0.34 initially and trended up to 0.60. ECG did not show any ischaemic changes and he was admitted to coronary care unit for Non ST elevation myocardial infarction (NSTEMI) treatment. His chest pain initially resolved with nitrates, however 4 hours after admission his pain acutely worsened.

A repeat ECG showed ST-segment elevation in V1-V4, AVR. Patient was taken for left heart catheterization which revealed a 90% stenosis of the mid left anterior descending artery (LAD) and 80% stenosis of the proximal diagonal branch. Left ventriculogram showed ejection fraction of 25%–30% with inferior, anterior, septal and lateral mid to distal wall hypokinesis, with hyperdynamic bases and apical ballooning. He received a drug eluting stent to LAD and diagonal branch. His troponin T peaked a 0.27 and trended down. EKG developed dynamic changes (figure). Transthoracic echocardiogram (TTE) done after re-vascularisation showed EF of 30%–35%, with same wall motion abnormalities as on Left ventriculogram. He was discharged in stable condition on aspirin, ticagrelor, atorvastatin and carvedilol. His TTE 3 months after showed complete recovery of LVEF and normal wall motion.

Conclusion Wall dysfunction in setting of myocardial injury in CAD should be limited to the region supplied by culprit artery. There may be possible additional stress induced catecholamine surge leading to a Takotsubo cardiomyopathy with concomitant ACS.