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 22, 2019

545A

IMPACT OF PORTAL PULMONARY HYPERTENSION IN THE COURSE OF HEPATORENAL ACUTE KIDNEY INJURY

¹M Rivera*, ¹J Velez, ²AE Mohammed. ¹University of Queensland, New Orleans, LA; ²Ochsner's Center for Outcomes and Health Services Research, New Orleans, LA

10.1136/jim-2018-000974.544

Purpose of study Porto-pulmonary hypertension is prevalent in cirrhotic patients. However its impact on outcomes of acute kidney injury (AKI) and cirrhosis has not been previously studied. We hypothesized that echocardiographic evidence of pulmonary hypertension affects the interplay between change in mean arterial pressure (MAP) and course of hepatorenal AKI during vasoconstrictor therapy as well as overall renal outcome.

Methods used We conducted a prospective observational study of hospitalized patients with AKI stage ≥ 2 and cirrhosis over 4 months. Daily MAP and serum creatinine (sCr) values were collected, as well as pulmonary arterial pressure (PAP) estimated by echocardiography at the time of AKI. Patients were divided into PAP tertiles: 1st ≤ 30 , 2nd 31–40, 3rd > 40 mmHg. Daily change in MAP (Δ MAP) and daily change in sCr (Δ sCr) from baseline were computed. Renal outcome chosen was need for renal replacement therapy (RRT).

Summary of results Among 52 patients, 19 (37%) were female, mean age was 56 (range 25–75). Baseline values were median MAP 76 (IQR 71–84) mmHg, median sCr 2.3 (IQR 1.7–3.7) mg/dL, median serum albumin 2.3 (IQR 1.8–3) g/dL and median total bilirubin 4.1 (IQR 1.8–27.2) mg/dL. A significant inverse correlation was found between Δ MAP and Δ sCr on the following day ($r = -0.20$, $p = 0.0003$) throughout the course of AKI. PAP was obtained in 36 patients. The correlation between Δ MAP and Δ sCr within each PAP tertile were: ≤ 30 : $r = 0.08$ ($p = 0.37$), 31–40: $r = -0.36$ ($p = 0.002$) and > 40 : $r = -0.40$ ($p = 0.0006$). Thus, as PAP increases, a negative correlation between Δ MAP and Δ sCr on the following day strengthens. Furthermore, there was a trend for an increased need for RRT within those in the highest tertile of PAP (need for RRT: 28.6%, 33%, and 70%, for the 1st, 2nd, and 3rd tertiles, respectively ($p = 0.0511$, chi-square for trend)).

Conclusions Cirrhotic patients with more severe pulmonary hypertension exhibit a significantly stronger negative correlation between Δ MAP and Δ sCr, suggesting that those with

higher PAP may display increased sensitivity to improved kidney function upon optimization of MAP with vasoconstrictors. Moreover, higher PAP is associated with greater need for RRT, adding complexity to the pathogenesis of hepatorenal AKI.

545B

EMERGENCE OF CLONAL NONTYPEABLE HAEMOPHILUS INFLUENZAE IN HIV+ BLACK MEN WHO HAVE SEX WITH MEN (MSM) IN METRO ATLANTA, 2017–18

^{1,2}LF Collins*, ^{1,2}A Tunali, ^{1,2}S Thomas, ¹Z Wiley, ^{1,2}S Satola, ^{1,2,3}M Farley. ¹Emory Univ., Atlanta, GA; ²Georgia EIP, Atlanta, GA; ³Atlanta VAMC, Atlanta, GA

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Purpose of study Nontypeable *Haemophilus influenzae* (NTHi) is genetically diverse and the most common cause of invasive Hi disease. Reported cases of invasive NTHi (iNTHi) in younger adult HIV +MSM increased in 2017–2018 in Atlanta. We characterized iNTHi isolates and compared iNTHi cases in persons living with HIV (PLWH) to HIV- adults.

Methods used Population-based surveillance for iNTHi was performed through Active Bacterial Core Surveillance. We analyzed clinical and epidemiologic data and performed pulsed-field gel electrophoresis (PFGE) for iNTHi cases aged 18–55 y from 1/1/2008–06/30/2018 in metro Atlanta. Data was stratified by HIV status and period (2008–16, 2017–18); PFGE patterns were examined for evidence of clonality.

Summary of results iNTHi incidence in PLWH remained stable from 2008–16, but significantly increased in 2017–18 ($p < 0.01$) (Figure). Compared to HIV- iNTHi cases in 2008–18 ($n = 113$), PLWH with iNTHi in 2017–18 ($n = 28$) were more likely to be male (93% vs 46%, $p < 0.01$), black (100% vs 51%, $p < 0.01$), reside in an urban county (82% vs 43%, $p < 0.01$) and develop septic arthritis (36% vs 1%, $p < 0.01$).

iNTHi isolates from PLWH in 2017–18 clustered by PFGE (96%), compared to HIV +cases in 2008–16 (44%, $p < 0.01$) and HIV- in 2008–18 (6%, $p < 0.01$). We identified 2 PFGE clusters: #1 ($n = 20$), median age 32 y, 95% PLWH [89% MSM], 95% male, 100% black, 95% diagnosed in 2017–18; and #2 ($n = 20$), median age 36 y, 80% PLWH [100% male, 83% MSM], 100% black, 44% diagnosed in 2017–18. Most PLWH with clustered iNTHi had CD4 > 200 , viral suppression, and frequent sexually transmitted infections.

Conclusions We document a significant emergence of clonal iNTHi in young, HIV +black MSM in Atlanta. Septic arthritis was common. The emergence suggests potential spread of NTHi within a social network. Further investigation is needed to determine the mode of transmission and to assess virulence of the closely related isolates.

Abstract 545B Figure 1

545C NITRIC OXIDE SYNTHASE INHIBITION STIMULATES RENIN SYNTHESIS INDEPENDENT OF CGMP IN COLLECTING DUCT CELLS

¹A Curnow*, ¹SR Gonzalez, ¹B Visniasukas, ¹SL Crabtree, ¹VR Gogulamudi, ²EE Simon, ³LD Lara Morcillo, ^{1,4}MC Prieto. ¹Tulane University-SOM, New Orleans, LA; ²Tulane University HSC, New Orleans, LA; ³Instituto de Biofísica Chagas Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; ⁴Tulane Hypertension and Renal Center of Excellence, Tulane University, New Orleans, LA

10.1136/jim-2018-000974.546

Purpose of study Nitric oxide (NO) synthase (NOS) inhibitors attenuate any stimulation of juxtaglomerular renin gene expression, regardless of the underlying challenge of the renin-angiotensin system. However, the regulation of renin in the collecting duct (CD renin) in response to NOS inhibition is unknown. We tested the hypothesis that NO inhibits renin synthesis and secretion via the NO/GC/cGMP pathway in M-1 cells.

Methods used Cultured cortical collecting duct (M-1) cells were treated with either: 1) PBS (control); 2) NO donor (NONOate, 1 mM); or 3) NOS inhibitor (L-NAME, 1 mM) to assess renin synthesis and secretion using qRT-PCR and Western blot, and ELISA in extracellular media. To elucidate the involvement of guanylyl cyclase (GC) on renin, we quantified intracellular cGMP levels in response to NONOate, as well as renin protein with concomitant treatment of NONOate and 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ), to inhibit GC. Renin immunohistochemistry in M-1 cells and kidney from eNOS-KO mice was also used.

Summary of results In M-1 cells, L-NAME increased renin transcript as compared to control (2.5 ± 0.6 vs 1.0 ± 0.1) but not NONOate (0.9 ± 0.2). These data paralleled increased renin immunoexpression in eNOS-KO mouse kidneys ($p < 0.05$). In M-1 cells, L-NAME and NONOate increased renin protein (1.0 ± 0.01 and 1.1 ± 0.1 vs 0.6 ± 0.1 au, $p < 0.05$) and its immunoexpression. Intracellular cGMP levels increased in response to NONOate (3.5 ± 0.5 vs 1.5 ± 0.2 pmol/mL; $p < 0.05$). Concomitant treatment with NONOate and ODQ increased renin protein compared to control (0.3 ± 0.04 vs 0.1 ± 0.01 au, $p < 0.05$), but not to NONOate alone. These data suggested that GC inhibition did not ameliorate this effect. No changes in renin extracellular media were found in any group.

Conclusions In M-1 cells, NO inhibition stimulates CD renin synthesis independent of cGMP. Although, NO *per se*, does not increase renin transcript, it seems to augment intracellular renin protein, possibly by inhibiting renin secretion.

545D EXAMINING THE EFFECT OF A CYCLIC PEPTIDE CXCR4 ANTAGONIST, LY2510924, IN AN ORTHOTOPIC XENOGRAFT MICE MODEL ON COLORECTAL CANCER TUMOR GROWTH AND METASTASIS

¹R Ahmad*, ¹D Levine, ²L Hellmers, ²G Maresh, ²R Moret, ²X Zhang, ²L Li, ^{2,3}D Margolin. ¹University of Queensland School of Medicine, Brisbane, Australia; ²Institution of Translational Research Ochsner, New Orleans, LA; ³The Ochsner Clinic, New Orleans, LA

10.1136/jim-2018-000974.547

Purpose of study Colorectal cancer (CRC) is a leading cause of mortality in the United States; with distant metastases, 5 year survival is 14%. Previously we found that CRC tumor-initiating cells (Co-TIC) expressing CD133 and CXCR4, support

extra-nodal metastasis (ENM) of CRC through interactions of CXCR4 with CXCL12 found on lymph node stromal cells (LNSCs). We hypothesized that blocking this interaction would prevent ENM. Our aim is to investigate the effect of a cyclic peptide CXCR4 antagonist, LY2510924 (LY), as a monotherapy or combination therapy with the chemotherapeutic drug (5FU) to test our hypothesis.

Methods used Our study utilized three luciferase-tagged human CRC cells (HCT-116, HT-29, and SW620) and one patient-derived tumor cell (CaCoPt302). These tumor cells were intrarectally injected $\pm$ LNSCs (HK) in NOD/SCID mice. LY was given subcutaneously qd for 14 days either -1 or +5 days after the cancer cells were injected into the mice. 5FU was administered intravenously qw from week 6-9 with leucovorin. Tumors, liver and lungs were harvested for bioluminescent imaging and weighing; additionally, H and E and immunohistochemistry (IHC) staining of these specimens were performed.

Summary of results HK cells significantly enhanced tumor growth and ENM in all cell lines. H and E and IHC showed that our orthotopic xenograft model recapitulated the histological structure and exhibited the characteristics of CRC. In both HCT-116 and SW620 models, while monotherapy of LY had a decrease of tumor progress similar to 5FU alone; combination therapy of LY and 5FU showed significant reduction in tumor weight and ENM in comparison to the control group. In both HT-29 and CoCaPt302 models, there was no significant difference in monotherapy or combination therapy.

Conclusions It is evident that LY therapy effects each model differently. Varying cell lines or patient tumors may have varying expression of molecule markers, which may affect their drug sensitivity. Further studies in their difference may guide us to an effective treatment for an individual patient.

545E METFORMIN INCREASES SURVIVAL IN T2DM PATIENTS WITH PANCREATIC CANCER AND LYMPHOMA

^{1,2}A Vacheron*, ^{1,2}A Wynn, ^{1,2}J Zuber, ^{1,2}S Solomon. ¹University of Tennessee Health Science Center, Memphis, TN; ²VA Medical Center Memphis, Memphis, TN

10.1136/jim-2018-000974.548

Purpose of study The biguanide drug metformin is one of the most commonly used drugs for treatment of T2DM. Diabetics are at an increased risk for cancer and metformin has been shown to possess anti-cancer properties. Previous studies using patient records have demonstrated improved outcomes in patients taking metformin suffering from prostate, colon, lung, thyroid, and esophageal cancers. Metformin's main anti-neoplastic mechanism of action is widely believed to be mediated through AMPK resulting in inhibition of mTOR, inhibition of HIF-1 alpha, and activation of p53. We investigated the overall survival of T2DM patients on metformin with pancreatic cancer and lymphoma using the Computerized Patient Record System (CPRS) at the VA Medical Center, Memphis.

Methods used Lymphoma and pancreatic cancer patients with DM2 were sorted into an experimental (metformin) group and a control (non-metformin) group. Patients were matched on baseline characteristics such as race, BMI, treatment, etc. Cancer outcomes, i.e. overall survival, metastasis, recurrences, incidence of new malignancies were recorded. Hemoglobin A1C and creatinine values were recorded and compared. Statistical analyses used included unpaired t-test and Chi-squared test.

Summary of results There was significantly greater overall long-term survival in the metformin group compared to the non-metformin group for lymphoma (5.89 vs 1.29 years, $p<0.001$) and for pancreatic cancer (0.68 vs 0.22 years, $p=0.016$). Treatment modalities in both groups, i.e. surgery, radiation, and chemotherapy were comparable.

Conclusions Metformin has a significant, positive therapeutic effect in T2DM patients with pancreatic cancer and lymphoma by increasing overall survival. The HbA1c values in both groups were comparable so greater mortality in the non-metformin group was not due to a lack of diabetic control. These results are very encouraging, and we would like to see a prospective study with metformin to confirm these results.

545F IMPACT OF THE ADULT CONGENITAL HEART DISEASE CLINIC ON PATIENT SURVIVAL IN MISSISSIPPI

S Kiparizoska*, C Richards, K Windham, F Han, WF Campbell, ME Hall, B Kogon, MR McMullan. *University of Mississippi Medical Center, Jackson, MS*

10.1136/jim-2018-000974.549

Purpose of study The University of Mississippi Medical Center (UMMC) opened Mississippi's first Adult Congenital Heart Disease (ACHD) clinic in January 2014. There is no published data assessing the rates of survival of MS ACHD patients. The aim of this work is to assess the impact of the ACHD clinic on patient survival in the last 5 years.

Methods used We retrospectively analyzed electronic health data from UMMC's ACHD patients ($n=3863$) and included the following: diagnosis name, age, sex, and race in our search from 2013–2017. Diagnosis name was further classified by anatomy complexity and an outcome of an all cause death was assessed. Death rates were calculated by dividing the total amount of all cause deaths of patients with CHD at UMMC by the total number of patients at UMMC who have a CHD diagnosis.

Summary of results Death rates of patients with a current or repaired CHD dropped from 6.6% in 2013 to 1.1% at the end of 2017. In the entire population, 60% of patients were female and 40% were male and 54% of total patients identified as white and 42% as black. There was no trends identified between death rates and age, sex, or race.

The death rate for those patients with complex or unspecified anatomy appeared to remain stable over the study period, while those with moderate anatomy appeared to increase.

Abstract 545F Figure 1

Most of the reduction in death rates appeared to occur in the simple anatomic subgroup (figure 1).

Conclusions The death rate has continued to decrease since the opening of the ACHD clinic supporting the model of specialized medical care for ACHD patients. Further longitudinal assessment is needed to determine the overall effect of this care on the aging ACHD population in MS.

545G METABOLIC CHANGES AFTER ONE YEAR OF BARIATRIC SURGERY IN OBESE HISPANIC PATIENTS

H Nuñez*, PI Altieri, A Suárez, HL Banchs. *University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico*

10.1136/jim-2018-000974.550

Purpose of study Bariatric surgery (B.S.) is a very useful method in the management of morbid obesity. The report of Clalit-Reseach Institute in Telaviv showed in a span of 4.5 years a mortality in the surgical group of patients (P) 1.3% compared to 2.3% in the non-surgical P. Our purpose is to compare the metabolic changes (M.C.) between the 2 types of B.S., sleeve (S.) and Roux-N-Y (R.).

Methods used A total of 34 P. who underwent S. and 102 P. who underwent R. were compared.

Summary of results The comorbidities were the same and the mortality 1.5%. The pre-op values in B.M.I., total cholesterol (C.), LDL, HDL and F.B.S. were the same in both groups. In the R. group a significant reduction of LDL (14%) vs. the S. group (7.62%) was observed, $p<0.0093$. The HDL was increased, R. (11.73%) in S. (23%) $p<0.9319$. The C. was reduced, R. (10.49%), S. (1.80%) $p<0.096$. The F.B.S. showed a reduction, R. (11.42%), S. (13.76%) $p<0.9916$. The B.M.I. showed a reduction in R. of (34.04%), and in S. (30.08%) $p<0.9315$. In comparison between the 2 groups, no differences were found in B.M.I., T.G., F.B.S and HDL.

Conclusions The P. with R. has greater benefits in losing weight, although B.M.I. changes were the same, but complications in R. surgery were greater. Follow up for 5 years have shown the same reduction in the metabolic parameters. Both groups showed an increase of C-reactive protein of 20%. Due to these findings we prefer S. over R. surgery. A longer follow up of more than 5 years will clarify if these changes persist longer.

545H INFLAMMATORY RESPONSE INDUCED BY NONTUBERCULOUS MYCOBACTERIA IS ASSOCIATED WITH ALTERED CELL ENERGY METABOLISM IN MACROPHAGES

¹Z Prasla*, ^{1,2}C Bedi, ^{1,2}RT Sadikot. *¹Emory University, Atlanta, GA; ²VA Hospital, Atlanta, GA*

10.1136/jim-2018-000974.551

Purpose of study The incidence of nontuberculous mycobacterial (NTM) lung disease is rising worldwide and accounts for most cases of NTM infection. *Mycobacterium avium* complex (MAI) is a well-known cause of infection in immunocompromised patients. However, pulmonary NTM infections are not limited to immunocompromised hosts, and *Mycobacterium abscessus* (MAB) is particularly difficult to treat in patients with COPD, non-CF bronchiectasis, and CF. Despite abundant

knowledge of the clinical significance of NTM, relatively little is known about host immune response to NTM infection. Our objective was to define the immune-metabolic response induced by NTM in macrophages.

Methods used We infected RAW cells (murine immortalized macrophages) and MH-S cells (murine alveolar macrophages) with clinical strains of MAI or MAB (MOI of 10, 25, or 50) for 6, 24, and 48 hours. We determined the expression of key inflammatory genes (COX-2, IL-1 β , and TNF α) that contribute to immune response to infections by using RT-qPCR to calculate their fold change relative to GAPDH. We used this infection model to perform a cell energy phenotype assay in MH-S cells infected by MAI.

Summary of results We found that in RAW cells, COX2 and TNF α were increased at 48 hours, with an increase in TNF α noted as early as 24 hours. There was no increase in IL-1 β production in RAW cells. In comparison, in MH-S cells, there was a robust increase in IL-1 β that was noted as early as 24 hours with a modest increase in TNF α seen at 24 hours. These results were confirmed with an IL-1 β ELISA assay, which showed peak concentration at 24 hours but was noted as early as 6 hours. Cell energy phenotype analysis showed that at baseline, ECAR was increased in infected MH-S cells relative to control cells.

Conclusions These data suggest that there is a difference in the immunologic phenotype of macrophage host response to NTM, which may be dependent on the type of macrophage. In MH-S cells, MAI appears to shift cells to a more glycolytic phenotype. The functional impact on bacterial killing and phagocytosis of changes in these inflammatory genes and their associated alterations in cell energy metabolism need to be further investigated to elucidate new mechanisms of host response that aid treatment of NTM infections.

546

SMOKING HISTORY AND PD-1/PDL-1 PATHWAY BLOCKADE: PREDICTING RESPONSE TO TREATMENT IN METASTATIC CANCER

¹CM Sullivan*, ²J Lu, ²J Kucharczyk, ²D Vesselinovitch, ²N Khurana, ²M Matrana. ¹LSU Health Sciences Center, New Orleans, LA; ²Ochsner Medical Center, Jefferson, LA

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Purpose of study Identifying patients who will benefit from immune-checkpoint inhibitor therapy is a challenge as proven predictive indicators remain to be elucidated. High tumor mutational burden (TMB) represents a possible biomarker for response to PD1 blockade such as in nivolumab or pembrolizumab. Genomic analyses have shown that patients with heavy smoking history are more likely to have high TMB. However smoking status alone has not been examined independently in relation to treatment response. We sought to determine whether a relationship existed between smoking history and response to treatment in metastatic non-small cell lung cancer (NSCLC), metastatic renal cell carcinoma (mRCC) and metastatic melanoma (mMelanoma).

Methods used A retrospective analysis was conducted of Ochsner Health System patients with mRCC, mMelanoma, and NSCLC receiving a minimum of two cycles of nivolumab or pembrolizumab between 12/2014 and 01/2018. Pre- and post-treatment target lesions were analyzed using RECIST criteria to calculate best response to treatment. Patient demographic information was gathered including age,

sex, smoking history, and performance status pre and post treatment. Kaplan-Meier method was used to estimate progression free survival (PFS) and overall survival (OS) outcomes.

Summary of results Heavy smokers (>10 packyears) had a higher response to immunotherapy than light (<10 years) and never smokers (p=0.0500). Heavy smokers with NSCLC treated with immuno-therapy also had significantly improved OS compared to light smokers with NSCLC (p=0.003). mRCC immuno-therapy patients with heavy smoking history showed increased PFS compared to light/never smokers (p=0.026).

Conclusions In summary, in response to PD-1 blockade heavy smokers showed improved survival compared to light and never smokers suggesting smoking history may represent a potential predictor of treatment response to PD-1 inhibitor therapy.

Legal entity responsible for the study Ochsner Medical Center and the University of Queensland, Ochsner Clinical School.

547

SMALL MOLECULE INHIBITOR SELECTIVELY REDUCES T FOLLICULAR CELLS AND ABROGATES JOINT INFLAMMATION IN A MOUSE MODEL OF RHEUMATOID ARTHRITIS

X Zhang*, N Bhatia, F Migliore, L Hellmers, G Olayemi, J Zakem, W Davis, R Quinet. Ochsner Medical Center, New Orleans, LA

10.1136/jim-2018-000974.553

Purpose of study Rheumatoid arthritis (RA) is an inflammatory autoimmune disease characterized by T cell infiltration in the joints and autoantibody production. T follicular helper (Tfh) cells are a unique subset of CD4⁺ T cells regulating antibody production in germinal center (GC). Our previous studies have shown that increased circulating Tfh cells were correlated with anti-CCP auto-antibody titer and disease activity in active RA patients, indicating that Tfh cells may play an important role in RA pathogenesis. Here we investigate the therapeutic potential of a small molecule inhibitor targeting Tfh cells (SMI-Tfh) in mice with collagen-induced arthritis (CIA).

Methods used CIA model was induced by administering chicken type II collagen in twenty-four DBA/1 mice. Arthritis progression was determined by measuring the swelling of paws weekly using caliper. Following the onset of clinical arthritis, mice were treated with SMI-Tfh (50 mg/kg). Blood, spleen, and affected paws were collected at the end of the study. Pathological changes of tissue sections were stained with H and E. Immunofluorescent histochemistry staining and flow cytometry analysis were performed to identify Tfh cells (CD4⁺CXCR5⁺ICOS⁺). IHC results were analyzed by Image-Scope and flow cytometry results were analyzed by FlowJo software.

Summary of results Mice developed arthritis between day 21–28 and reached peak on day 42 after initial immunization with type II collagen. The joints of CIA mice had increased inflammatory cells in the synovial tissues and destruction of articular cartilage in comparison with normal mice. Tfh cells (CD4⁺CXCR5⁺ICOS⁺) were observed in the blood and the GCs of mouse spleen. Mice treated with SMI-Tfh had significantly reduced paw swelling. SMI-Tfh treatment also reduced

Tfh cell infiltration in inflamed joints and in the GCs of spleen ($p<0.01$) in CIA mouse.

Conclusions The small molecule inhibitor SMI-Tfh selectively inhibits Tfh cells and abrogates activity of inflammatory arthritis in CIA mouse model. Treatment with our small molecule SMI-Tfh in CIA mice provides a potential strategy for joint protection and may be beneficial in RA patients.

Southern Society for Pediatric Research

Plenary Session

Young Investigator Award Finalists

8:00 AM

Friday, February 22, 2019

548 DOSE RESPONSES OF VITAMIN K₂ SUPPLEMENTATION ON BLOOD LIPIDS IN OVERWEIGHT CHILDREN: A RANDOMIZED PLACEBO-CONTROLLED TRIAL

L Rodriguez*, M Fain, CF Williams, R Bassali, C Davis, NK Pollock. *Medical College of Georgia, Augusta University, Augusta, GA*

10.1136/jim-2018-000974.554

Purpose of study Given that dyslipidemia predisposes children to cardiovascular disease in adulthood, it is critical to identify novel, safe, and inexpensive strategies for dyslipidemia prevention. Vitamin K₂ has been recently focused as a pivotal nutrient in improvement in lipid metabolism, possibly via increased carboxylation of matrix Gla-protein (MGP). This study determined the dose-response effects of vitamin K₂ supplementation on lipid profile and the inactive form of MGP (desphospho-uncarboxylated MGP, dp-ucMGP) in overweight children.

Methods used Twenty-seven overweight children aged 8–17 years were randomly assigned to either the control group receiving placebo ($n=9$) or the low-dose (45 mcg/d, $n=9$) or high-dose group (90 mcg/d, $n=9$) receiving vitamin K₂ for 8 weeks. At baseline and posttest, fasting blood samples were collected for assessment of triglycerides, total cholesterol, HDL-cholesterol, non-HDL-cholesterol and LDL-cholesterol, and dp-ucMGP.

Summary of results After 8 weeks, plasma dp-ucMGP concentrations decreased significantly and dose-dependently in the low-dose and high-dose vitamin K₂ groups by 10% and 32%, respectively ($p=0.03$). A dose-response benefit of vitamin K₂ supplementation was also observed for triglycerides, total cholesterol, non-HDL-cholesterol, and LDL-cholesterol as indicated by significant downward trends (all $p<0.05$). There was no dose-response effect on HDL-cholesterol. Multivariate linear regression, adjusting for age and sex, revealed that changes in triglycerides ($b=0.52$) and non-HDL cholesterol ($b=0.48$) were associated with changes in dp-ucMGP (both $p<0.04$).

Conclusions In overweight children, vitamin K₂-induced carboxylation of MGP demonstrated dose-response benefits on lipid profile. Our study provides the rationale that larger trials are needed to determine the effectiveness of vitamin K₂

supplements as an alternative non-pharmacological approach to dyslipidemia prevention and treatment in children likely to incur dyslipidemia.

549 INTERKINGDOM MICROBIAL RELATIONSHIPS IN THE HUMAN PRIMORDIAL MICROBIOME VARY BY GESTATIONAL AGE

KA Willis*, JH Purvis, CK Gomes, AJ Talati, JF Pierre. *The University of Tennessee Health Science Center, Memphis, TN*

10.1136/jim-2018-000974.555

Purpose of study Meconium was traditionally considered sterile. Following advances in molecular sequencing techniques, recent evidence suggests that bacterial communities may exist in the gut prior to birth. Here, we describe the presence of multi-kingdom microbial communities in meconium immediately following birth.

Methods used We prospectively enrolled premature (gestational age <32 weeks') very low birthweight (VLBW <1500 g) and full term (FT, gestational age 37–41 weeks') newborns and collected the initial meconium. We examined the interkingdom community structure using 16S and ITS rDNA-based amplicon sequencing.

Summary of results We enrolled 57 VLBW and 35 FT newborns. Bacteria were found in meconium of 90% of VLBW and 82% of FT samples (χ^2 $p=0.325$) and fungi in 93% of VLBW and 62% of FT samples (χ^2 $p=0.003$). The bacterial and fungal communities differed significantly between VLBW and FT (bacteria: PERMANOVA $p=0.006$, fungi: PERMANOVA $p=0.013$). Fungal communities of VLBWs were dominated by Ascomycota, including *Candida*, while FT meconium contained greater Basidiomycota and taxonomic diversity. Bacterial communities in VLBW meconium were also less diverse and contained on average a third as many taxa compared with FT.

Conclusions Human meconium contains complex interkingdom microbial communities that mature with gestational age, suggesting host-microbe interkingdom relationships may exist during pregnancy. Intriguingly, fungi are 50% more commonly observed in premature meconium than in full term neonates.

Abstract 549 Figure 1 Phylogenetic distribution of fungal taxa

550

PULMONARY FUNCTION USING NON-INVASIVE FORCED OSCILLOMETRY RESPIRATORY (PUFFOR) TESTING IN TERM NEONATES: AN OBSERVATIONAL COHORT STUDY

A Klinger*, C Travers, A Martin, A Saadoon, WT Harris, WA Carlo, N Ambalavanan.
University of Alabama at Birmingham, Birmingham, AL

10.1136/jim-2018-000974.556

Purpose of study Forced oscillometry technique (FOT) is a non-invasive method for testing respiratory mechanics. Superimposition of a gentle, oscillatory signal over spontaneous tidal breathing for a short time provides estimates of respiratory Resistance (R) and Reactance (X). The objectives were to demonstrate feasibility of FOT, determine normative data in term infants without respiratory disease, and compare to those with transient tachypnea of the newborn (TTN).

Methods used A cohort of term infants without respiratory disease and another with TTN born at the University of Alabama at Birmingham were evaluated on postnatal days 1 through 3. FOT was measured daily via a TremoFlo C-100 Airwave System™, custom fitted and calibrated with a filter and infant anesthesia face mask. R, X, and area under the reactance curve (AX) were measured at prime frequencies 7 to 41 Hz for 8 s.

Summary of results Of the enrolled 114 term infants, 78% had adequate measurements on day 1, 61% on day 2, and 58% on day 3. R and X measurements for term infants days 1 through 3 are shown in figure 1. AX was 621 cmH₂O s/L (95% CI 562 to 680) on day 1, 674 (95% CI 615 to 733) on day 2, and 719 (95% CI 643 to 794) day 3. Figure 2 shows a comparison of day 1 measurements of controls and a 12 infant cohort with TTN in which there is increased

Abstract 550 Figure 1

Abstract 550 Figure 2

resistance and decreased reactance in the TTN group. There were no statistically significant changes in measurements on day 2 and 3 between TTN and controls.

Conclusions Estimation of respiratory mechanics non-invasively in term infants is feasible using FOT but is dependent on cooperation from the infant and provider skill for adequate results. There are no statistically significant changes in R, X, and AX over the first 3 days. There are statistically significant differences in R and X between infants with TTN and controls at specific frequencies. This study provides normative data for future studies in infants with respiratory disease.

551

REDUCTION OF HYPOXIA-ISCHEMIA INDUCED EARLY BRAIN DAMAGE AND SENSORIMOTOR BEHAVIORAL DISTURBANCES BY INTRANASAL INSULIN TREATMENT IN NEONATAL RATS

C Talati*, JW Lee, S Lu, T Nielson, R Raval, V Prakash, N Ojeda, Y Pang, AJ Bhatt, L Fan.
University of Mississippi Medical Center, Ridgeland, MS

10.1136/jim-2018-000974.557

Purpose of study There is an urgent need for additional therapies to improve outcomes of infants with hypoxic-ischemic (HI) encephalopathy. Recent *in vitro* and *in vivo* animal studies and clinical investigation suggest that insulin could be a neuroprotective agent. The neuroprotective effect of insulin against HI brain injury is unexplored. We hypothesized that intranasal insulin (InInsulin) is neuroprotective against HI brain injury in neonatal rats. The objectives of this study were to examine whether InInsulin attenuated HI-induced brain injury and neurobehavioral dysfunction in neonatal rats.

Methods used On postnatal day 10 (P10), rat pups were randomly divided into four groups with equal male to female ratio: HI +Insulin; HI +Vehicle(Veh); Sham +Insulin; Sham +Veh. Pups either had HI by permanent ligation of the right carotid artery followed by 90 min of hypoxia (8% oxygen) or Sham surgery followed by room air. Immediately after HI or Sham, rat pups were given Insulin (25 µg) or an equal volume of vehicle in each nare under light anesthesia. A blinded observer performed sensorimotor neurobehavioral tests and evaluated the microscopic brain injury by estimations of brain damage following Nissl staining and Fluoro-Jade C staining at P11. Statistical analysis was performed via two-way ANOVA followed by the Student-Newman-Keuls method. The sample size was determined to find a difference of 30% between means with the power of 85% and significance of $p < 0.05$.

Summary of results HI caused ipsilateral brain damage (35.8%, $p < 0.001$, $n = 4-6$ pups) and increased Fluoro-Jade C positive cells (448,000 cells; HI +Veh vs. 0 cells; Sham+Veh; $p < 0.001$, $n = 4-6$ pups). InInsulin reduced the HI-induced ipsilateral brain damage volume (35.8% vs. 7.0%; $p < 0.001$, $n = 4-6$ pups) and the Fluoro-Jade C positive cells in the newborn brain (448,162 cells vs. 52,444 cells; $p < 0.002$, $n = 4-6$ pups). InInsulin attenuated HI-induced sensorimotor behavioral disturbances as seen in negative geotaxis, wire hanging, hind limb suspension, and righting reflex tests at P11 ($p < 0.002$, $n = 16$ pups).

Conclusions InInsulin reduced early brain injury and sensorimotor behavioral disturbances following neonatal HI. Further experiments are planned to examine sex-specific outcomes.

552

MAGNETIC RESONANCE PERFUSION IMAGING/ SPECTROSCOPY TO VISUALIZE EARLY INJURY IN A RAT MODEL OF NEONATAL HYPOXIC ISCHEMIC ENCEPHALOPATHY: SEX DIFFERENCES IN MRI/S

¹MG Melek*, ²R Towner, ¹J Kung, ²D Saunders, ²M Zalles, ¹F Bhatti. ¹OU Children's Hospital, Oklahoma City, OK; ²OMRF, Oklahoma City, OK

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Purpose of study Perinatal hypoxic ischemic encephalopathy (HIE) results in variable neurodevelopmental outcomes. Early diagnosis relies on clinical criteria and not a definite objective tool. Changes in magnetic resonance (MR) images are important for diagnosis but most findings are only detectable late after the onset of injury. We hypothesized that MR modalities, including perfusion, diffusion, and magnetic resonance spectroscopy (MRS), would detect early changes (within 6 hours) in a rat model of HIE. We also analyzed the male/female differences.

Methods used Sixteen 10-days-old Sprague Dawley rats were divided into sham and Hypoxic/Ischemic (HI) groups. Each group was further subdivided into male and female subgroups (n=4 per group). HI was induced using a modified Rice-Vanuucci model with right carotid artery ligation followed by hypoxia (8% O₂) for 45 min. MR including perfusion, diffusion, and spectroscopy was done within 6 hours of HI. Spectroscopy metabolites include Lactate, N-acetyl Aspartate (NAA), Glutamate, Creatine (Cre), Choline (Cho), Taurine (Tau), and Myoinositol (Myo-Ins), and are expressed as metabolite/Cre ratios. Percentage changes were calculated for the right (ligated) side compared to the left (control) side of each brain. Differences between sham and HI were analyzed via chi square analysis with p<0.05.

Summary of results Change in perfusion was higher in HI (104.9%) vs sham (22.1%) (p=0.02) with the change in males twice of that seen in females (p=0.03). For diffusion, change in HI (8.9%) was greater than sham (3.3%) but not statistically significant (p=0.18), with no difference between males and females. For MRS, Myo-Ins was significantly increased, while Cho and NAA were decreased in the HI group vs sham. Myo-Ins was significantly lower (50%) in females vs males, and while not significant, trended lower for Tau and Cho as well.

Conclusions Perfusion scans and MRS show early changes 6 hours after HI injury. Myo-Ins, Cho, and NAA can be used as reliable early radiologic markers for neonatal HIE. Male and female rats show a differential pattern of expression of metabolites as well as in changes in perfusion. The pathophysiology of these sex differences requires further investigation.

553

AIRWAY MICROBIAL DYSBIOSIS INDUCED NEUTROPHILIC INFLAMMATION LEADS TO BRONCHOPULMONARY DYSPLASIA-LIKE PHENOTYPE IN MICE

K Dolma*, G Rezonzew, T Jilling, N Ambalavanan, CV Lal. University of Alabama at Birmingham, Birmingham, AL

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Purpose of study Airway microbial dysbiosis and neutrophilic inflammation are associated with BPD. Our group has previously found that γ proteobacteria abundance is increased and

lactobacilli abundance is decreased in infants developing severe BPD. The mechanism by which airway microbial dysbiosis contributes to BPD is poorly understood. We hypothesized that airway microbial dysbiosis leads to neutrophilic inflammation causing BPD-like phenotype in mice.

Methods used

1. Gnotobiotic (GN; germ-free) mice and non-GN (NGN) mice were exposed to 21% O₂ versus 85% O₂ for baseline comparison
2. GN and NGN mice were monoclonized with γ proteobacteria (*E coli* 1 $\times$ 10⁶ cfu/20 ul of saline intranasally) versus saline at P3, P6 and P9 and P12 to determine the effect of γ proteobacteria monoclonization in both 21% and 85%
3. GN and NGN mice exposed to 85% O₂ + γ proteobacteria (double hit model of BPD-JCI *Insight*, 2018; PMID:29515035) were treated with a respiratory probiotic combination (total 1 $\times$ 10⁶ cfu/20 ul of saline intranasally) versus saline at P3, P6, P9 and P12 to evaluate the therapeutic potential of the respiratory probiotic combination.

Lungs were harvested for histology, protein, and RNA following pulmonary function test (PFT) at P14. Echo were done at P28. Markers of neutrophilic inflammation were tested.

Summary of results

1. GN mice in 85% O₂ showed protected lung structure (RAC) and function (PFT) compared to NGN mice in 85% O₂. NGN mice lungs in 21% vs 85% O₂ showed no baseline differences in microbial diversity and abundance based on 16S sequencing and bioinformatics
2. γ proteobacteria monoclonization in NGN and GN mice induced alveolar hypoplasia (decreased RAC), decreased function (PFT), increased neutrophilic inflammation (Ac-PGP, MPO, neutrophil counts), and evidence of pulmonary hypertension (PH) in both 21% vs 85% O₂
3. Respiratory probiotic combination treatment in the double hit BPD murine model, improved lung structure and function, decreased neutrophilic inflammation, and decreased signs of PH.

Conclusions Airway microbial dysbiosis (increased γ proteobacteria and decreased respiratory probiotic bacteria) cause neutrophilic inflammation leading to BPD in mice. Use of respiratory probiotic combination provides therapeutic benefits in murine BPD.

554

EFFECT OF BREAST MILK EXOSOMES ON POSTNATAL TRANSMISSION OF HUMAN CYTOMEGALOVIRUS

N Arora*, S Pati, B Sims, W Britt, S Boppana. University of Alabama at Birmingham, Birmingham, AL

10.1136/jim-2018-000974.560

Purpose of study Human cytomegalovirus (HCMV) is a frequent cause of congenital infection and a leading cause of sensorineural hearing loss in children. Most HCMV seropositive mothers shed CMV in breast milk (BM) (>90%), and half of the breast-fed infants will be infected, providing us a unique setting to understand virus transmission at the mucosal surface. Exosomes are small membranous nanovesicles secreted by diverse mammalian cell types. They facilitate cell-cell communication and shuttle molecular cargo from donor to a

recipient cell. Their role in augmenting HIV-1 infection was recently shown. However, exploitation of exosomes by HCMV in human BM has not been studied.

Methods used We used BM samples collected in a prospective study in which infants were monitored for HCMV infection during the 1st 6 months of life. HCMV PCR, exosome separation and analysis were done using a previously described protocol.

Summary of results Preliminary analysis shows that the peak viral load in BM of seropositive transmitting mothers was significantly higher as compared to non-transmitters ($p < 0.001$). The mean number of BM exosomes (5.10×10^8 /ml of BM) were higher in the transmitting mothers as compared to the non-transmitters (1.20×10^8 /ml of BM), when we compared 3 samples with the highest viral load from each group ($p = 0.06$).

Abstract 554 Figure 1

Conclusions Our findings reveal that seropositive transmitting mothers have a higher mean peak viral load. However, the overlap in viral load between the groups suggests other factors may play a role in viral transmission. Our preliminary analysis reveals increased number of exosomes in the breast milk of transmitting mothers. We plan to further characterize the samples from the cohort including imaging data (Electron Microscopy) to identify biomarkers of transmission and shed light on fundamental exosome characteristics.

Adolescent Medicine and Pediatrics

Concurrent Session

2:00 PM

Friday, February 22, 2019

555 LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS WITH DIAPHRAGMATIC PARALYSIS IN AN INFANT

L Thai*, O Sanchez. *University of South Alabama, Mobile, AL*

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Case report Pediatric transverse myelitis (TM) is a rare autoimmune, demyelinating disorder, which most commonly involves inflammation of the spinal cord; only about 20% of TM cases occur in children and fewer cases being longitudinally extensive transverse myelitis (LETM). This condition leads to temporary and sometimes permanent flaccid paralysis. TM is a

diagnosis of exclusion and is treated with high-dose steroids, IVIG or plasmapheresis with variable results.

4-month-old female with no significant medical history presented in acute respiratory distress. She was healthy with no associated symptoms, who suddenly became 'limp' after a nap. On initial evaluation, patient had respiratory failure, right-sided extremity paralysis, torticollis, and asymmetrical chest wall movement. She was immediately intubated but was eventually extubated and weaned to nasal cannula. C-spine and brain MRI showed moderate diffuse edema on the right side, extending from the medulla oblongata down to the cervical C6-C7 level. IVIG treatment and steroids were given due to concern of TM. Full work-up was performed to identify an etiology of her symptoms, which was overall unremarkable for an infectious or autoimmune etiology. Diaphragmatic paralysis persisted despite treatment. She could not tolerate feeds well and was not able to be wean off supplementary O2. Patient had right diaphragmatic plication which helped to improve her respiratory status as well as being able to tolerate feeds, resulting in discharge.

Discussion Pediatric transverse myelitis is rare and LETM is even rarer. Our patient is very interesting due to her age, acute onset, LETM, association with diaphragmatic paralysis, and minimal response to treatment. Although TM is a diagnosis of exclusion, it is imperative to include transverse myelitis in the differential diagnosis since early implementation of treatment appears to improve outcomes. Current treatment options have variable outcomes, but overall most show at least some improvement. Plasmapheresis has been documented to be beneficial in cases that are not highly responsive to steroids, however, due to our patient's age, the risks outweighed the benefits. There are no clear guidelines when TM is associated with diaphragmatic paralysis, therefore experts' opinions should be taken into consideration.

556 THE IMPACT OF THE RESULT OF MULTIPLEX POLYMERASE CHAIN REACTION TESTING FOR RESPIRATORY PATHOGENS ON THE LENGTH OF HOSPITAL STAY AND THE INITIATION AND DURATION OF ANTIBIOTICS IN PEDIATRIC INPATIENTS

A Bishara*, C Barton, P Windham, S Tengsupakul. *University of South Alabama, Mobile, AL*

10.1136/jim-2018-000974.562

Purpose of study To assess whether there is a difference in outcome (length of stay, antibiotic initiation, and antibiotic duration) in pediatric, non-intensive care unit (ICU) inpatients with positive viral respiratory multiplex polymerase chain reaction (mPCR) test results compared to those with negative results.

Methods used Retrospective chart review with statistical analysis comparing length of hospital stay and initiation and duration of antibiotics in pediatric, non-ICU, inpatients at University of South Alabama Children and Women's Hospital in those with a positive viral respiratory mPCR result to those with a negative result from September 1, 2016 to September 30, 2017. Of the total respiratory mPCRs obtained ($n = 664$), ICU patients were excluded ($n = 228$: 37 neonatal intensive care unit and 197 pediatric intensive care unit); those with positive bacterial pathogens were excluded ($n = 2$), and those with multiple mPCRs obtained upon same admission were excluded ($n = 7$). Antibiotic duration was measured using days

of therapy administered via intravenous, intramuscular, enteral, and/or nebulized routes.

Summary of results Of the 427 respiratory mPCR tests that met inclusion criteria, 231 were positive, and 196 were negative. Subjects with a positive viral respiratory mPCR result were found to have a significantly decreased length of stay (median of 3 vs. 4 days; $p=0.0025$) and decreased duration of antibiotics (median of 1 vs. 3 days; $p=0.0016$) compared to those with a negative result. Additionally, a significantly higher percentage of patients with a positive mPCR result were never started on antibiotics compared to those with a negative result (60% vs. 40%).

Conclusions Viral pathogens identified by mPCR can diagnose an etiology for respiratory symptoms for which antibiotic therapy is not indicated. This implies that if there is clinical suspicion for a respiratory viral illness as the primary source and cause of morbidity in a non-ICU, pediatric patient, a respiratory mPCR should be obtained since the identification of a viral respiratory pathogen has the potential to reduce antibiotic initiation, antibiotic course duration, hospital length of stay, and hospital resource expenditure.

557 REACHING CHILDREN FROM LOW-INCOME FAMILIES THROUGH A SCHOOL-BASED OBESITY PREVENTION INITIATIVE

K Head*, K Morella, S Beasley, J Key. *Medical University of South Carolina, Charleston, SC*

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Purpose of study Children in low-income families are more likely to become obese and are more difficult to reach by traditional health care means. School based obesity prevention programs that impact all children enrolled may be an effective way to intervene. However, Title 1 schools with a high percentage of children from low-income families tend to have fewer resources and parental support. Thus, Title 1 schools may be less likely to participate or may participate at a lesser level in school-based wellness programs compared to schools enrolling children from higher income families. The purpose of this study was to determine participation of Title 1 schools in the South Carolina Docs Adopt School Health Initiative® (DASHI), an evidence-based program that motivates schools to make changes in policies, environments, and systems, while competing in a wellness ‘contest’ with other schools, earning points for implementing items on the School Wellness Checklist® (SWC).

Methods used This outcome evaluation of DASHI examined Title 1 versus non-Title 1 schools in 3 comparisons:

1. participation in DASHI,
2. achievement of Wellness Awards and
3. overall SWC scores and subscores.

Data included SWC scores for the 2016–17 school year. Analysis used chi-square and ANOVA.

Summary of results 11 school districts participated in DASHI in 2016–17, with all schools in each district eligible for participation. 87 of 123 non-Title 1 schools (70%) and 100 of 126 Title 1 schools (79%) participated ($p=0.115$). Of participating schools, 74 of 87 non-Title 1 schools (85%) and 93 of 100 Title 1 schools (93%) earned Wellness Awards ($p=0.079$). Mean SWC points for Title 1 schools totaled 94.4 versus 93.8 points for non-Title 1 schools ($p=0.935$). There was no

significant difference between Title 1 and non-Title 1 subscores in the 7 subcategories of the SWC.

Conclusions DASHI is as successful in Title 1 schools enrolling students at higher risk of obesity as in non-Title 1 schools. Title 1 schools are as likely to participate in DASHI and they implement the same number of wellness changes as non-Title 1 schools enrolling students from higher income families. This indicates that school-based obesity prevention programming may be an effective method to reach at-risk children.

558 IMPACT OF SLEEP HABITS ON QUALITY OF LIFE IN OBESE CHILDREN

HE Rodriguez*, K Gray, M Pearson, J Shadlow, A Hendrix, E Hemming, M Condren, LH Ali. *OU Tulsa Health Science Campus, Tulsa, OK*

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Purpose of study Quality of life (QL) is decreased in children with obesity. The contribution of sleep habits to QL in these patients has not been thoroughly evaluated. This study hypothesized that different types of sleep habits would moderate quality of life in obese children.

Methods used This is a retrospective chart review including Body Mass Index (BMI) z-score and 6 parent-reported answers to sleep questions, as well as parent and child Pediatric QL Inventory TM scores. Data was collected from the electronic medical records for children ages 3–18 years with BMI ≥ 95 percentile for age. The sleep questionnaire allocated habits into 2 categories: Consistency in Bedtime Routine (Consistency) and Arousal-Related Pre-Bedtime Behaviors (Arousal) with higher scores indicating better sleep. Multiple regression analyses examined the effect of sleep habits on the patients’ self- and parent-reported QL.

Summary of results Forty females and 59 males with mean age of 9.82 ± 2.97 had complete data for inclusion. Participants were 58% Hispanic. Consistency in Bedtime Routines predicted higher child-reported psychosocial QL scores [$F(2, 73)=4.83$, $p<0.05$], [HEJ(1)] parent-proxy reported psychosocial QL scores [$F(2, 92)=4.50$, $p<0.05$], child reported physical QL scores [$F(2, 73)=6.22$, $p<0.01$] and parent-proxy reported physical QL [$F(2, 91)=4.95$, $p<0.01$]. Arousal-Related Pre-Bedtime Behaviors predicted higher child-reported psychosocial QL scores [$F(2, 73)=3.41$, $p<0.05$], parent-proxy reported psychosocial QL scores [$F(2, 92)=4.50$, $p<0.05$], child reported physical QL scores [$F(2, 73)=4.79$, $p<0.05$] and parent-proxy reported physical QL [$F(2, 91)=4.87$, $p<0.01$].

Conclusions Better sleep habits are associated with improved QL in obese children in both physical and psychosocial functioning. Future research targeting sleep habits for intervention may impact sleep hygiene, and consequently improve QL of obese children.

559 BRIDGING PROVIDER PERCEPTION AND DELIVERY OF TRANSITION OF CARE FROM PEDIATRIC TO ADULT MEDICINE

S Leung*, M Walgrave, S Mennito. *Medical University of South Carolina, Charleston, SC*

10.1136/jim-2018-000974.565

Purpose of study A transition of care (TOC) process from pediatric-to-adult medicine ensures adolescents receive ongoing

healthcare into young adulthood, a time for increased risk of preventable mortality and morbidity. This project explores provider perspectives on TOC for healthy adolescents, who account for 75% of pediatric patients, to complement the predominant transition research for adolescents with special health care needs.

Methods used Surveys were developed based on prior literature and piloted before dissemination. Primary care providers (physicians, social workers, nurses, clerical) from Pediatrics, Internal Medicine (IM) and Family Medicine (FM) completed surveys from April-July 2018. Questions explored perceptions of TOC, value of TOC components, and expectations for patient autonomy. Two-tailed Z-test was used to compare responses between providers from different departments.

Summary of results A total of 131 surveys were returned: 41% Pediatrics, 28% IM, and 31% FM. Participants included 79% physicians, 58% female, and 79% Caucasian. Only 37% of providers expressed being knowledgeable about TOC, with FM ($p=0.02$) and Pediatric providers ($p=0.02$) significantly more knowledgeable than IM providers. Most noted TOC should begin between ages 16–18 y. Only 25% of pediatricians stated the majority of their patients had identified an adult provider at the time they were leaving the practice. Pediatric providers were statistically more likely than FM or IM providers to assert that the patient knowing the names of and how to take their medications, having knowledge about their own health, and where to see a provider for preventive care were important components of the TOC process. FM and IM providers (41% vs 46%) were more likely than Pediatric providers (32%) to expect patients age 17 y and older to make independent health care decisions, but the difference was not significant.

Conclusions The transition to adult medicine is a critical stage in any adolescent's life, including those who are healthy. Understanding the perceptions of both pediatric and adult primary care providers allows for the development of processes that can ensure the receipt of ongoing care for this vulnerable population.

560

REASONS FOR HESITANCY AND ACCEPTANCE OF HUMAN PAPILLOMAVIRUS VACCINATION AMONG LATINA IMMIGRANT MOTHERS

AB Khodadadi*, I Scarinci. University of Alabama at Birmingham, Birmingham, AL

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Purpose of study Latinas have the highest incidence of cervical cancer in the U.S. Despite its link to cervical cancer prevention, HPV vaccination rates continue to be lower than other immunizations administered in adolescence. Since Latinos are generally in favor of vaccinations, understanding the parental attitudes towards the HPV vaccination could provide information on how to target this at-risk population.

Methods used This study was part of a larger effort to examine the efficacy of an intervention to promote HPV vaccination among daughters (9–12 years of age) of Latina immigrants ($n=317$) through a group randomized trial. Baseline data of Latina immigrant mothers with unvaccinated daughters was collected prior to this intervention. Only mothers who indicated a 'yes' or 'maybe' response to intention to vaccinate their daughters were included, leading to a final sample size of 309 participants.

Summary of results Of the 309 participants, 117 reported intention to vaccinate (37.9%) while 191 reported hesitancy (defined as an answer of 'maybe') to vaccinate their daughters (61.8%). Demographic differences between the two groups of mothers were significant for years of education completed ($p=0.03$). There were no significant differences with regard to the mothers' age, marital status, or years in the U.S. Frequently endorsed reasons for hesitancy included: the safety of the vaccine (78%), discomfort or pain their daughter might have receiving the vaccine (60.2%), and worry that the vaccine would promote sexual activity (50%). Frequently cited reasons for willingness to administer the HPV vaccine to their daughters included: the need for general vaccinations (98.3%), prevention of cervical cancer (92.2%), and their daughter needing the vaccine (85.3%).

Conclusions Only 38% of Latina immigrant mothers intended to vaccinate their daughters against HPV, despite research showing Latinos are pro-vaccination. Frequently endorsed reasons for reluctance were safety, discomfort, and promotion of sexual activity. Future efforts should focus on addressing these identified barriers while maximizing motivators among mothers willing to vaccinate their daughters.

561

A COLLABORATIVE PROGRAM TO IMPROVE ADOLESCENT HEALTH LITERACY AND STRENGTHEN DIALOGUE SKILLS BETWEEN TEEN PATIENTS AND MEDICAL PROVIDERS

¹E Oddo*, ^{1,2}MM Bowden, ¹D Burroughs-Ray, ²K Cox. ¹University of Tennessee Health Science Center, Memphis, TN; ²Le Bonheur Children's Hospital, Memphis, TN

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Purpose of study During adolescence, teens are learning skills to interact with physicians as they transition from pediatric to adult care. Physicians have significant deficits in discussing sensitive issues with teens, and few programs exist to provide appropriate training. Residency serves as an ideal time to pursue such training, as the effects may last throughout a provider's career. Additionally, teens benefit from non-clinical encounters with physicians acting as a trusted source for health information.

Methods used Pediatric residents and faculty collaborated with adolescent representatives from a hospital-affiliated teen pregnancy prevention program to develop a health literacy workshop. The workshop consisted of a presentation defining health literacy concepts, interactive scenarios, and an assessment tool. Residents participated in groups of 4–8 students from a local teen leadership program. Groups discussed scenarios including sexual activity, sexual orientation, and mental health. Students identified areas of health literacy deficits and implemented newly acquired skills.

Summary of results Six residents and 21 students participated in the workshop; each completed pre- and post-surveys. Paired t-tests were used to identify areas of significant improvement. Residents gained knowledge about helping students discuss health issues with parents ($p=0.002$). Students gained knowledge about where to get accurate health information ($p=0.000$) and asking a physician about sexual health ($p=0.003$). Follow-up surveys were conducted six months later. Response rates were 61.9% and 100% for students and residents, respectively. Residents initiated a discussion about sexual health with teen patients 90.3% of the time, while

students felt comfortable asking their doctors about sexual health 91.7% of the time.

Conclusions This program provides an innovative and effective approach to improving adolescent health literacy and resident communication with adolescents. Teens gained improved knowledge of health care resources and were empowered to engage with providers. Concurrently, residents became more comfortable initiating conversations about sexual health with adolescent patients and discussing confidentiality policies.

562 HEALTH-RISK BEHAVIORS IN EARLY ADOLESCENTS ADMITTED FOR PSYCHIATRIC CARE

EA Brew*, S Dumas. *LSUHSC School of Medicine, New Orleans, LA*

10.1136/jim-2018-000974.568

Purpose of study Early adolescence (10–13 years) is a developmental stage characterized by rapid changes. Health-risk behaviors, such as substance use and sexual activity, may emerge during this stage and increase throughout the teenage years. An increase in health-risk behaviors has also been associated with mental health diagnoses in adolescents. We sought to determine the prevalence of health risk behaviors in early adolescents admitted for psychiatric care.

Methods used We conducted a retrospective chart review of 13-year-old patients admitted to an inpatient adolescent psychiatric facility between January 2015 to June 2016. Data was extracted from the initial medical assessment conducted on each patient, and included patients' self-reported history of substance use and sexual history. Data was managed with Redcap and analyzed with Stata 14.0. We compared our cohort to CDC reports of adolescent health behaviors from the Youth Risk Behavior Survey (YRBS).

Summary of results There were 291 13-year-olds admitted during the study period, 71% of whom were female. The prevalence of patients with a history of sexual activity was 23.4%, of which 22% had a history of non-consensual sex. The prevalence of sex among 9th graders in the YRBS was 20.4%, and only 9.7% had experienced non-consensual sex. The overall prevalence of patients in our cohort with a history of substance use was 31%, among whom the use of tobacco was 41%, alcohol was 54%, and illicit drugs was 64% (93% of which was marijuana, specifically). Ninth graders in the YRBS had a prevalence of cigarette, alcohol, and marijuana use of 21%, 48%, and 24%, respectively.

Conclusions Our cohort experienced higher rates of non-consensual sex and drug use than similar aged adolescents in the US, which is consistent with higher rates of health-risk behaviors in adolescents with mental health diagnoses. Future research is needed to investigate the directional relationship between non-consensual sex and depression, in particular, to help prevent these outcomes in such a vulnerable group of young teens.

563 POST-CONCUSSION AND POST-TRAUMATIC STRESS SYMPTOMS IN INJURED PATIENTS: ADOLESCENT GIRLS ARE VULNERABLE

ER Fisher*, L Ewing-Cobbs, G Duque. *University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX*

10.1136/jim-2018-000974.569

Purpose of study Traumatic brain injury (TBI) is a major cause of disability and death in children. We assessed post-concussion symptoms (PCS; fatigue, somatic, cognitive, emotional) and post-traumatic stress symptoms (PTSS; re-experiencing, avoidance, emotional numbing, hyperarousal), which are understudied but have profound implications for the management of children's psychological health.

Methods used The study used a prospective cohort design with assessment 6 weeks following a motor vehicle accident. From 2011–2016, patients ages 8–15 years old who sustained a TBI (n=89) or an extracranial injury (EI; n=40) were recruited from the ED at a Level 1 trauma center. TBI was divided into mild, complicated-mild/moderate, and severe groups. Parents completed standardized measures at baseline to retrospectively rate patients' preinjury 'concussion-like' symptoms and internalizing behavior. Patients completed validated rating scales. Spearman correlations examined relations between PCS and PTSS. Generalized linear models (GzLM) with a negative binomial distribution and log link function examined the main effects of age at injury, sex, injury group, and their interactions on outcomes controlling for preinjury ratings of child behavior.

Summary of results PCS and PTSS total scores were significantly correlated for all groups but severe TBI. GzLM indicated significant group effects for PCS total, somatic, cognitive, and fatigue scores. Symptoms varied across TBI severity groups, but EI did not differ from TBI. Girls had more emotional symptoms than boys. GzLM for PTSS indicated significant age by gender interactions; adolescent girls had more total, avoidance, and hyperarousal symptoms. Hyperarousal symptoms varied by age and group; adolescents in complicated-mild/moderate TBI group had fewer symptoms. PTSS did not differ between TBI and EI.

Conclusions Significant PCS and PTSS were found in patients with either TBI or EI. Symptoms were influenced by demographic and injury factors. PCS and PTSS were related to both injury group and severity of the injury. Female adolescents were particularly vulnerable to developing both sequelae. Patients with symptoms that persist over a month should be monitored by a pediatrician to be referred for appropriate psychological health care.

564 IMPROVING HPV VACCINE COVERAGE FOR DETAINED YOUTH

¹AP Hoang*, ^{1,2}LJ Benjamins, ^{3,4}V Oyegunle, ³A Aladejare. ¹McGovern Medical School – UT Health Science Center at Houston, Houston, TX; ²Juvenile Detention Center, Houston, TX; ³UT School of Public Health, Houston, TX; ⁴University of Illinois at Chicago, Chicago, IL

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Purpose of study Detained youth often lack HPV vaccination coverage compared to the general population. The immunization protocol at a large urban juvenile detention center was revised to provide catch-up immunizations at the time of adjudication. We set out to see if this change had an impact on the rate of adolescent immunizations, including HPV.

Methods used After IRB approval, a retrospective chart review was conducted. Immunization records were accessed to determine HPV, MCV, and Tdap vaccination rates. Sexual history was also abstracted from the intake history and physicals.

Summary of results 329 records from January through April of 2017 were reviewed. 111 (33.7%) subjects identified as White, 164 (49.8%) identified as Black or African-American, one

(0.3%) identified as Asian, and 4 (1.2%) identified as Other. 80% of subjects were male. Subjects ranged in age from 11 to 18 years, with an average age of 15 years. Among the 147 (44.7%) subjects whose immunization records could be accessed, nearly 97% had initiated the MCV series, 94.6% had completed Tdap, and 78.2% had started the HPV series. In 2014, these numbers were 79%, 74%, and 18%, respectively at the same facility. In 2017, 88.7% of subjects who had initiated the HPV series completed it; in 2014 only 22% of youth had received more than one HPV vaccine and only 7% had completed all three doses. 62.3% of subjects reported being sexually active, and only 28.6% of subjects had used condoms at their last sexual encounter.

Conclusions Rates of MCV and Tdap vaccination, as well as HPV series completion markedly improved in this facility under the revised protocol. This improvement in coverage against HPV could be a result of promoting the initiation and completion of the series once adjudicated but may also be influenced by nationwide trends. The revised CDC and ACIP guidelines from 2016 recommend that adolescents initiating the HPV under 15 years of age receive two doses instead of three, which may also positively affect vaccine series completion.

565 EMERGENCY CONTRACEPTION AVAILABILITY IN LOUISIANA

EN Chiccarelli*. *LSU, New Orleans, LA*

10.1136/jim-2018-000974.571

Purpose of study Since FDA approval of oral emergency contraceptives (EC) in 1998, accessibility of these medications has been a focal point for legislation. Over the last twenty years, options have expanded and patients can access EC both over the counter (levonorgestrel, LTG) and by prescription (ulipristal acetate, UA). Today, all patients including minors and males are legally permitted to access LTG without a prescription or age requirement. UA is available to similarly available to anyone, but requires a prescription. These products can be of particular aid in preventing teen pregnancy, which continues to be higher than the national average in Louisiana. This project seeks to define and document EC accessibility for various geographical areas in Louisiana based on same-day availability of EC at local pharmacies.

Methods used Using a secret shopper method whereby participants called local retail pharmacies in four Louisiana municipalities, researchers gathered information posing as adolescents and physicians. They obtained information on current stock and cost of EC, and additional barriers to access using a scripted dialogue.

Summary of results We found overall poor availability of UA at 5%, which may reflect prescribing practices. Availability was better for LTG at 65%, which had an average cost of \$49. There is a strong correlation (Pearson=0.96) between metropolitan area population and EC availability. Regionally operated pharmacies are less likely to stock EC compared with national chains (OR=8.5). Additionally, 1 in 3 pharmacy staff members quoted inappropriate age restrictions during calls. Availability did not vary by socioeconomic parameters.

Conclusions The poor availability of UA represents a significant health disparity for overweight women in Louisiana, for whom this is a more effective form of EC compared to LTG.

Availability of LTG is reduced in our sample compared with previous national studies, which may represent challenges specific to Louisiana or to more rural areas. Our results indicate a need for further directives to bring pharmacy policy in line with the current EC access laws. We can also drive market demand for EC by improving medical education on this topic.

Allergy, Immunology, and Rheumatology I Concurrent Session

2:00 PM

Friday, February 22, 2019

566 ERYTHRODERMIC PSORIASIS SECONDARY TO SYSTEMIC CORTICOSTEROID USE AND CESSATION

¹M Heinrich*, ²RM Medrano, ²D Payne, ¹S Bijlani. ¹Texas Tech University Health Science Center, Lubbock, TX; ²TTUHSC, Lubbock, TX

10.1136/jim-2018-000974.572

Case report Erythrodermic psoriasis is an uncommon, potentially life-threatening, variant of psoriasis. We present a 58 year old woman with psoriasis who, after an abrupt discontinuation of steroids, developed erythrodermic psoriasis with extensive body surface involvement (>90%). Erythrodermic psoriasis requires a high index of suspicion to timely diagnose, treat and prevent complications.

Characterized by generalized erythema of the skin and frequently involves >75% of body surface area. Pustules, scaling, and exfoliation of the skin are commonly seen. Only occurring in 3% of psoriasis patients and requires a high index of suspicion to timely diagnose, treat and prevent progression to complications such as water-electrolyte imbalance and secondary infections. The differential diagnosis includes: Drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome, and Lyell's syndrome.

Case presentation 58 year-old female consulted a dermatologist for a 2 month history of rash involving her left lower extremity which progressed cephalad. A clinical diagnosis of psoriasis was made, and oral corticosteroids were prescribed. After 5 months of oral corticosteroid use, symptoms persisted. After developing hematemesis, steroids were stopped. Over the following two weeks, the rash generalized, involving >90% of her body surface. The rash was erythematous and exfoliative with significant sloughing of skin. Accompanied by pruritus, burning pain, occasional clear discharge, and xerophthalmia. Notably, mucosal surfaces were spared by the rash. A skin biopsy of the left upper extremity was obtained, revealed erythrodermic psoriasis. During hospitalization the patient was treated with topical triamcinolone ointment 0.1%, topical hydrocortisone 2.5% for eyelid involvement, and IV fluids. The rash improved significantly with topical treatment and hydration.

Conclusion This case illustrates the potential for erythroderma in psoriasis patients who use or abruptly withdraw systemic corticosteroids use. Although rare, the prompt biopsy diagnosis and treatment of this potentially life-threatening disease is imperative. A history of psoriasis, eczema, or a drug eruption is an important clue to the onset of an erythrodermic phenotype.

567

AN INTERESTING CASE OF NECROTIZING AUTOIMMUNE MYOPATHYR Bahloul*, H Patel, I Serrano, E Sottlie. *UF Health Jacksonville, Jacksonville, FL*

10.1136/jim-2018-000974.573

Case report Necrotizing autoimmune myopathy (NAM) is a new and rare type of idiopathic inflammatory myopathies, which presents with subacute symmetrical muscle weakness and very elevated levels of serum creatine kinase (CK). Risk factors for NAM include statin exposure, mixed connective tissue disease, viral infection and paraneoplastic syndromes.

A 39-year-old male with a history of obstructive sleep apnea presented to the hospital with gradually worsening proximal muscle weakness and 30 lb weight loss of 2 months duration. His weakness was worse in the upper extremities and associated with exertional myalgias. On physical exam, the patient had decreased strength bilaterally; more pronounced in deltoids, biceps and quadriceps. Labs ordered were notable for elevated CK at 20,000, transaminitis and elevated ESR/CRP. Myositis panel was remarkable for positive anti-SRP antibodies. Anti-HMGCR antibodies were negative. An MRI of the thighs revealed evidence of abnormal muscle signal enhancement bilaterally, most severe in the left proximal rectus femoris. A biopsy from that location revealed mild necrotizing myopathy with denervation without inflammation or vasculitis. The patient was started on 1 g daily of intravenous steroids, followed by prednisone 40 mg orally twice daily. He showed significant symptomatic improvement and was discharged to follow-up outpatient with Rheumatology.

Necrotizing autoimmune myopathy is a rare type of acquired idiopathic myopathy that has only recently been discovered. It is important to distinguish from other forms of myocyte necrosis, where treatment can have very little to no effect. In NAM, studies have shown that treating with 2 or more agents within 3 months significantly improves the odds of recovery, especially in patients with anti-SRP and/or anti-HMGCR antibodies, like our patient. The usual treatment regimen of steroids and steroid-sparing immunosuppressants allow recovery in over 50% of patients. Our patient was able to regain significant muscle function and quality of life with this combination of medications. Further prospective studies are needed to quantify the most effective regimens. We conclude that, while NAM is a potentially debilitating disease, an accurate diagnosis and rapid treatment can restore a remarkable amount of quality to our patients' lives.

568

A DEBILITATING PRESENTATION OF SARCOIDOSISA Burkenstock*, A Shalaby, D Lennep, L Weatherly. *University of Mississippi Medical Center, Jackson, MS*

10.1136/jim-2018-000974.574

Case report Sarcoidosis is a non-infectious, granulomatous inflammatory disorder known to affect multiple organ systems of the body.

A 39-year-old African American female presented to her primary care physician with a three-month history of progressive lower extremity pain and weakness limiting her to a wheelchair. Creatine kinase levels were significantly elevated at 11,626 U/L, and she was referred to the emergency department for further in-patient work-up. The physical examination was significant for 2/5 strength bilaterally of the proximal

upper and lower extremities with increased strength distally, non-pitting lower extremity edema, and reduced bilateral patellar reflexes. Further laboratory work-up was performed and demonstrated significant muscle break down indicative of possible rhabdomyolysis. Electromyography (EMG) was obtained demonstrating inflammatory myositis, greatest in the proximal musculature. A deltoid muscle biopsy demonstrated necrotic myofibers as well as focal chronic inflammatory infiltrate. Interestingly, laboratory myomarker auto-antibody panel was negative for autoimmune processes such as polymyositis. Computed tomography (CT) of the chest was significant for enlarged mediastinal and bilateral hilar lymph nodes. Subsequently, bronchoalveolar lavage (BAL) and endobronchial ultrasound (EBUS) guided lymph node biopsy were performed, which returned with benign lymphoid tissue and multiple non-necrotizing granulomas. Additionally, BAL flow cytometry results were also consistent with the diagnosis of sarcoidosis. Following lymph node and deltoid biopsies, treatment was initiated with high dose intravenous steroids. Her symptoms of muscle pain and proximal weakness steadily improved with each day of in-patient treatment.

The clinical picture of sarcoidosis is highly variable and symptomatic myopathy is an uncommon presenting complaint. Only one of the presentations of sarcoid myopathy is acute myositis, and it is clinically indistinguishable from polymyositis. While sarcoid myopathy is uncommon, a simultaneous presentation of both sarcoidosis and polymyositis would be even more infrequent.

569

SARCOID WITHOUT THE LUNGS Mohini*, M Hess. *SUNY Upstate, Syracuse, NY*

10.1136/jim-2018-000974.575

Introduction Sarcoidosis is a granulomatous disorder that affects multiple organ systems, however primarily the lung. The disease is characterized by the detection of noncaseating granulomas. Sarcoidosis typically presents with pulmonary symptoms or is incidentally detected with radiographic evidence. The following is a case presentation of patient who presented with only extrapulmonary manifestations.

Case presentation A 27-year-old African-American woman presented to emergency room after being found to be anemic at her PCP's office. Patient also had complaints of LUQ abdominal pain, decrease appetite, and weight loss. Patient was found to have an H/H of 7.5/23.6 with previously normal levels. Her lab work also showed an elevated creatinine of 4.40. Initially she was evaluated for a possible gastric ulcer, however her EGD was negative. She was seen by nephrology who thought she may have ATN from her anemia and recommended work up for her anemia. Her basic anemia work-up did not show a cause of her anemia. She eventually was evaluated by hematology and underwent a bone marrow biopsy after additional lab work was negative. The patient's blood counts and creatinine stabilized allowing her to be discharge home with outpatient follow up. Her bone marrow biopsy showed noncaseating granulomas suspicious for sarcoidosis. She also had a renal biopsy done as outpatient which showed granulomatous interstitial nephritis which helped lead to her diagnosis. The patient was seen by pulmonary as well and was found to have no pulmonary involvement in her sarcoidosis.

Discussion Sarcoidosis is a multisystem disease that is characterized by noncaseating granulomas. Sarcoidosis most commonly affects the lungs. Patients typically present with pulmonary and systemic complaints. Other organ systems that can be involved include skin, lymph nodes, eye, liver, bone marrow, and renal.

Conclusion This case represents an unusual presentation of Sarcoidosis without lung involvement. Sarcoidosis usually involves the lung in about 95% of cases. Disease involving the bone marrow was seen in 3.9% of cases while renal disease was seen around 0.7% of cases. The diagnosis of sarcoidosis is difficult in the absence of pulmonary findings. Patient's with suspected sarcoidosis should have multiple test to rule in or out sarcoidosis. Ultimately, biopsies are often required to confirm the disease.

570 HYPOPHOSPHATEMIC MICE ARE PROTECTED FROM COLLAGEN-INDUCED ARTHRITIS

JD Kee*, LD Quarles, A Kang, L Myers. *University of Tennessee Health Science Center, Memphis, TN*

10.1136/jim-2018-000974.576

Purpose of study Rheumatoid Arthritis (RA) is the most common form of autoimmune arthritis, and with the high prevalence of RA in the United States, it is important to understand the pathophysiology. Fibroblast growth factor 23 (FGF-23), which is secreted by osteocytes, leads to poor mineralization of bone and appears to affect the immune system by upregulating macrophage differentiation. Our hypothesis was that hypophosphatemic (*Hyp*) mice, which have high levels of FGF-23, would develop a more severe arthritis in the collagen-induced arthritis model.

Methods used Six hypophosphatemic (*Hyp*) mice and five C57BL/6 mice were immunized with type II collagen (CII/CFA) and observed for the onset of arthritis. The mice were evaluated for antibody production, cytokine production, and phenotype.

Summary of results The *Hyp* mice did not develop any arthritis, while the wild type had an 80% incidence rate. Antibody production levels were significantly decreased in the *Hyp* mice group compared to wild type ($p=0.04$) and cytokine analysis showed a decrease in the proinflammatory IL-17, mIFN- γ , and IL-5 cytokines upon stimulation with no effect on the anti-inflammatory IL-10 cytokine. Flow cytometry showed that NK cells and B cells are decreased in *Hyp* mice, while M1 macrophages are upregulated.

Conclusions Taken together, these data indicate that *Hyp* mice do not develop autoimmune arthritis and are unable to mount inflammatory T cell and antibody responses to the immunizing antigen. Identification of the mechanisms by which *Hyp* mice are protected from autoimmunity should lead to improved therapeutic options for autoimmune arthritis.

571 HAIR CHEMICAL USAGE AND SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

J English*, TD Faith, D Kamen. *Medical University of South Carolina, Johns Island, SC*

10.1136/jim-2018-000974.577

Purpose of study Systemic lupus erythematosus (SLE) is a complex chronic autoimmune disease of unknown etiology. Previous studies of beauty products as potential triggers of SLE development have shown conflicting results. Our study evaluates the use of hair chemicals in patients with SLE and controls and the relationship of use with disease severity among patients.

Methods used Data was obtained from an ongoing longitudinal registry of patients with SLE and non-SLE population-matched controls. Information on demographics, medical and social histories, types of hair chemicals used, and SLE characteristics (if applicable) was gathered from in-person interviews. Chart review and telephone follow-up was done for missing values. Disease damage was determined by SLICC/ACR Damage Index ('damage present' if score ≥ 1). Males were excluded from the study population. Pearson's chi-squared testing was performed for categorical measures and two-sample t-tests for continuous measures. Significance was set at $\alpha=0.05$.

Summary of results A total of 726 SLE patients and 474 controls were included. Demographics and hair chemical use described in table 1. Hair chemical use did not differ by race. Patients with SLE were significantly more likely to use hair chemicals compared to controls (74.6% vs. 25.4%, $p<0.01$), specifically with higher proportions of patients using hair relaxers/straighteners ($p=0.02$), hair dyes ($p<0.01$), and permanent wave products ($p<0.01$). SLE damage was more common among patients who use hair chemicals compared to those who do not, though not statistically significant (57.4% vs 50.1%, $p=0.08$).

Conclusions In conclusion, we found that hair chemical use among females was significantly higher in patients with SLE compared to controls, especially hair dyes and permanent wave products. These results provide a basis to look further in to hair chemical use and its relation to autoimmunity. Ongoing analyses are examining the timing and duration of hair chemical use and the development of autoimmunity, as well as SLE characteristics, such as alopecia.

Abstract 571 Table 1

Characteristics	SLE n=726	Controls n=474	p-value
Current age (mean years $\pm$ sd)	48.5 $\pm$ 15.6	51.5 $\pm$ 16.9	<0.01
African American (%)	72.7	88.4	<0.01
Insured, any (%)	93.6	94.1	0.76 (NS)
High school graduate (%) (adults)	86.2	86.3	0.99 (NS)
Any hair chemical usage (%)	74.6	25.4	<0.01

572 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT PRESENTING WITH PYODERMA GANGRENOSUM

L Hayward*. *University of Mississippi Medical Center, Madison, MS*

10.1136/jim-2018-000974.578

Introduction Multiple skin manifestations can be encountered in patients with SLE. These manifestations include acute cutaneous lupus erythematosus, subacute cutaneous lupus erythematosus, and chronic cutaneous lupus erythematosus. This case illustrates another skin manifestation that may be seen in these patients.

Case report A 36 year old African American female with a past medical history of Graves' disease, resultant post-

surgical hypothyroidism, and systemic lupus erythematosus compliant on Hydroxychloroquine 200 mg BID and Azathioprine 100 mg daily presented with new bilateral lower extremity skin lesions. Prior to these findings, patient reported a flare of diffuse arthralgias, worsening of her Raynaud's, and then small lesions that resembled mosquito bites. Patient reported these lesions rapidly grew, became necrotic, and then ulcerated. Physical exam was unremarkable except for 3 well defined full thickness ulcerations of bilateral lower extremities ranging in size from 3–8 cm. At the time of presentation, white blood cell count low at 2.4TH/cmm (near baseline), erythrocyte sedimentation rate mildly elevated at 31 mm/hr, c-reactive protein normal at 0.20 mg/dL, C3 complement normal at 149 mg/dL, C4 complement normal at 39 mg/dL, and anti-neutrophil cytoplasmic antibody panel negative. Initial differential diagnosis included pyoderma gangrenosum, calciphylaxis, vasculitis, and infection. Patient evaluated by dermatology and punch biopsies obtained which favored pyoderma gangrenosum with a broad ulceration with underlying acute and chronic inflammation impinging on the subcutaneous fat with no evidence of calciphylaxis or leukocytoclastic vasculitis. Patient was immediately started on short course of Prednisone with slow improvement in lesions. She was subsequently started on Infliximab to escalate therapy as these lesions occurred while she was compliant on therapy. Patient continues to improve on more aggressive therapy.

Discussion This case illustrates other skin manifestations that can be seen in patients with autoimmune diseases. While common disorders associated with pyoderma gangrenosum include inflammatory bowel disease, inflammatory arthritis, malignancy, and hematological disorders, it is important to keep a wide differential in patients with autoimmune disorders.

573

IGE-MEDIATED MILK ALLERGY IN INFANTS WITH FOOD PROTEIN-INDUCED ALLERGIC PROCTOCOLITIS

GM Jeha*, LA Wall. *Louisiana State University Health Sciences Center, New Orleans, LA*

10.1136/jim-2018-000974.579

Case report Food protein-induced allergic proctocolitis (FPIAP) is a transient non-IgE-mediated allergic condition that presents with bloody stools in otherwise healthy infants. Patients with FPIAP typically achieve clinical resolution and tolerance of an unrestricted diet by twelve months of age. Within the current literature, development of IgE-mediated hypersensitivity against the implicated food antigen is not of concern. We present two infants with cow's milk-induced proctocolitis who experienced IgE-mediated hypersensitivity reaction to cow's milk within the first year of life. To our knowledge this phenomenon has not been previously reported.

Method Retrospective chart review.

Results Documented are two breast-fed male infants who developed FPIAP and experienced resolution of bloody stools with maternal cow's milk avoidance as they continued to breast-feed. Case 1 developed FPIAP at two weeks old. By nine months of age, his mother gradually reintroduced foods containing trace amounts of baked milk into her diet. Additionally, the infant was able to consume foods containing milk as a trace baked ingredient by one year of age. At 12 months of age, ingestion of cow's milk-based yogurt led

to an anaphylactic emergency. Case 2 was diagnosed with FPIAP at three months old. While transitioning to a milk-based formula at six months old, he developed a severe allergic reaction involving hives and angioedema immediately after consuming his first bottle. Both patients had detectable levels of cow's milk-specific IgE before one year of age.

Conclusion FPIAP is generally considered a benign, transient, non-IgE-mediated condition. However, these cases demonstrate that there is potential for infants with dairy-induced FPIAP to develop a severe IgE-mediated hypersensitivity reaction to cow's milk within the first year of life.

574

FAILURE OF B CELL REPOPULATION FOLLOWING REPEATED RITUXIMAB INFUSIONS

C Mitchell, C Crayne*, R Cron. *University of Alabama Birmingham, Birmingham, AL*

10.1136/jim-2018-000974.580

Purpose of study Rituximab (RTX) is a chimeric monoclonal antibody that binds to CD20, found predominantly on B cells, resulting in reduced B cell activity and immune suppression. It is most commonly used to treat select antibody-mediated autoimmune diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). While the safety and efficacy of RTX in rheumatic diseases is well-established, the long-term effects of RTX, specifically on B cell repletion, are variable. This study explores the association between demographic characteristics and the effects on B cell depletion following RTX infusion. The primary outcome was defined as persistent failure to repopulate B cells after ≥ 12 months following last RTX infusion.

Methods used A retrospective chart review of 112 children ≤ 18 years treated with RTX at Children's of Alabama from 2007 to 2018 was performed. Exclusion criteria included patients with a diagnosis of malignancy. Demographic, clinical, and laboratory data were extracted and compared using JMP Pro 13.1 statistical software.

Summary of results Of the 112 children included, 8 (7.21%) remained B cell depleted at 12 months following RTX. Half of those who failed to repopulate at 12 months had connective tissue disease (CTD) (n=4). Nine patients (8.11%) failed to achieve normalization of B cells more than one year following RTX, and all of these patients had underlying CTD. There was no statistically significant association between age, sex, or the number of RTX rounds and the frequency of B cell depletion. The association between race and B cell depletion approached significance ($p=0.0555$), suggesting that black and asian race may be less likely to repopulate B lymphocytes. There was no association between the number of rounds of RTX and failure to normalize ($p=0.8553$) at ≥ 12 months following last RTX.

Conclusions The results of this study suggests that children treated with RTX may fail to repopulate B cells and may remain depleted for more than 12 months following last infusion. Patients with connective tissue disease may be at higher risk of persistent depletion with failure to repopulate. Persistent B cell depletion appears to be independent of the number of RTX rounds, suggesting repletion may vary with respect to underlying disease.

575

IVIG-REFRACTORY KAWASAKI DISEASE: DISTILLING THE LITERATURE TO PREDICT OUTCOMESC Crayne*, T Beukelman. *University of Alabama Birmingham, Birmingham, AL*

10.1136/jim-2018-000974.581

Purpose of study Kawasaki disease (KD) is an acute, self-limited medium vessel vasculitis, complicated by coronary artery lesions (CAL) in roughly 25% of untreated disease. If IVIg (2 g/kg) is given during the first 10 days of fever, CAL risk is reduced to <5%. Refractory KD, defined as the return of fever at least 36 hours and <7 days following completion of initial IVIg infusion occurs in about 10%–20%. Persistent fever is associated with a significantly higher risk of developing CAL. Evidence remains contradictory regarding next-line therapy and risk of cardiac sequelae. The objective of this study is to evaluate the efficacy and safety of three treatments [i.e. a 2nd IVIg infusion, glucocorticoids (GC), and infliximab (IFX)] in patients with refractory KD using decision analysis methods.

Methods used A systematic review of literature published from 1990 to November 2017 was performed to extract outcome probabilities for a decision analysis model. Primary outcomes were resolution of fever within 36 hours and reduction in size of CAL within 8 weeks. Eligibility criteria included articles written in English and original clinical research, including cases not previously reported.

Summary of results Thus far, 9 manuscripts have been identified and reviewed. Four were prospective, randomized studies, and two were prospective, non-randomized. Three of the published studies were retrospective reviews. This combined cohort included 188 patients from Japan, 130 from North America, and 43 from Korea. In total, 209 patients received a 2nd IVIg, 89 received GC, and 63 received IFX. Treatment response was 72% with IVIg, 72% with GC and 89% with IFX. Overall, the total number of patients with CALs was 17 (8.13%) with IVIg, 10 (11.24%) with GC, and 24 (38.1%) with IFX. The number of patients with moderate-severe or persistent aneurysms was zero with IVIg, 7 with GC, and 3 with IFX.

Conclusions Preliminary literature review suggests a second dose of IVIg is used more frequently in refractory KD and response to treatment is comparable to GC. The reported differences in reduction of CALs among each treatment group is of unclear significance. The results of this systematic review of the literature will be used to populate a computerized decision analysis model to determine the most cost-effective second-line therapy for IVIg-refractory Kawasaki Disease.

576

ASSESSING THE ROLE FOR VACCINE ADJUVANT SELECTION IN DRIVING ANTIGEN-SPECIFIC B CELL ACTIVATION AND MEMORYJT Prior*. *Tulane University School of Medicine, New Orleans, CT*

10.1136/jim-2018-000974.582

Purpose of study There has been a global rise of antibiotic resistant pathogens and these pathogens are causing a significant increase in morbidity and mortality. Regrettably, this rise in resistance has been accompanied by a decrease in the amount of new antibiotics and even our last line of defense antibiotics are no longer able to kill certain extensively drug

resistant bacteria. Vaccines offer one of the best ways to combat and prevent infections with resistant bacteria. Antibody responses are usually the most effective and sought after aspects of vaccine-induced immunity and the one with the greatest capacity to protect against the highest number of pathogens. Many new efforts are being made to develop new vaccines through the use of new adjuvants. However, many questions remain about the changes B cells undergo when exposed to vaccine antigens and adjuvants. It is possible that adjuvant choice can direct the location and type of immune response towards one that is most desired for a particular infection.

Methods used Flow Cytometry, ELISA, ELISPOT, and RNA Sequencing.

Summary of results The addition of adjuvants to vaccines helps improve the number of antigen specific B cells generated as well as improves the isotype switching of these B cells.[MJB1] Of note, double mutant liable toxin (dmLT), a detoxified liable toxin of *E. Coli*, was able to direct a more mucosal immune response as compared to alum.

Conclusions Learning the role that adjuvants play in altering the immune response to vaccines is invaluable to improving their efficacy. dmLT could be used as a potent adjuvant to improve vaccines against *Salmonella* or *E. Coli*.

Cardiovascular I**Concurrent Session****2:00 PM****Friday, February 22, 2019**

577

EARLY AND LATE ADULTHOOD RISK FACTORS IN THE DEVELOPMENT OF CAROTID PLAQUE: THE BOGALUSA HEART STUDYRK Trivedi*, X Wang, J Xu, Z Fang, F Smart, G Berenson. *LSU Health Sciences Center – New Orleans, New Orleans, LA*

10.1136/jim-2018-000974.583

Purpose of study Carotid plaque (CP) is a precursor lesion of cerebrovascular and general cardiovascular disease (CVD) burden. Ultrasound (U/S) screening for CP is now an effective tool given its cost and availability. Despite clinical utility, little investigation has gone into associations between CP and CVD risk factors at time CP was seen or prior to lesion development.

Methods used The Bogalusa Heart Study is a longitudinal epidemiological study of early CVD with 12 000 subjects followed continuously since 1972. A subset of these subjects underwent U/S of the carotids serially from 2000 to 2008 (n=914, age 44.4±4.4 years). Data regarding patient health status was simultaneously collected. Statistical analysis was done by t-test or chi square; reported as odds ratio with 95% CI.

Summary of results At time CP was first identified in late adulthood (2008), there was an association between CP and smoking [SMK, 2.87 (1.64,5.01)], white ethnicity [2.67 (1.26,5.65)], and co-morbid states. A personal history (PHx) of hypertension [HTN, 2.30 (1.45,3.65)] and current blood pressure (BP) were increased. There was increased PHx of

diabetes [DM, 2.74 (1.48,5.09)] and elevated blood glucose (BG). There was also elevated serum LDL [1.01 (1.00,1.01)] and triglyceride [TGY, 1.00 (1.00,1.01)] although PHx of hyperlipidemia (HLD) was not significantly increased.

During early adulthood (2000), prior to CP presence, we observed associations with family history (FHx). There was increased FHx of DM [1.97 (1.18,3.28)] and heart disease [HD, 2.36 (1.42,3.93)]. Similar to later adulthood there was increased BP, BG, and TGY but not LDL. Additionally, serum uric acid was significantly increased at this earlier timepoint [1.17 (1.00,1.37)] suggesting early inflammatory response may lead to CP formation. As before, SMK was significantly increased [3.34 (1.79,6.24)] although the absolute risk was greater than seen at time CP was identified.

Conclusions Known CVD risk factors such as SMK, HTN, DM, and HLD are associated with presence of CP. Further, risk factors during earlier adulthood such as early SMK, increased BP, elevated BG and TGY, and FHx of HD and DM are associated with CP. Lastly, serum uric acid may predispose CP incidence later in adulthood.

578 OUTCOMES WITH ELECTRONIC PERIOPERATIVE CARDIAC RISK ASSESSMENT IN NONTHORACIC NONVASCULAR SURGERY

¹L Singh*, ¹R Hasan, ^{1,3}S Vallurupalli. ¹University of Arkansas for Medical Sciences, Little Rock, AR; ²Central Arkansas Veterans Healthcare System, Little Rock, AR

10.1136/jim-2018-000974.584

Purpose of study To study post-operative outcomes in patients who underwent nonthoracic nonvascular surgeries after electronic perioperative cardiac risk assessment.

Methods used Electronic consultation was requested by the surgeon and reviewed by a cardiology fellow following the 2014 ACC/AHA guidelines on perioperative risk assessment. If cardiac symptoms and functional status was unclear, patients were contacted by telephone and if indicated, additional testing and clinic follow-up was arranged. 162 electronic consultations for perioperative cardiac risk assessment

Abstract 579 Figure 1 Kaplan-Meier survival curve for death, MI or late CR

were performed between 2014–2017. Primary outcomes of interest were postoperative myocardial infarction (MI) and 30 day mortality.

Summary of results Our study included an elderly cohort with mean age of 68.9 years. 97.4% of them were males. 56% of them had known coronary artery disease (CAD). Perioperative assessment was completed within a median of 1 day (IQR 0–2) from the date of request. Mean risk of MACE predicted using the Gupta score was 0.45%±0.44%. No additional testing was recommended in 95.1%. Stress testing was performed in 8 patients, 4 were positive for ischemia and evaluated in clinic and 2 of whom subsequently underwent coronary angiography. Surgery was performed within a median of 20 days (IQR 7–41) after completion of consultation (65.4% elevated risk surgery, 15% time sensitive). There were no post-operative myocardial infarctions or deaths within 30 days.

Conclusions Our study demonstrates that electronic perioperative risk assessment in adherence with current guidelines can be performed safely in a population with significant burden of CAD undergoing nonthoracic, nonvascular surgery.

579 THE PROGNOSTIC VALUE OF MYOCARDIAL PERFUSION IMAGING IN PATIENTS WITH TYPE 2 MYOCARDIAL INFARCTION

CM Colon*, R Marshall, C Roth, A Farag, AE Iskandrian, FG Hage. University of Alabama at Birmingham, Birmingham, AL

10.1136/jim-2018-000974.585

Purpose of study Type 2 myocardial infarction (T2MI) is an increasingly common diagnosis in clinical practice. The management of this condition is controversial and the prognostic value of myocardial perfusion imaging (MPI) in these patients has not been adequately studied.

Methods used We retrospectively studied T2MI patients (troponin I levels >99th percentile) who underwent vasodilator MPI within 3 months of T2MI at a single institution. Abnormal perfusion was deemed present when it involved ≥5% of left ventricular (LV) myocardium. Abnormal LV ejection fraction (EF) was defined as <50%. The primary outcome was a composite of death, myocardial infarction or coronary revascularization.

Summary of results Our cohort consisted of 234 patients (62 ±14 years, 57% men) with T2MI (peak troponin 0.2 ng/ml, interquartile 0.1–1.4) of whom 136 (58%) had abnormal MPI. During a median follow-up of 20 months, 155 patients (66%) had the primary outcome (39% death, 42% myocardial infarction, 5% coronary revascularization). An abnormal MPI was associated with increased risk of the primary outcome during follow-up with a hazard ratio of 1.56, 95% CI (1.12 to 2.18), p=0.008 that remained significant after multivariate adjustment (1.45, 95% CI (1.02 to 2.06), p=0.04).

Conclusions Patients with T2MI are at high risk for death or cardiac events in the intermediate term. More than one-half of patients with T2MI have an abnormal MPI and this is associated with increased risk of cardiac events during follow-up. Risk stratification with MPI after T2MI may identify patients that would benefit from aggressive risk reduction.

580

MULTIPLE ANTIHYPERTENSIVE THERAPY AND RISK OF FALLS IN GERIATRIC PATIENTS

C Mulloy*, KN Rezkallah, EA Aguilar, S Barry, L Ali, TM Reske. *LSUHSC, New Orleans, LA*

10.1136/jim-2018-000974.586

Purpose of study HTN management in elderly adults is demanding due to the tendency to develop orthostatic hypotension. Fall risk factors include autonomic instability, comorbidities and volume depletion. We are seeing an increase in comorbid older adults and the issue of drug safety is critical, as falls are a common source of morbidity. We investigate if antihypertensive meds, when used in combination, increase fall risk.

Methods used With IRB approval a cross-sectional chart review of 139≥60 yo patients at PACE-GNO for ≥3 months were divided in 2 groups: falls and no falls. Antihypertensive meds and number of falls were counted for each group. Patients on a single med were the comparator and we calculated the odds ratio/relative risk of falls with additional meds.

Summary of results With 1 drug as baseline, RR and OR values>1 represent a regimen associated with higher fall risk. An OR >1 was seen with 2 medications (OR=1.7, RR=1.5) and >3 medications (OR=1.4, RR=1.3). BPs were not available.

Conclusions Data suggests that use of a single medication has less fall risk than 2 or >3 meds. 3 meds have a different relationship with OR and RR=0.9. A trend points toward additional meds conferring additional risk, but the CIs cross 1, and P values are>0.05—indicating statistically insignificant findings; likely due to small sample, comorbidities, concurrent drugs, or other fall risks. These data can inform future studies in specific drug combinations that pose risk. Polypharmacy must be avoided, and benefits of BP control must be weighed against the risks of adverse events. There is a need for large trials studying management of HTN in elderly adults.

Abstract 580 Table 1 Number of medications in each group of patients

Medications	Falls	No Falls	Total (N)
1 Med	4	21	25
2 Meds	11	34	45
3 Meds	6	34	40
>3 Meds	6	23	29

Abstract 580 Table 2 Odds ratio and relative risk of multiple agents vs. single agent

	OR	95% CI	RR	95% CI	P
2 Meds	1.7	0.5–6.0	1.5	0.5–4.3	0.4
3 Meds	0.9	0.2–3.7	0.9	0.3–3.0	0.9
>3 Meds	1.4	0.3–5.5	1.3	0.4–4.1	0.7
All	1.3	0.4–4.2	1.3	0.4–3.3	0.6

581

THE YOGA-MEDITATION HEART CONNECTION: A PILOT STUDY LOOKING TO IMPROVE WOMEN'S HEART HEALTH

S De Jesus*, E Schultz, R Bond. *Lenox Hill Hospital, New York, NY*

10.1136/jim-2018-000974.587

Purpose of study Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in the United States for women. Although there has been a decline in mortality in older women from heart disease, recent data suggests a stagnation among women<55 years. It is imperative that we continue to increase awareness, understand and research the unique pathophysiology of women's CVD, and increase recognition of nontraditional risk factors that are more common in women such as stress, anxiety and depression, and the alternative measures that can help decrease them such as yoga and meditation.

Methods used An anonymous survey was provided to the participants of a weekly complimentary chair yoga/meditation workshop supervised by a trained cardiac yoga therapist. The surveys were distributed on day 1 and on week 24 to assess any changes in their reported level of stress, depression, anxiety and lifestyle.

Summary of results A total of 16 and 10 female participants with or at risk for CVD completed the initial and follow up survey respectively, which included validated screening tools for depression, anxiety and stress. The Patient Health Questionnaire-9 from the initial session to the follow up survey showed an overall increase in the mean score (2.25 vs 3.2 [p=0.199]). Despite this increase, the severity remained as minimal depression. The mean Generalized Anxiety Disorder-7 went from 7 down to 4.9 (p=0.138) for the follow up survey (decreased from a definition of mild to no clinical anxiety). Lastly, the Perceived Stress Score demonstrated a mean reduction from 18.25 to 15.2 (p=0.106), both remaining as moderate perceived stress. Participants also endorsed a trend towards integrating more low saturated fat foods, and 37.5% endorsed a 3–9 lbs weight loss.

Conclusions Although more research and larger studies are yet to be done to demonstrate a definitive benefit in meditation and chair yoga in CVD risk reduction, our pilot study demonstrated a trend towards overall improvement of novel risk factors for CVD, which predominantly affect women. Given the low harm and cost of these measures, they can be done as adjuvants to our standard of care to increase the patient's overall well being by improving the psychological aspect of their lives which in turn could reflect on their physical health.

582

A COMPREHENSIVE META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS COMPARING DRUG-ELUTING STENTS WITH BARE-METAL STENTS IN SAPHENOUS VEIN GRAFT INTERVENTIONS

¹KG Hesterberg*, ²PS Jagadish, ²AK Butt, ¹K Najib, ¹SB Latham, ^{1,3}R Shah. ¹UTHSC, Memphis, TN; ²UTHSC, Memphis, TN; ³VA Medical Center, Memphis, TN

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Purpose of study Several large randomized controlled trials (RCTs) have proven the superiority of drug eluting stents (DESs) over bare metal stents (BMSs) for native coronary stenosis. However, RCTs comparing DESs with BMSs for saphenous vein graft (SVG) lesions have predominantly been small in size and have yielded conflicting results. Therefore, we performed an updated meta-analysis with the largest sample to date by including trials from recent months.

Methods used Scientific databases and websites were searched to find RCTs. Data from six RCTs involving 1582 patients were included. Pooled risk ratios (RRs) were calculated using

Abstract 582 Figure 1 A) Early MACE; B) Early TVR; C) Late MACE; D) Late TVR

random-effects models. Early outcomes (with median follow up of 12 months) as well as late outcomes (with a median follow up of 2 to 3 years) were examined.

Summary of results Data from six RCTs involving 1582 patients were included. Saphenous vein graft interventions with DESs reduced early MACE rate (RR, 0.60; 95% CI, 0.42–0.87; $p < 0.007$) (figure 1A), driven by decreased rate of target vessel revascularization (TVR; RR, 0.52; 95% CI, 0.30–0.88; $p = 0.017$) (figure 1B) compared to BMSs. However, no difference between the stents were found for the rate of early MI, all-cause mortality or cardiac mortality. Finally, there was no difference found for any late outcomes (including MACE and TVR) between the two stent strategies (figure 1C, figure 1D).

Conclusions For SVG intervention, DESs appear to be the better stent at short term follow up, as they are associated with decreased rate of TVR, compared to BMSs. However, the early benefit of DESs seem to disappear with long term follow up.

583 DECISIONS FOR SURGICAL INTERVENTIONS: A NATIONAL PERSPECTIVE ON CONGENITAL HEART DISEASES IN CHILDREN WITH TRISOMY 13 AND 18

D Dillistone*, A Parnell, J Desai. University of Mississippi Medical Center, Jackson, MS

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Purpose of study We aimed to study a national perspective on practices of surgical interventions and factors predicting surgical decisions for congenital heart disease (CHD) in patients with Trisomy 13 (T13) and Trisomy 18 (T18).

Methods used We used the Kid's Inpatient Database for the years 2000, 2003, 2006, 2009, and 2012. Pediatric patients admitted with a diagnosis of T13 or T18 were included while transfer-out, stillbirth, and a combined diagnosis of T13 and T18 were excluded. Statistical analysis was performed using SAS 7.1.

Summary of results Among non-critical CHDs, VSD (77%) and secundum ASD (17%) were most common while TOF (35%) and CoA (23%) were most common among critical CHDs. Total of 205 surgical procedures were performed: 3.2% in T13 non-critical CHDs and 9.0% in critical CHDs; 3.9% in T18 non-critical CHDs and 7.4% in critical CHDs (figure 1). Predictors for surgical interventions are described in figure 2. Mortality was significantly lower in children who received cardiac interventions, white race, female and if term gestation at birth.

Abstract 583 Figure 1 Factors predicting surgical interventions

Abstract 583 Figure 2 Surgical interventions for T13 and T18

Conclusions To our knowledge this is the largest study cohort describing surgical intervention of CHDs in patients with T13 and T18 which can be useful for prenatal/postnatal counselling and decision making. We were unable to identify mosaicism as there is no separate ICD-9 code for it.

584 PERCUTANEOUS REPAIR OF CORONARY ARTERY FISTULAS IN ORTHOTROPIC HEART TRANSPLANT RECIPIENTS

¹CA Castro-Soto*, ^{2,3}E Rodriguez, ⁴C Diaz, ^{2,5}HL Banchs, ^{2,5}PI Altieri, ²IF González-Cancel. ¹San Juan Bautista School of Medicine, San Juan, Puerto Rico; ²Cardiovascular Center of Puerto Rico and the Caribbean, San Juan, Puerto Rico; ³San Jorge Children's Hospital, San Juan, Puerto Rico; ⁴Ponce Health Sciences University School of Medicine, Ponce, Puerto Rico; ⁵University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico

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Purpose of study Coronary fistulas (CAFs) prevalence has been reported to be 0.2% in the normal population. Orthotopic heart transplant (OHT) recipients tend to have a higher 8% prevalence. CAFs are associated with myocardial ischemia, bacterial endocarditis, right cardiac overload resulting in pulmonary hypertension and sudden cardiac death. Even though, most are initially asymptomatic, symptoms may include: dyspnea, fatigue, cardiac arrhythmias, or chest pain; and a murmur upon auscultation.

Methods used We present 3 cases of heart transplant patients who had percutaneous repair of CAFs.

Summary of results The first patient was an 18 year old male, who developed a continuous murmur 1 year post OHT. A

transthoracic echocardiogram showed a continuous flow entering the apical area of the right ventricle (RV). Coronary arteriogram confirmed a fistula from the left coronary artery to the RV by various openings. A covered stent (Graft Master, Abbot, USA) was implanted with complete closure of the defect. The second patient was a 38 year old male found with a continuous murmur 8 years after OHT. Coronary arteriogram revealed a fistula arising from the proximal right coronary artery (RCA) emptying into the RV. Two vascular occlusion devices (Amplatzer Vascular Occluder II, Abbot, USA) were used to close the fistula. The last case was a 75 year old male, OHT recipient complaining of dull chest pain, and during an exercise stress test had ventricular tachycardia. Arteriogram showed a dilated RCA from the ostium down to the area where a fistula was connecting to the right atrium. In this case, an Amplatzer Vascular plug II (Abbot, USA) was implanted successfully with no residual shunt, using an arteriovenous wire approach.

Conclusions The percutaneous repair of acquired fistula in OHT recipients is a feasible procedure that offers an alternative to open heart surgery and has proven to show good results.

585

ANALYSIS OF RACIAL DISPARITIES IN CONGENITAL HEART DISEASE

K Windham*, C Richards, S Kiparizoska, WF Campbell, F Han, ME Hall, B Kogon, MR McMullan. *University of Mississippi Medical Center, Ridgeland, MS*

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Purpose of study Critical congenital heart disease (CCHD) is a subset of heart disease that requires intervention within the first year of life and is associated with increased morbidity and mortality. The most prevalent CCHD diagnoses include: tetralogy of Fallot (TOF), d-transposition of the great vessels (TGA), hypoplastic left heart syndrome (HLHS), pulmonary atresia (PA), tricuspid atresia (TA), total anomalous pulmonary venous return (TAPVR), common truncus (CT). Previous investigations showed a similar overall prevalence of CHD in Mississippi between white and African American patients, but a substantially higher mortality in the African Americans. We hypothesized that this

higher mortality rate was related to a higher prevalence of CCHD in African Americans.

Methods used We retrospectively reviewed data from the University of Mississippi Medical Center's Research Data Warehouse using a patient cohort explorer (Epic QlikView) from 2013–17. Patients ≤ 17 years with CCHD ($n=2486$) were included in the analysis. Statistical analysis was performed with SPSS software.

Summary of results Prevalence of the individual CCHD diagnoses was variable between whites and African Americans. Regardless of this variability, African Americans exhibited higher mortality in 6 of 7 subgroups. This increased mortality achieved significance in three of the subgroups (TOF, $p=0.031$; TGA, $p=0.027$; and HLHS, $p=0.001$) (table 1).

Conclusions Given the variability in prevalence of CCHD amongst whites and African Americans, increased complexity does not seem to account for the increased mortality in African American patients. That being said, increased mortality in the African American population translates into the CCHD patients, just as it did for the overall CHD population. Larger patient cohorts and additional risk factor analyses may be needed to identify the etiologies of the disparate African American mortality.

586

IMPORTANCE OF CARDIAC MAGNETIC RESONANCE IMAGING IN VENTRICULAR TACHYCARDIA

F Ashraf*, N Yedlapati. *UTHSC, Memphis, TN*

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Case report 66 year old man with past medical history of hypertension and osteoarthritis presented with an 8 hour history of palpitations. He never lost consciousness and had no chest pain. Heart rate on arrival was 160 beats/min, blood pressure was 70/30 mmHG. Physical examination was unremarkable. Laboratory work up was remarkable for troponin of 0.08. In the emergency department, the electrocardiogram (EKG) showed wide complex tachycardia determined to be ventricular tachycardia (VT). He successfully cardioverted back into a normal rhythm. Afterward, he maintained normal sinus rhythm (NSR).

Abstract 585 Table 1

Diagnosis	Total Patients	(%) AA Prevalence	(%) White Prevalence	Total Deaths	(%) AA Mortality	(%) White Mortality	P Value
TOF	847	53	41	28	64	18	.031
TGA	477	33	58	16	50	25	.027
HLHS	421	41	54	52	73	25	.001
PA	254	61	19	19	74	11	.058
TA	242	67	27	14	79	21	.545
TAPVR	143	41	48	24	67	25	.069
CT	102	42	55	11	36	45	.949

Transthoracic Echocardiogram (TTE) revealed mild concentric hypertrophy, left ventricular ejection fraction (LVEF) of about 50%. Cardiac catheterization was done as work up of VT, and showed no coronary artery disease. A Cardiac Magnetic Resonance Imaging (MRI) was then done after consultation with electrophysiology (EP) to rule out scar as cause of VT. Cardiac MRI revealed epicardial delayed enhancement representative of scar in the inferior septal, inferior and inferolateral segments at the base of the heart.

An electrophysiology study was then done, which was positive for VT, most likely epicardial. He was eventually given an ICD and sent home on anti-arrhythmic.

Discussion Recognizing scar in VT patients is of utmost importance. Cardiac MRI can identify scar as substrate for VT. It can also be used pre-procedure to improve outcomes for VT ablation. Recent studies have shown scar identification and extent to predict VT cycle length, hence optimizing settings and timings for ICD to prevent inappropriate shocks. TTE and coronary angiography remain first-line diagnostic imaging modalities in patients presenting with VT according to the 2015 ESC guidelines and 2017 AHA guidelines. The image resolution of TTE however is not sufficient for detailed scar analysis, as illustrated by our case above. Therefore, it is important to investigate VT with cardiac MRI when there are no obvious reasons.

587 TAKOTSUBO CARDIOMYOPATHY AS A COMPLICATION OF MARIJUANA INDUCED MYOPERICARDITIS

W Vutthikraivit*, M Arevalo, C Carrasco, M Ansari. *Texas Tech University Health Sciences Center, Lubbock, TX*

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Case report Takotsubo cardiomyopathy (TC), known as a transient apical ballooning syndrome is an uncommon presentation of non-ischemic cardiomyopathy. Recent case reports have revealed that preceding myopericarditis can be the cause of TC. We describe a patient who presented with marijuana induced myopericarditis and then developed TC.

Case description A 20-year-old man presented to the hospital with a continuous, sharp, non-radiating middle chest pain for one day that was aggravated with leaning forward and deep breathing. He denied prior viral infection symptom, diaphoresis, nausea, vomiting, and palpitations. He had no past medical history or risk factors for cardiac disease except a history of regular marijuana use. Last marijuana use was 2 days ago. His vital signs and physical examination were unremarkable. Laboratory testing showed mildly elevated C-reactive protein and elevated troponin-T (1.03 ng/mL). Laboratory tests for viral infection and hepatitis were negative. Urine drug screening was positive for marijuana. Electrocardiography (ECG) showed a normal sinus rhythm and diffuse, non-specific ST segment elevations in all leads except aVR and V1 and PR segment depression in every lead except aVR. TTE revealed normal left ventricular ejection fraction (LVEF) with no regional wall motion abnormality. No pericardial effusion was presented. A diagnosis of myopericarditis was made. The next day, the patient developed worsening chest pain with dyspnea on exertion. Repeat ECG showed diffuse ST segments elevation like the initial ECG. Troponin T was increased to 2.95 ng/mL. Repeat TTE showed

depressed LVEF, mid to apical hypokinetic segments. Takotsubo Cardiomyopathy diagnosis was made based on his clinical presentation and TTE findings. He was discharged on day 5 with 3 months of colchicine and 2 weeks of ibuprofen. The follow-up TTE demonstrated normal LVEF and no regional wall motion abnormalities.

Discussion In conclusion, marijuana use should be considered in adults who present with myopericarditis without a history of viral infection. TC can potentially be associated with myopericarditis; however, the exact mechanism is still unclear.

588 DIAGNOSIS OF PLASMABLASTIC LYMPHOMA VIA PERICARDIOCENTESIS

A Bailey*, Dwight D. Eisenhower Army Medical Center, Grovetown, GA

10.1136/jim-2018-000974.594

Purpose of study Broaden medical knowledge.

Methods used Thoracentesis, Pericardiocentesis, EKG, Echocardiogram, Chest X-Ray, RUQ ultrasound, PET scan, CT Chest.

Summary of results 75 year old male who was diagnosed with Plasmablastic lymphoma via fluid analysis from pericardiocentesis despite recent thoracentesis demonstrating no evidence of malignancy. Patient initially presented to the ED for evaluation of shortness of breath, orthopnea, and peripheral edema that had been worsening over a month. Chest X-ray obtained in the ED was notable for a large right sided pleural effusion. Furthermore, the patient was found to have a moderate pericardial effusion in the ED via bedside ultrasound. The patient did not have any evidence of cardiac tamponade on physical exam, EKG, or bedside ultrasound. A formal Echocardiogram was performed on 13Apr2018 which confirmed moderate to large pericardial effusion along with LVEF 45%±5% and no evidence of tamponade physiology. A thoracentesis was performed on 14Apr2018 to further investigate etiology of the pleural effusion which lab analysis showed a transudative etiology with no evidence of malignancy. The patient endorsed significant improvement in his symptoms after thoracentesis and approximately 6 liters of diuresis with the use of IV and oral Lasix.

On 23 Apr 2018 the patient was re-admitted from the Cardiology clinic for worsening of his pericardial effusion. Echocardiogram at that time showed that the pericardial effusion was larger with possible signs of early tamponade physiology (RV and RA early diastolic partial collapse). He underwent therapeutic as well as diagnostic pericardiocentesis on 27Apr2018 with resolution of pericardial effusion. Unexpectedly laboratory analysis of pericardial fluid resulted in malignant cells consistent with Plasmablastic lymphoma. This was an unexpected finding given Plasmablastic lymphoma is a rare malignancy, especially in a patient without a history of HIV or other immunocompromised condition. Furthermore, in addition to a thoracentesis being performed a non-contrast CT Chest, RUQ ultrasound, and PET scan were obtained during his prior admission all of which had no evidence of a culprit malignancy.

Conclusions Thorough investigation of all abnormal findings should take place in order to not inadvertently miss a potentially life threatening etiology.

Gastroenterology

Concurrent Session

2:00 PM

Friday, February 22, 2019

589

TRANSCRIPTOME PROFILING OF INFLAMMATORY BOWEL DISEASE PATIENTS REVEALS SHARED AND UNIQUE ALTERATIONS IN IMMUNE CELLS, MOLECULAR PATHWAYS, AND TRANSCRIPTS

HM Penrose*, SD Savkovic. Tulane University School of Medicine, New Orleans, LA

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Purpose of study Inflammatory Bowel Disease (IBD), characterized by chronic inflammation of the intestine, is driven by an altered immune profile and inflammatory mediators. However, the heterogeneous nature of IBD requires better understanding of common and distinct changes within individuals for more precise diagnostics and tailored therapeutic regimens. Using publicly available IBD transcriptomes from American and European patient cohorts, we aimed to elucidate alterations, both similar and distinct, in the immune cell landscape, molecular pathways, and transcripts in affected tissue.

Methods used Whole transcriptomes from healthy controls, active or non-active IBD cohorts were utilized (~500 patient endoscopic biopsies, NCBI GEO). Immune profiles were assessed by the core LM22 signature (CIBERSORT, $p < 0.05$). Pathway analysis was performed using Ingenuity Pathway Analysis (IPA, Qiagen, $p < 0.05$).

Summary of results In healthy human colon, immune cell profiling revealed a consistent abundance of B cells (plasma), T cells (CD4 memory resting), mast cells (resting), and macrophages (M2). In active-IBD involved tissue, we observed substantial alterations in the immune profile including increased neutrophils, T CD4 memory activated cells, active dendritic cells, M0/M1 macrophages, B naïve cells, as well as reduced T CD8 cells, Tregs, and M2 macrophages. Next, relative to healthy control IPA of differentially expressed transcripts from IBD cohorts revealed similarly altered pathways linked to bacterial (TLR, LPS/IL-1), inflammasome, and inflammatory signaling (NF κ B, ERK/MAPK, p38, iNOS, PI3K). However, pathways that differed among IBD cohorts included select signaling linked to inflammation (IL17A, OX40), growth (TGF β , PTEN, p53), and metabolic (PPAR α , leptin) functions. At the transcript level, we found several novel genes consistently altered in IBD affected tissues including KYNU, LPCAT1, CLDN8 as well as those differentially altered including MASPIN, FGFR2, AGRP, INSR.

Conclusions We determined the global immune cell landscape and molecular pathways both similarly and differentially altered, highlighting the complex, heterogeneous nature of IBD pathobiology. Utilization of this approach may provide clues for development of precise diagnostic and personalized therapeutics for IBD.

590

BRAIN MRI ANALYSIS FOR NEUROANATOMICAL ABNORMALITIES IN CYCLIC VOMITING SYNDROME FOCUSING ON MARIJUANA USE

¹RA Mandania*, ¹MI Ramirez, ²TH Davis, ¹R McCallum. ¹Texas Tech University Health Sciences Center, El Paso, TX; ²Texas Tech University, Lubbock, TX

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Purpose of study Cyclic vomiting syndrome (CVS) in adults, is a disorder characterized by recurrent bouts of nausea, vomiting, and abdominal pain separated by symptom-free periods lasting days to months. Marijuana use (MU) has been recognized as a major etiological factor. Literature regarding changes in the central nervous system (CNS) during CVS attacks is limited. This study investigated whether there are CNS neuroanatomical differences (Dif) identified by brain MRI, in acutely symptomatic CVS patients (PTs) reporting chronic MU, compared to non-MU CVS, as well as healthy controls (HC).

Methods used 14 CVS-MU, 9 non-MU CVS, and 20 HC age and gender matched subjects (SU) participated. CVS-MU reported chronic MU (>3 years). All CVS PTs completed MRI scans during a symptomatic episode. High-resolution anatomical Magnetization-Prepared Rapid Gradient-Echo1 (MP-RAGE) images were obtained, preprocessed, and tested from all SU for Dif in subcortical volume. Surface-based results were thresholded and corrected for multiple comparisons using Monte Carlo simulation.

Summary of results In the MRI analysis, non-MU CVS PTs had significant (Sig) Dif in subcortical grey matter volume (figure 1), left and right hippocampus, $p = 0.0069$; $p = 0.00078$; and left amygdala, $p = 0.0309$, compared to CVS MU PTs who were similar to HC. Marginally Sig results were also observed in the left and right putamen, left and right caudate, left pallidum, and left accumbens.

Abstract 590 Figure 1 Mean and SEM bars indicate 95% confidence intervals

Conclusions Based on MRI analysis we conclude that non-MU CVS differ from CVS-MU in having Sig reductions of hippocampus, amygdala, putamen, caudate, pallidum, and accumbens; regions associated with pain, emotion, stress, and dopaminergic innervation. CVS-MU seems to be protected from this reduced grey matter volume, consistent with the concept that Cannabinoid Hyperemesis seems to be a separate entity.

591

FECAL INCONTINENCE IN CHILDREN WITH ADHD, BEFORE AND AFTER ADHD TREATMENT: THE ROLE OF STIMULANT MEDICATION

L McCann*. University of South Alabama, Mobile, AL

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Purpose of study The aim of this study is to compare the resolution of FI in children with ADHD before and after treatment with ADHD stimulants. We hypothesize that FI will be higher prior to initiation of ADHD stimulants and lower after initiation.

Methods used A retrospective chart review from 2011–2017, using ICD 9–10 codes for FI, constipation, and ADHD. Children aged 5yo–19yo were included. Patients excluded if

Abstract 591 Figure 1

deceased, severe neurological diagnoses, anorectal malformations, or previous GI surgery. Statistical analysis was done using Fisher's exact test and logistic regression analysis.

Summary of results This study included 174 patients with ADHD. There were 106 males (61%) and 68 females (39%). Data showed 171 of 174 patients (98%) had constipation and 22 patients (12%) had FI and ADHD. Of these 22 patients, all were currently being treated for FI with laxatives. Among the 19 patients with results, 14 (73%, 95% CI[48%, 89%]) did not have recurrence of FI after stimulants. 18 (82%) were on stimulants, and 4 (18%) were not. The effect of stimulant on FI is not significant ($p=0.15$) with an odd ratio of 0.13. 133 patients out of 174 patients (76%) were currently on ADHD stimulant medications. Mean length of constipation treatment and ADHD stimulant treatment were similar, at 3 years. Fisher's exact test and logistic regression analysis were used.

Conclusions Children with ADHD have a higher incidence of FI. Treatment of ADHD with stimulants helps in resolution of FI.

592 DOES CYCLIC VOMITING SYNDROME CREATE A NEW CHALLENGE IN CLINICAL CARE?

J Wilson*, P Williams, N Shankar, I Sarosiek, K Espino, S Tonarelli. *Texas Tech University Health Sciences Center, El Paso, TX*

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Purpose of study Cyclic Vomiting Syndrome (CVS) is characterized by intermittent episodes of nausea and vomiting followed by asymptomatic periods lasting days to months. Lack of awareness of CVS may result in decreased quality of care and delayed diagnosis. This study focuses on understanding the impact of CVS with a patient perspective on illness experience.

Methods used 737 CVS patients completed an anonymous survey through Qualtrics from September 2016 to May 2017. The survey included patient demographics, medical history, medications, and social history. Specific questions for CVS focused on illness experience, healthcare utilization, and quality of life. Individual questions were analyzed separately as each item was voluntary.

Summary of results Mean age of onset of CVS symptoms was 18.5 years. 79.4% had symptoms for more than 12 months prior to CVS diagnosis. During evaluation, patients frequently received studies including gastric emptying (50.4%), endoscopy (18.8%), ultrasound (15.4%), x-ray (14.9%), or MRI (13.3%). Many were misclassified as gastroparesis (19.3%), dyspepsia (15.9%), or cholecystitis (12.5%) prior to CVS diagnosis. 31%

were unable to maintain employment. 18% left school due to medical expense. 88.6% attempted to reduce stress to alleviate symptoms. 69% had at least one emergency department (ED) visit in the last year with an average of 4 visits in the past 12 months. 67% had at least one hospital admission in the past year with a mean duration of 4.6 hospital days. When comparing patients prescribed Amitriptyline, Ondansetron, and Promethazine to those not on conventional treatment, there was no significant difference in number of ED visits or duration of hospitalization.

Conclusions Delayed diagnosis can be an immense burden for CVS patients. With an average of 4 ED visits per year, our patients had substantial utilization of healthcare services. Further studies should focus on potential targets for treatment to reduce healthcare utilization and improve quality of life. Diagnostic delay in CVS can be minimized by improving clinician awareness of CVS in hospitals, clinics, and the ED.

593 RUMINATION SYNDROME IS A TREATABLE ENTITY: A SINGLE-CENTER EXPERIENCE

¹A Robles*, ²HD Quezada, ²E Tatro, ¹R McCallum. ¹Department of Medicine, Texas Tech University Health Sciences Center, El Paso, TX; ²Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, TX

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Purpose of study Rumination syndrome (RS) is an under-recognized gastrointestinal functional disorder characterized by effortless regurgitation of food and/or liquids that starts within minutes of eating. Lack of awareness of this condition leads to a delay in diagnosis and in initiation of appropriate therapies, impacting a patient's quality of life. We highlight the clinical aspects of RS and report the outcomes of a single-center case series of RS utilizing two primary treatments options: Tricyclic Antidepressants (TCAs) and diaphragmatic breathing/relaxation techniques (DB/RT).

Methods used Patients referred to an academic motility center for vomiting of unknown origin and who met Rome IV criteria for RS were identified from 2017 to 2018. At the time of presentation, their main working diagnosis was gastroparesis. All received an electronic file with instructions on how to perform DB/RT and started pharmacotherapy with TCAs (nortriptyline 10–50 mg). Patients having completed a minimum of 3 months of therapy were interviewed and asked to complete a questionnaire detailing their response.

Summary of results A total of 14 patients (10 female, mean age 44.7 [range 26–71]) having met the criteria for RS underwent the treatment protocol and then completed a follow-up questionnaire. Median time from reported onset of symptoms to diagnosis was 33 months [range 2–180], weight loss prior to treatment ranged from 10–60 lbs., 2 had a jejunostomy feeding tube, and one was receiving TPN. The majority of patients (71.4%) reported improvement with the treatment regimen: 14.3% complete resolution of symptoms while 57.1% had partial improvement.

Conclusions RS is an under-recognized gastrointestinal functional disorder with a characteristic history and presentation. Inability to recognize RS leads to both a delay in diagnosis and in initiation of appropriate therapies, thus increasing patient morbidity. The combination of diaphragmatic breathing/relaxation techniques with TCAs (nortriptyline) can effectively suppress rumination events, reduce accompanying comorbidities, and improve quality of life.

594 RECURRENT HEPATITIS C AFTER ANTIVIRAL THERAPY

¹YK Reddy*, ^{1,2}LC Thornton, ^{1,2}B Waters. ¹University of Tennessee, Memphis, TN; ²VA Medical Center, Memphis, TN

10.1136/jim-2018-000974.600

Purpose of study Direct acting antiviral (DAA) therapy has resulted in high rates of sustained viral response (SVR) of Hepatitis C. There have been concerns of reinfection of Hepatitis C (HCV) in patients with previous substance abuse. In a study of 8558 VA patients, 83% reported a history of intravenous drug abuse (Cheung, 2000). The objective of this study was to assess the frequency of documented HCV recurrence in patients treated with DAA with a previous SVR.

Methods used Retrospective chart review of HCV patients who received DAA therapy at the Memphis VA Medical Center from 1/1/2014 and 9/22/2018. Patients with a SVR were studied for documentation of recurrence of HCV viremia. The review utilized the VA Hepatitis C registry and VA Computerized Patient Record System (CPRS).

Summary of results 1305 HCV patients were treated with DAA. 1158 were followed >14 weeks posttreatment and 1017 (87.8%) returned for repeat HCV RNA testing. Of the 1017 tested, the SVR rate was 97.5%. Only 4 of the 1017 had documented recurrent HCV viremia following SVR. All four patients were male with a median age of 64.5 (range 43 to 68). Three were African-American and one was Caucasian. 1 HIV+, 3 HIV-. One patient had liver transplantation from a known HCV viremic cadaveric donor. One patient was coinfecting with HIV with ongoing sexual risk factors. One patient reported recurrent cocaine use. One patient did not report any HCV risk factors. Median duration from time of SVR to recurrent positive HCV RNA was 17.5 months (1 month, 10 months, 25 months, 28 months).

Abstract 594 Table 1

	Patient 1	Patient 2	Patient 3	Patient 4
HCV genotype of first occurrence	1b	3a	1a	1a
Treatment	ledipasvir/ sofosbuvir	daclatasvir/ sofosbuvir	ledipasvir/ sofosbuvir	ledipasvir/ sofosbuvir
Viral load detected during recurrence	9580	9950	570	59
Age at recurrent viral load detection	43	69	61	68
HCV genotype during recurrence	1a	1a	Unknown	Unknown

Conclusions In this series of Hepatitis C patients monitored after antiviral therapy, the sustained response rate was 97.5%. There have been concerns regarding the risks of reinfection in Hepatitis C patients. Fortunately following a sustained viral response, few patients in this study had documented recurrent Hepatitis C viremia.

595 HEMORRHAGIC ASCITES AS A MANIFESTATION OF HEPATIC ANGIOSARCOMA

A Penmetsa*, J Sweeney, S Rawlins. SUNY Upstate, Syracuse, NY

10.1136/jim-2018-000974.601

Case report Hemorrhagic ascites (HA) often poses a diagnostic dilemma due to its broad differential diagnosis and rare presentation. We present the case of a 75 year old male with a complicated medical history and occupational exposure to arsenic and polyvinyl chloride. He initially went to an outside hospital for worsening abdominal distension and dyspnea and was found to have HA, a liver mass, and newly found cirrhosis. He was discharged in stable condition, however presented to our institution with re-accumulation of ascites. Paracentesis yielded fluid with a serum ascites albumin gradient <1.1, a total fluid protein of 3.2, an erythrocyte count of 575,030/ μ L, with cell count negative for spontaneous bacterial peritonitis. Fluid cytology was negative for malignancy on repeated studies.

Computed tomography (CT) angiography revealed a 3 cm hepatic lesion with decreased arterial enhancement and no active extravasation. Magnetic resonance (MRI) with liver mass protocol confirmed these findings as well as several smaller hepatic lesions. Evaluation for underlying etiologies of cirrhosis was negative and tumor markers were unremarkable. Serial imaging also ruled out portal and hepatic vein thrombosis, but did demonstrate omental caking. Due to bleeding risk from liver lesions, a biopsy of the greater omentum was performed, revealing high-grade angiosarcoma, likely with hepatic primary.

The literature has defined HA as the presence of an ascitic fluid erythrocyte count greater than 50,000/ μ L. HA is most commonly associated with malignancy; including primary gastrointestinal tumors, angiosarcomas, lymphoma, or metastases. Liver cirrhosis, endometriosis, trauma, iatrogenic injury, and infectious etiologies should also be considered. More serious causes associated with acute abdomen include intraperitoneal organ rupture, mesenteric ischemia with bowel gangrene, and acute necrotizing pancreatitis. Rare etiologies include sarcoidosis, Henoch-Schönlein purpura, and systemic lupus erythematosus.

Upon recognition of HA, an aggressive search for an underlying diagnosis is imperative. In our patient, angiosarcoma remained high in our differential despite negative fluid studies due to his occupational exposure and the known correlation. This prompted serial abdominal imaging with CT and MRI to facilitate an eventual biopsy and final diagnosis.

596 EARLY INTRAUTERINE TRANSFUSION IN RH ISOMMUNIZATION ASSOCIATED WITH CHOLESTATIC HEPATIC DISEASE AND IRON OVERLOAD TREATED WITH DEFEROXAMINE CHELATION THERAPY: A CASE REPORT

¹I Varier*, ²MB Fletcher, ³M Serrano. ¹Tulane – Ochsner Residency Program, New Orleans, LA; ²Pediatric Hematology and Oncology, Ochsner Health System, New Orleans, LA; ³Pediatric Gastroenterology, Hepatology and Nutrition, Georgetown University Hospital, Washington DC

10.1136/jim-2018-000974.602

Case report Antenatal management of fetal anemia in hemolytic disease of fetus and newborn (HDFN) by intrauterine transfusions (IUT) is well understood, although there is paucity of data on postnatal management of complications of IUT including iron overload. We discuss a 34 w 4 d male neonate with isoimmune hemolytic anemia who was treated with 9 IUTs including 8 intraperitoneal transfusions and developed significant iron overload and cholestatic jaundice. At birth he

presented with a total bilirubin (TB) of 7.3 mg/dl and direct bilirubin (DB) of 1.2 mg/dl. He had a rapid rise in DB to >14 mg/dl (TB to 25 mg/dl) at 20 days of life. He peaked his TB at 26.8 mg/dl at 2 months of age. Hyperbilirubinemia in this setting was treated with failed phototherapy and ursodiol 15 mg/kg/dose BID. At 2 weeks of life he developed anemia (Hb-7.6 g/dl, Hct 21%) with very low reticulocyte count requiring packed red blood cell (pRBC) transfusions. He also received 2 doses of IVIG (750 mg/kg) at day of life 0 and 1. rHuEPO 250 units/kg three times a week was started at 40 days of life to minimize the number of transfusions. Despite treatment, there was a dramatic increase in ferritin from 2294 ng/ml to 12,244 ng/ml at 27 days. He received 4 pRBC transfusions which accounted to 166 ml by volume. Liver function tests: AST ranged from 23–679 units/L, ALT 6–339 units/L, INR <1.1. Further comprehensive work-up including genetic studies for cholestasis were unremarkable. Liver biopsy showed 4450 mcg/g of iron, confirming iron overload. Iron chelation therapy with deferoxamine 30 mg/kg was initiated at 2 months of age. He completed 11 weeks of daily deferoxamine treatment with improvement in cholestasis (TB 2.5 mg/dl and DB 1.6 mg/dl) and ferritin levels decreased to <1500 ng/ml. In conclusion, chelation therapy with deferoxamine should be considered in iron overload which can be a consequence of intrauterine transfusions and cause severe cholestatic liver disease.

597

ASSESSMENT OF MOTILITY PARAMETERS CAPTURED BY WIRELESS MOTILITY CAPSULE IN GASTROPARETIC PATIENTS WITH AND WITHOUT UTILIZATION OF GASTRIC ELECTRIC STIMULATION THERAPY

P Loganathan, R McCallum*, N Vega, K Espino, M Bashashati, I Sarosiek. *TTUHSC El Paso, El Paso, TX*

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Purpose of study Gastroparesis (GP) is a syndrome with delayed gastric emptying resulting in symptoms without any evidence of obstruction in the gastrointestinal tract (GI). The SmartPill or wireless motility capsule (WMC) assesses intraluminal pH, temperature, pressure, and records transit time and contractile activity throughout the GI tract. The aim of this study is to analyze the differences captured by the SmartPill in the phasic pressure profiles including amplitude, contractions and gastric motility index (MI) of the stomach in GP subjects with and without gastric electrical neurostimulation (GES).

Methods used SmartPill results of 6 GP patients with a gastric electric stimulator (GES) were compared with a control group consisting of 6 GP patients without gastric electric stimulator. All 12 patients were categorized as severe based on symptom index. Control patients underwent surgery after the SmartPill study for GES implantation, therefore an antral smooth muscle biopsy was obtained from all patients. The motility index (MI) was calculated as $\ln(\text{sum of pressure amplitudes} \times \text{number of contractions} + 1)$ based on values obtained during the SmartPill studies.

Summary of results The mean 30 min pre-gastric emptying MI in patients with GES was 0.93 vs. 0.39 for patients without GES ($p=0.13$). The mean 30 min post gastric emptying MI was 0.4950 vs. 0.2783 ($p=0.37$). The 30 min

pre-gastric emptying amplitude (24.6 vs. 10.8, $p=0.09$) and 30 min post-gastric emptying amplitude (11.1 vs. 7.6, $p=0.1$), 30 min pre-gastric emptying contractions (1.8 vs. 2.0, $p=0.9$) and 30 min post-gastric emptying contractions (2.8 vs. 2.8, $p=0.9$) from SmartPill study were also not statistically significant between patients with and without gastric electrical stimulator. We found that the mean number of interstitial cells of Cajal per high power field in antrum biopsy taken at the time of surgery was not statistically different between these two groups (10 vs. 6, $p=0.1$).

Conclusions

1. Gastric electric neurostimulation does not improve the parameters of gastric motility as assessed by the WMC method;
2. The depleted ICC present in severe GP patients may contribute to impaired gastric neuromuscular function.

598

PRIMARY PEDIATRIC NON-HODGKIN LYMPHOMAS OF THE GASTROINTESTINAL TRACT: A POPULATION BASED ANALYSIS

B Naeem*, S Jain. *University of Texas Medical Branch Galveston, Texas City, TX*

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Purpose of study Primary gastrointestinal non-Hodgkin lymphomas (PGINHL) are a heterogeneous group of rare GI tumors with very limited available data. Here, we present the clinical characteristics, natural history and survival outcomes of these tumors in the pediatric population utilizing a large population cohort.

Methods used Surveillance, Epidemiology, and End Results (SEER) database was queried for patients aged 0 to 19 years with PGINHL between 1973 and 2014.

Summary of results A total of 452 cases were identified (mean age 11.0 [± 5.1] years, whites 84.1%, males 76.5%). The majority of tumors were noted in the small bowel (SB) (47.6%), followed by large bowel (LB) (28.5%) and the stomach (10.0%). In the SB and LB, respectively, ileum and cecum were the most common sites of tumor involvement. Overall, the most common histological subtype at all locations was Burkitt lymphoma (51.8%), followed by diffuse large B-cell lymphoma (DLBCL) (26.1%). In the stomach however, DLBCL was the most common histological subtype. No significant differences were noted in term of age, gender, disease stage at all tumor sites. Mean overall survival (OS) of the entire cohort was 400 months with a 5 year, 10 year and 30 year survival rate of 86%, 86% and 79% respectively. Large bowel tumors had the best long-term survival rates whereas; gastric tumors had the worst (30 year survival rate 84% and 74%, respectively). Similarly, 30 year survival rates for patients with Burkitt lymphoma, DLBCL and other histologies were 83%, 77% and 75%, respectively. Overall, 328 (72.6%) patients received surgery. No significant survival difference was noted between patients who underwent surgery and those who did not.

Conclusions Our study presents the largest data set of PGINHL and describes the clinical features and outcomes of these patients in addition to summarizing the literature.

599

SEVERE HYPERTRIGLYCERIDEMIA AND PANCREATITIS WITH DRAMATIC RESPONSE TO INSULIN THERAPYN Merza*, T Lindgren, D Lin, K Cutts, T Naguib, M Saadaldin. *Texas Tech Univ HSC, Amarillo, TX*

10.1136/jim-2018-000974.605

Case report Severe hypertriglyceridemia is frequently associated with acute pancreatitis. The level of triglycerides (TG) is usually controlled with fibrates but, with poor adherence to therapy, a resultant peak in triglycerides can precipitate acute pancreatitis. Insulin therapy has been employed to control TG levels but has not been the mainstay of therapy. We report a case where insulin therapy alone has resulted in dramatic improvement of both TG levels and pancreatitis.

A 26-year-old female with known history of Type 2 DM, came in with severe epigastric abdominal pain, nausea, and vomiting without hematemesis. The abdominal pain was, described as ‘stabbing,’ and radiates to back with no precipitating or alleviating factors. Also states that she has had a pink-orange, maculopapular, itchy rash on the arms, back, buttocks was noted for 3 months. Initial labs were showing blood glucose of 885, normal ALT and AST, lipase of 1,232, amylase of 891, lactate of 2.9, WBC of 20 000. Cholesterol was 648, triglycerides 5,738, HDL 37, and LDL 111. CT revealed acute pancreatitis and severe fatty infiltration of the liver with mild hepatomegaly and no evidence for cholelithiasis or cholecystitis.

In addition to supportive care in the form of bowel rest, fluid infusion, and pain control, we had multiple treatment options including heparin, insulin, fibrates, and apheresis. Fibrates therapy was not possible due to emesis, and insulin therapy was initiated in view of hyperglycemia. Our patient was treated successfully with regular insulin drip of 1 Unit/kg/24 hour and 5% Dextrose in water infusion. A dramatic response in TG levels dropping to 1705 mg/dl resulted in 2 days. On the fourth day of the hospitalization liver enzymes and leukocyte count were normalized and the patient was started on Fenofibrate and was discharged to home.

Insulin infusion may produce dramatic improvement in hypertriglyceridemia-induced acute pancreatitis through upregulation of lipoprotein lipase. This modality is better than heparin infusion that may lead to deterioration of hemorrhagic pancreatitis, and fibrate intake that is limited by emesis. It can also spare the use of apheresis.

Hematology and Oncology**Concurrent Session****2:00 PM****Friday, February 22, 2019**

600

QUANTIFICATION OF THE INFLUENCE OF LYMPH NODE STROMAL MICROENVIRONMENT ON THE PROTEIN EXPRESSION AND REGULATION OF RENAL CELL CARCINOMA PROGRESSION

^{1,2}GD Unis*, ²R Moret, ²Q Nguyen, ³C Morais, ²X Zhang, ²G Maresh, ²L Hellmers, ⁴D Margolin, ⁴S Talwar, ⁴M Latsis, ⁴M Variano, ³G Gobe, ⁴D Canter, ⁴S Bardot, ²L Li. ¹The University of Queensland – Ochsner Clinical School, Jefferson, LA; ²Ochsner Health System, Jefferson, LA; ³University of Queensland, Woolloongabba, Australia; ⁴Ochsner Health System, Jefferson, LA

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Purpose of study Renal cell carcinoma (RCC) is the most common solid tumor of the adult kidney, with cancer specific mortality of 30%–40%. Lymph node (LN) involvement is a strong negative prognostic marker in RCC. Previous experiments using orthotopic xenograft models, LN stromal cells (LNSCs, HK) were found to alter parameters associated with RCC progression. Two different RCC cell lines were used in this study. ACHN dependent on HK cells, while SN12K1 cells are independent of HK cells. This study evaluates alterations in protein expression in RCC cells induced by LNSC and correlates this alteration and promotion of RCC progression via expression of proteins on cancer cells.

Methods used RCC cell lines (ACHN, SN12K1) were cultured with or without HK cell supernatant and cell lysates were subjected to proteomic analysis. Vital protein markers were selected using information from a public database <http://www.proteinatlas.org>. Differentially expressed proteins that were significant in RCC or other cancers were confirmed and quantified by Western Blotting.

Summary of results Based on proteomic analysis, 128 proteins were present in both cell lines with or without HK cell sup. treatment. Protein markers including CTSD, SAMHD1, FAM114A1, RFC5, NAPA, SRP68, SNX6, AIMP1, PSMD6, and YWHAE, were selected for further investigation on their published significance in cancer survival data. Quantification validated early proteomic findings showing differential expression of proteins between the two RCC cell lines and altered by HK sup. to identify mechanistic pathways of HK sup. on RCC progression and metastases.

Conclusions Conditioned media from LNSC HK cell alters expression levels of proteins in RCC which may promote tumor progression and metastases. Further studies into the interplay between LNSC and malignancies and, subsequently, blocking those pathways may lead to novel treatments for RCC and other solid tumors.

601

SARCOMA IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS: EXAMINING OUTCOMES AND SURVIVAL FROM 2005–2015

¹K Fahimipour*, ^{1,2}R Gardner, ^{1,2}D Leblanc, ^{1,2}C Morrison, ^{1,2}MC Velez, ^{1,2}RG Watts, ^{1,2}L Yu, ^{1,2}P Prasad. ¹LSU Health Sciences Center New Orleans, Kenner, LA; ²Children's Hospital-New Orleans, New Orleans, LA

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Purpose of study Dramatic improvements in survival have been achieved for children and adolescents with cancer. Sarcomas are a rare form of mesenchymal tumors that can be divided into two categories: soft tissue sarcomas and cancers of the bone. Over 20% of patients diagnosed with solid malignant cancers are sarcomas in the pediatric population and less than 1% are sarcomas in the adult population. A retrospective chart review was conducted in which survival outcomes and mortality rates of sarcomas of the bone were analyzed in order to determine a link amongst the different types of sarcomas.

Methods used The cases of sarcomas in patients ages 0–22 years treated at Children's Hospital New Orleans (CHNOLA) from January 1, 2005 to January 1, 2015 were examined and compared to the treatment and outcome to national survival data from the Surveillance, Epidemiological and End Results (SEER) study. The items collected include: Information regarding sarcoma type, site of diagnosis, year of diagnosis,

treatment received (Chemotherapy, Radiation, Surgery), Alive/Dead, cause of death, survival months.

Summary of results Overall, a trend was observed where CHNOLA patients had higher survival outcomes (14.3% higher) and lower mortality outcomes (10.84% less) when compared to SEER database; $p=0.08$. ($p<0.05$). CHNOLA patients diagnosed with osteosarcoma had decreased survival, when compared to SEER; $p=0.48$. Ewing's Sarcoma patients treated at CHNOLA had increased survival when compared to SEER; ($p=0.27$). CHNOLA chondrosarcoma patients had increased survival when compared to SEER ($p=0.07$). CHNOLA male patients had increased survival when compared to SEER ($p=0.07$). The majority (61%) of patients with sarcomas were white in SEER and CHNOLA.

Conclusions CHNOLA patients diagnosed with sarcoma had higher survival outcomes (14.3% higher) and lower mortality outcomes (10.84% less) when compared to SEER database; $p=0.08$. ($p<0.05$)

602 EXAMINING THE EFFECT OF A CYCLIC PEPTIDE CXCR4 ANTAGONIST, LY2510924, IN AN ORTHOTOPIC XENOGRAFT MICE MODEL ON COLORECTAL CANCER TUMOR GROWTH AND METASTASIS

¹R Ahmad*, ¹D Levine, ²L Hellmers, ²G Maresh, ²R Moret, ²X Zhang, ²L Li, ^{2,3}D Margolin. ¹University of Queensland School of Medicine, Brisbane, Australia; ²Institution of Translational Research Ochsner, New Orleans, LA; ³The Ochsner Clinic, New Orleans, LA

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Purpose of study Colorectal cancer (CRC) is a leading cause of mortality in the United States; with distant metastases, 5 year survival is 14%. Previously we found that CRC tumor-initiating cells (Co-TIC) expressing CD133 and CXCR4, support extra-nodal metastasis (ENM) of CRC through interactions of CXCR4 with CXCL12 found on lymph node stromal cells (LNSCs). We hypothesized that blocking this interaction would prevent ENM. Our aim is to investigate the effect of a cyclic peptide CXCR4 antagonist, LY2510924 (LY), as a monotherapy or combination therapy with the chemotherapeutic drug (5FU) to test our hypothesis.

Methods used Our study utilized three luciferase-tagged human CRC cells (HCT-116, HT-29, and SW620) and one patient-derived tumor cell (CaCoPt302). These tumor cells were intra-rectally injected $\pm$ LNSCs (HK) in NOD/SCID mice. LY was given subcutaneously qd for 14 days either -1 or $+5$ days after the cancer cells were injected into the mice. 5FU was administered intravenously qw from week 6–9 with leucovorin. Tumors, liver and lungs were harvested for bioluminescent imaging and weighing; additionally, H and E and immunohistochemistry (IHC) staining of these specimens were performed.

Summary of results HK cells significantly enhanced tumor growth and ENM in all cell lines. H and E and IHC showed that our orthotopic xenograft model recapitulated the histological structure and exhibited the characteristics of CRC. In both HCT-116 and SW620 models, while monotherapy of LY had a decrease of tumor progress similar to 5FU alone; combination therapy of LY and 5FU showed significant reduction in tumor weight and ENM in comparison to the control group. In both HT-29 and CoCaPt302 models, there was no significant difference in monotherapy or combination therapy.

Conclusions It is evident that LY therapy effects each model differently. Varying cell lines or patient tumors may have

varying expression of molecule markers, which may affect their drug sensitivity. Further studies in their difference may guide us to an effective treatment for an individual patient.

603 SUPPORTING CARE FOR LONG-TERM SURVIVORS OF PEDIATRIC CANCER IN THE ELECTRONIC HEALTH RECORD

^{1,2}LT Ber*, ³C Petersen, ²CU Lehmann. ¹Meharry Medical College, Nashville, TN; ²Vanderbilt University, Nashville, TN; ³Mayo Clinic, Rochester, MN

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Purpose of study Health outcomes research conducted in the last three decades established that survivors of childhood cancer are at increased risk for morbidity and mortality during their late childhood and young adult years, largely due to therapies that treated their primary malignancies (Hudson, Ness, Guney, et al, 2013; Robinson LL. 2014). Despite ample research and knowledge on the long-term effects of the treatments received, there is a lack of long-term follow up and surveillance (Hewit, Weiner, & Simone, 2003). Suh and colleagues revealed that internists were uncomfortable treating these patients and made poor medical decisions, partly due to a lack of comprehensive treatment history being obtained. Physicians were also unaware of current guidelines in treatment and preferred to conduct follow-up care in conjunction with a national cancer institutes. The purpose of this project was to combine and analyze data on the long-term effects of cancer treatments and required screening to develop data elements and logic for electronic health record (EHR) functionalities supporting decision support to care for long-term survivors of pediatric cancer.

Methods used We conducted a literature review and extracted long-term effects of childhood cancer from published articles and the Long-Term Follow-Up Guidelines published by the Children's Oncology Group into an Appendix.

Summary of results In total 858 long term effects were described, and 728 key action statements and conditional triggers for each exposure were defined. Data fields to measure exposure elements were also described. Radiation caused the greatest number of adverse effects and the urogenital system was the most widely affected organ system. A total of 399 action statements were lacking important information to be decidable (e.g., at what time they should be performed).

Conclusions We recommend that the authors from the Children's Oncology Group revisit their work product in order to disambiguate and increase decidability. The decision support rules for EHRs outlined will support physicians in conducting more effective surveillance and practicing preventive medicine once adopted by EHR vendors.

604 THE RELATIONSHIP BETWEEN OXYCODONE AND QTC INTERVAL IN SICKLE CELL DISEASE

¹J Schaub*, ¹JD Pollard, ¹J Knudson, ¹C Carroll, ¹T Tanawuttiwat, ¹W Wang, ²G Kato, ³S Majumdar, ¹J Maher. ¹University of Mississippi Medical Center, Ridgeland, MS; ²University of Pittsburgh School of Medicine, Pittsburgh, PA; ³Children's National Health System, Washington, DC

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Purpose of study Persons with sickle cell disease (SCD) have increased risk of sudden cardiac death, risk factors for

which include QTc interval prolongation on the electrocardiogram (ECG), a measure of abnormal cardiac repolarization. Some medications are well-known risk factors for QTc interval prolongation. Patients with SCD are commonly prescribed opioid medications, such as oxycodone or methadone, for pain management. Although QTc prolongation by methadone is well-described, there are several inconclusive reports suggesting that oxycodone may prolong QTc.

Methods used We are conducting a study QTc-modifying genetic and secondary factors in SCD, targeting enrollment of 500 (250 adults and 250 children) patients with SCD, at baseline status, from sickle cell clinics in the University of Mississippi Medical Center. In addition to a resting 12-lead ECG and numerous labs, we collected demographic information and a detailed list of medications, including opioid use and any use in the prior 24 hours. In this interim analysis, complete data on oxycodone use and baseline ECG were available for 229 participants (181 adults, 48 children). We investigated the correlation of oxycodone use with the QTc interval, and its sub-components QRS and JTc interval.

Summary of results Among all participants analyzed, oxycodone use was associated with a small but non-significant increase of the QTc interval (431.06 vs 433.58 msec, $p=0.230$) and increase in prevalence of prolonged QTc (14.05% vs 17.5%, $p=0.495$); analysis of the effects of oxycodone use on the QRS and JTc also revealed no significant difference for either one. With further analysis of adults only, the differences remained non-significant. Additionally, a subset analysis of those having taken, versus not having taken, oxycodone within the prior 24 hours also revealed no significant difference (QTc 433.22 vs 433.84 msec, $p=0.89$).

Conclusions Although several prior reports have proposed that oxycodone prolongs QTc, this study found no significant effect of oxycodone on QTc in patients with SCD.

605 EFFICACY OF ADJUVANT VERSUS NEOADJUVANT CHEMOTHERAPY IN HISPANIC/LATINO WOMEN WITH EARLY STAGE, TRIPLE NEGATIVE BREAST CANCER (TNBC)

A Philipovskiy*, J Corral, R Heydarianna, S Gaur. *Texas Tech University Health Science Center, El Paso, TX*

10.1136/jim-2018-000974.611

Purpose of study The aim of this study was to investigate the efficacy of adjuvant chemotherapy versus neoadjuvant chemotherapy in Hispanic/Latino women diagnosed with an early stage TNBC.

Methods used We retrospectively reviewed 115 charts of women diagnosed with TNBC stages I–III, that were treated at Texas Tech University Health Science Breast Cancer Center from 2006 to 2016. We divided all treated patients into two groups: those that received adjuvant chemotherapy (ACT) versus those treated with neoadjuvant chemotherapy (NACT). For statistical analysis, we used unadjusted and adjusted COX proportional hazards model. Kaplan–Meier survival curves were generated.

Summary of results Of the 115 patients diagnosed with TNBC – 32 (28.5%) received NACT while 83 (71.5%) received ACT. Patients undergoing NACT were found to be

younger, with a mean age of 51 (range 22–67) compared with those in the ACT group that had a mean age of 54 (range 32–80) ($p=0.05$). Additionally, the women in the neoadjuvant group had more advanced cancer, stage III (56%) II (29%) in contrast to the adjuvant group, stage III (21%), II (48%). Women in the group that received ACT were found to have progression-free survival (PFS) at 3 and 5 years of 89% and 59%, respectively. Women that received NACT had PFS at 3 and 5 years of 75% and 43%, respectively. There was no statistically significant difference in PFS between the two groups. In our study, we reported pathological complete response (pCR) after NACT at 37.5% which is higher than that reported in the literature (20%–30%). Surprisingly, we found that patients that received ACT were less likely to die from breast cancer during the observation period, as to compare with patients that did receive NACT (overall HR 0.62 (0.399, 0.962) 95% CI).

Conclusions Despite the robust pCR to NACT at 37.5% among Hispanic/Latino women with TNBC, we did not find any statistically significant difference in PFS at 3 and 5 years. However, patients that received adjuvant chemotherapy were less likely to die from breast cancer compared to those treated with neoadjuvant chemotherapy. At this point, we do not have the explanation for these findings, but we believe that a prospective study will elicit more insight into these phenomena.

606 IMPLICATIONS OF TOTAL PLATELET COUNT IN HEALTH AND DISEASE: A LARGE POPULATION STUDY ON DATA FROM NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

S Ball, S Wongsangskak*, M Arevalo, J Dennis, K Nugent. *Texas Tech University Health Sciences Center, Lubbock, TX*

10.1136/jim-2018-000974.612

Purpose of study Platelets are important mediators of coagulation, inflammation, and atherosclerosis. We conducted a large population study with National Health and Nutrition Examination Survey (NHANES) data to understand the relationship of total platelet count (TPC) with health and disease in humans.

Methods used The NHANES is a cross-sectional survey of the non-institutionalized United States adult population, administered every 2 years by the Centers for Disease Control and Prevention. Participants answer a questionnaire, receive a physical examination, and undergo laboratory tests. Values of TPC were collected over a 6 year period (2011–2016). Weighted 10th and 90th percentiles were calculated, and logistic regression was used to predict likelihood [Odds ratio (OR)] of being in categories with TPC <10th percentile or >90th percentile. Statistical analysis was performed using the Stata/SE 15.1.

Summary of results In our study including 17 969 individuals, mean TPC was 236.67/ μ L [SD=59.10], 10th percentile 170/ μ L and 90th percentile 311/ μ L. Hispanics (other than Mexican Americans) and obese individuals had lower odds of a TPC <10th percentile. Males, Blacks, people aged ≥ 45 years, and those with a recent (last 12 months) hospital-stay were more likely to have a TPC <10th percentile. Obese individuals and Mexican Americans had higher odds of having TPC >90th percentile. Individuals with a congestive heart

failure (CHF) or coronary heart disease (CHD) diagnosis had over twice the odds [OR 2.06, 95% CI: 1.50 to 2.82, $p \leq 0.001$, and 2.11, 95% CI: 1.48 to 3.01, $p \leq 0.001$, respectively] of having TPC <10th percentile. Individuals with emphysema or asthma diagnosis were more likely to have TPC >90th percentile [OR 1.84, 95% CI: 1.08 to 3.13, $p = 0.026$, and 1.25, 95% CI: 1.00 to 1.56, $p = 0.046$, respectively]. A diagnosis of chronic obstructive pulmonary disease and cancer didn't have significant associations with total platelet count.

Conclusions Our study showed that obese individuals are more likely to have higher TPC. Individuals with CHF and CHD had higher odds of having TPC <10th percentile and those with emphysema and asthma were more likely to have TPC >90th percentile.

607 SMOKING HISTORY AND PD-1/PDL-1 PATHWAY BLOCKADE: PREDICTING RESPONSE TO TREATMENT IN METASTATIC CANCER

¹CM Sullivan*, ²J Lu, ²J Kucharczyk, ²D Vesselinovitch, ²N Khurana, ²M Matrana. ¹LSU Health Sciences Center, New Orleans, LA; ²Ochsner Medical Center, Jefferson, LA

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Purpose of study Identifying patients who will benefit from immune-checkpoint inhibitor therapy is a challenge as proven predictive indicators remain to be elucidated. High tumor mutational burden (TMB) represents a possible biomarker for response to PD1 blockade such as in nivolumab or pembrolizumab. Genomic analyses have shown that patients with heavy smoking history are more likely to have high TMB. However smoking status alone has not been examined independently in relation to treatment response. We sought to determine whether a relationship existed between smoking history and response to treatment in metastatic non-small cell lung cancer (NSCLC), metastatic renal cell carcinoma (mRCC) and metastatic melanoma (mMelanoma).

Methods used A retrospective analysis was conducted of Ochsner Health System patients with mRCC, mMelanoma, and NSCLC receiving a minimum of two cycles of nivolumab or pembrolizumab between 12/2014 and 01/2018. Pre- and post-treatment target lesions were analyzed using RECIST criteria to calculate best response to treatment. Patient demographic information was gathered including age, sex, smoking history, and performance status pre and post treatment. Kaplan-Meier method was used to estimate progression free survival (PFS) and overall survival (OS) outcomes.

Summary of results Heavy smokers (>10 packyears) had a higher response to immunotherapy than light (<10 years) and never smokers ($p = 0.0500$). Heavy smokers with NSCLC treated with immuno-therapy also had significantly improved OS compared to light smokers with NSCLC ($p = 0.003$). mRCC immuno-therapy patients with heavy smoking history showed increased PFS compared to light/never smokers ($p = 0.026$).

Conclusions In summary, in response to PD-1 blockade heavy smokers showed improved survival compared to light and never smokers suggesting smoking history may represent a potential predictor of treatment response to PD-1 inhibitor therapy.

Legal entity responsible for the study Ochsner Medical Center and the University of Queensland, Ochsner Clinical School.

608 HEAD AND NECK CANCER DISPARITIES IN AN UNDERSERVED POPULATION

W Hoover*, DR Marshall. Meharry Medical College, Nashville, TN

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Purpose of study The SEER Program (seer.cancer.gov) estimated that 64 150 cases of oral cavity/oropharyngeal (OC/OP) and laryngeal cancer (LaCa) would be diagnosed in 2018, accounting for roughly 3.8% of all cancers. Men are diagnosed three times more often than women and African American/black (AA/B) men die at a higher rate than white (Wh) men. SEER data strives to represent as many demographic groups in the U.S. as is statistically possible (and these data can be mined at that level), yet the homogenized numbers, like those just presented, are often those used to determine therapy or to drive health policy. This is to the detriment of patients seen at clinics like those at Nashville General Hospital at Meharry (NGH@M). Presented here is a small part of a comprehensive program addressing disparities in outcome for head and neck cancers in underserved populations. Here we hypothesize that both black and white men and women, who use the services of a safety-net hospital, will differ substantially in age and stage at diagnosis compared to broader numbers generally seen.

Methods used We gathered IRB-approved information associated with demographics and risk or outcomes, from the medical records of 347 patients at NGH@M. These data were entered into a comprehensive database using REDCap (project-redcap.org) and, for this report, a summary analysis within REDCap was utilized. The patients in this group are 48% AA/B and 50% Wh with 2% not disclosed. Men represent 74% of the group and women, 26%.

Summary of results The median age at diagnosis for OC/OP is 57 years and for LaCa it is 56, compared to 63 and 65 years for all races, including both sexes from SEER18 data. NGH@M patients were also more likely to be diagnosed with regional metastasis than the national population at 58% and 47% respectively.

Conclusions Young age or metastatic stage at diagnosis are predictors of poorer outcome. These data suggest that socioeconomics are important in promoting disparities in prognosis. Future analysis will include incorporation of mortality as well as risk/etiology (including HPV presence and subtypes) and tumor subsite by race.

609 FIRST MOLECULAR TUMOR PROFILING OF HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMA (EHE)

EC Bourgeois*, K McQueen, A Fuentes, A Garcia. LSUHSC School of Medicine, New Orleans, LA

10.1136/jim-2018-000974.615

Purpose EHE case report and investigation of molecular profile.

Methods Review of Electronic Health Records.

Results A 32 year old female presented with shortness of breath and RUQ pain. CT showed multiple, bilateral small lung nodules and numerous hepatic masses. Results of liver and lung biopsies showed atypical epithelioid and spindle cells strongly positive for CD31, CD34, Factor VIII, and Fli-1 transcription factor and negative for CK7 and CEA, consistent with EHE. She was treated with metronomic oral

cyclophosphamide and bevacizumab with marked symptomatic improvement but no changes on imaging. Her disease has remained stable for two years after.

EHE is a rare vascular sarcoma with a prevalence of less than one in one million individuals. Patients can present with locally aggressive or widely metastatic disease, commonly involving the liver, lung, and bone. Most patients have an indolent disease course, and the 5 year disease-specific survival is 81%. While there is no treatment consensus due to paucity of cases in the literature, current treatment modalities include surgery, liver transplant, and chemotherapy. Tumor profiling was performed using next generation sequencing (NGS), and no actionable mutations were identified. The tumor was found to have a very low mutation burden and an unusual tumor infiltrating lymphocyte composition with a low number of CD8 +T cells and a high number of CD4 +FOXP3+T cells. There was no expression of PDL-1 in the tumor cells but a high expression in the surrounding immune cells. High expression of ADORA2A and CD39 were identified, reflecting a metabolic immune escape pathway.

Conclusions This case is fairly representative of EHE's clinical presentation, immunohistochemistry, and morphology. As these tumors are highly vascular we chose to treat with antiangiogenic therapy. Tumor molecular profiling suggests that treatment with PD-1 and ADORA2A/CD39 inhibitor may be active. This case contributes to the documentation of this rare tumor's diagnosis, prognosis, and treatment. To our knowledge, this is the first reported case of tumor molecular profiling in EHE, which may help us understand better its biology and treatment options.

610 DETERMINING RISK FACTORS FOR ANAL DYSPLASIA IN HIV+ INDIVIDUALS

J Ellison*, M Hagensee. Louisiana State University School of Medicine- New Orleans, New Orleans, LA

10.1136/jim-2018-000974.616

Purpose of study HPV infection and its related precursor lesions, anal intraepithelial neoplasia (AIN), are seen in increased rates in HIV +people. There is no established standard for determining who should be screened for anal cancer. These factors necessitate the development of additional biomarkers to identify high risk individuals. In cervical cancer, co-shedding of Epstein Barr Virus (EBV) has been shown to increase the risk of cervical dysplasia by 30%. EBV may play a role in the progression of anal dysplasia and could possibly serve as a biomarker for anal disease. This study aims to investigate this as well as identify other risk factors for anal dysplasia and anal cancer in HIV +people.

Methods used HIV +individuals attending HIV clinics at UMC and OMC were approached and consented. A history, and questionnaire involving demographics and behavior was administered. Anal swabs were collected for Pap smear analysis and high-risk HPV and EBV detection by reverse line blot and conventional PCR respectively. Individuals with abnormal anal cytology were given high resolution anoscopy and biopsied when clinically indicated. Within three months of the study visit HIV viral loads and CD4 counts were obtained via the electronic medical record. Risk factors for anal dysplasia were assessed using SPSS software. The clinic visit with all lab parameters available were used for analysis.

Summary of results The sample included 189 HIV +individuals, of which 88.4% were male, and 67.9% were African American. The mean age was 48.5, CD4 count was 523.8 cells/ml, and median HIV viral load of 39 copies/ml. The samples viable for testing showed 74.5% high risk HPV detection and 32.1% positive for EBV. Abnormal Pap smears were found in 58.6% of participants and anal dysplasia (low and high grade) was seen in 30.3%. The presence of HR-HPV alone was found in 43% of participants with anal dysplasia, whereas 75% of patients with co-shedding of EBV and HR-HPV were found to have anal dysplasia. Lower CD4 counts (average 415 cells/ml) and women were more likely to have concurrent anal dysplasia.

Conclusions Four variables were indicated as risk factors for dysplasia in HIV +individuals, of which anal dysplasia was prevalent at 30.3%. The variables included HRHPV, EBV and HPV co-shedding, CD4 counts, and women. Multivariate analysis of these factors will be attempted.

Infectious Diseases

Concurrent Session

2:00 PM

Friday, February 22, 2019

611 EMERGENCE OF CLONAL NONTYPEABLE *HAEMOPHILUS INFLUENZAE* IN HIV+ BLACK MEN WHO HAVE SEX WITH MEN (MSM) IN METRO ATLANTA, 2017–18

^{1,2}LF Collins*, ^{1,2}A Tunali, ^{1,2}S Thomas, ¹Z Wiley, ^{1,2}S Satola, ^{1,2,3}M Farley. ¹Emory Univ., Atlanta, GA; ²Georgia EIP, Atlanta, GA; ³Atlanta VAMC, Atlanta, GA

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Purpose of study Nontypeable *Haemophilus influenzae* (NTHi) is genetically diverse and the most common cause of invasive Hi disease. Reported cases of invasive NTHi (iNTHi) in younger adult HIV +MSM increased in 2017–18 in Atlanta. We characterized iNTHi isolates and compared iNTHi cases in persons living with HIV (PLWH) to HIV- adults.

Methods used Population-based surveillance for iNTHi was performed through Active Bacterial Core Surveillance. We analyzed clinical and epidemiologic data and performed pulsed-field gel electrophoresis (PFGE) for iNTHi cases aged 18–55 y from 1/1/2008–06/30/2018 in metro Atlanta. Data was stratified by HIV status and period (2008–16, 2017–18); PFGE patterns were examined for evidence of clonality.

Summary of results iNTHi incidence in PLWH remained stable from 2008–16, but significantly increased in 2017–18 ($p<0.01$) (Figure). Compared to HIV- iNTHi cases in 2008–18 ($n=113$), PLWH with iNTHi in 2017–18 ($n=28$) were more likely to be male (93% vs 46%, $p<0.01$), black (100% vs 51%, $p<0.01$), reside in an urban county (82% vs 43%, $p<0.01$) and develop septic arthritis (36% vs 1%, $p<0.01$).

iNTHi isolates from PLWH in 2017–18 clustered by PFGE (96%), compared to HIV +cases in 2008–16 (44%, $p<0.01$) and HIV- in 2008–18 (6%, $p<0.01$). We identified 2 PFGE clusters: #1 ($n=20$), median age 32 y, 95% PLWH [89% MSM], 95% male, 100% black, 95% diagnosed in 2017–18; and #2 ($n=20$), median age 36 y, 80% PLWH [100% male, 83% MSM], 100% black, 44% diagnosed in 2017–18. Most

Abstract 611 Figure 1

PLWH with clustered iNTHi had CD4 >200, viral suppression, and frequent sexually transmitted infections.

Conclusions We document a significant emergence of clonal iNTHi in young, HIV +black MSM in Atlanta. Septic arthritis was common. The emergence suggests potential spread of NTHi within a social network. Further investigation is needed to determine the mode of transmission and to assess virulence of the closely related isolates.

612 CHOLINE-BINDING PROTEIN A ASSOCIATED WITH RESISTANT SEROTYPES OF INVASIVE STREPTOCOCCUS PNEUMONIAE

¹I Fuwape*, ^{1,2}R Stanek, ¹NB Norton, ^{1,2}MA Mufson. ¹Marshall University Joan C. Edwards School of Medicine, Huntington, WV; ²Hershel Woody Williams Veterans Administration Medical Center, Huntington, WV

10.1136/jim-2018-000974.618

Purpose of study *Streptococcus pneumoniae*, the cause of invasive pneumococcal disease (IPD), contains multiple choline-binding proteins in its cell wall and membrane. One of those choline-binding proteins, choline-binding protein A (CbpA), is a highly-variable, cell-surface protein and virulence factor. Functions of CbpA include adherence to the nasopharyngeal mucosa, evasion of the host immune response and formation of biofilms. We investigated the relationship of CbpA to penicillin resistance in *S. pneumoniae*.

Methods used We recovered 199 *S. pneumoniae* isolates from normally sterile sites of patients with IPD admitted to three affiliated hospitals from 1981 to 2014. For this study, 46 isolates of the total were serotyped by quelling reaction and penicillin susceptibility determined by ETEST.[®] We extracted genomic DNA from all isolates and amplified the *cbpA* gene with PCR. PCR products were visualized with gel electrophoresis and sequenced. Of the 46 isolates, we successfully amplified and sequenced the *cbpA* gene in 38 isolates. For analysis, we combined the results of this study with the CbpA amino acid sequences obtained from 140 isolates of our original 199 isolates. We used EMBL-EBI Clustal Omega to align DNA and amino acid sequences. Phylogenetic trees were generated with Phylo dendron Phylogenetic Tree Printer, iubio.bio.indiana.edu.

Summary of results We examined the amino acid sequences of 155 isolates that clustered together in a phylogenetic tree. A sequence of 8–10 amino acids inserted in the N-terminal segment of CbpA was identified in nine serotypes that develop intermediate and resistance to penicillin. This insert was identified in 16 of 18 resistant isolates, 7 of 28 intermediate and 14 of 109 susceptible isolates and was absent from all 60 isolates of four serotypes that do not develop resistance.

Conclusions An altered amino acid sequence of the CbpA protein identified in nearly all penicillin-resistant isolates and in

intermediate and susceptible isolates of serotypes known to develop penicillin resistance suggests that a function of the altered cell surface protein has influenced the development of penicillin resistance in *S. pneumoniae*.

613 EMERGENCY DEPARTMENT OPT-OUT SCREENING OF HEPATITIS C IN NEW ORLEANS, LA

¹AT Jones*, ²L Moreno-Walton, ²K Okeke-Eweni, ¹K McGonigle, ²D Yang, ¹M Kim, ²J Miller, ²K Fletcher, ¹P Kissinger. ¹Tulane University, New Orleans, LA; ²LSU Health Sciences Center, New Orleans, LA

10.1136/jim-2018-000974.619

Purpose of study Hepatitis C Virus (HCV) has surpassed HIV in annual mortality and infects approximately 3.5 million Americans. With nearly half of patients unaware of their infection, diagnosis is the primary barrier to receiving curative treatment. In response, New Orleans established the first emergency department (ED) opt-out HCV screening program in March 2015. This aim of this study is to identify the HCV +patient population captured by this novel screening model.

Methods used Patients who tested HCV antibody-reactive at the University Medical Center ED from March to October 2015 were included in the study. Information was obtained through retrospective chart review. Data collected includes patient demographic information as well as secondary HCV testing results, including viral RNA load and genotype.

Summary of results In these six months, 757 patients screened HCV antibody-reactive. The mean age was 50.8 years (SD=11.4). Patients were predominantly male (73.2%) and African American (59.6%). The most common insurances were Medicaid (42.5%) and Medicare (21.5%), followed by the uninsured (15.5%). Reported history of intravenous drug use was present in 37.1% of our population. The majority of patients (68.7%) had no prior HCV screening, while 29.5% had previously tested positive for HCV. Although less than HCV, a majority (58.0%) had never been tested for HIV, while 1.7% were previously diagnosed HIV+. Of the 757 HCV antibody-reactive patients, 681 (90.0%) patients received a quantitative viral load. Spontaneous clearance of the virus occurred in 145 (21.3%) of the antibody-reactive patients, while 536 (78.7%) were chronically infected. The most prevalent HCV genotype was 1A (70.4%) followed by 1B (17.6%). Genotypes 1A/1B, 1C, 2, 2B, 3A, 4A/4C/4D, and 6A amounted for a combined 12.1%.

Conclusions Screening in the emergency department presents a unique model of healthcare delivery to non-whites and those of low socioeconomic status, a marginalized population at highest risk for HCV infection. Our study demonstrates the feasibility of ED screening programs to successfully capture undiagnosed patients.

614 PENTAMIDINE PLUS RIFAMPIN DEMONSTRATES *IN VITRO* SYNERGY AGAINST ENTEROBACTERIACEAE CARRYING THE MCR-1 GENE

A Kamal*, RM Brown, DS Ashcraft, GA Pankey. Ochsner Clinic Foundation, New Orleans, LA

10.1136/jim-2018-000974.620

Purpose of study The plasmid-mediated polymyxin resistance gene *mcr-1* was first identified in China from a pig *Escherichia coli* (Liu et al 2015). The *mcr-1* gene has since been

Abstract 614 Table 1 Pentamidine and rifampin MICs and synergy testing by time-kill assay ($\log_{10}$ change in CFU/ml at 24 h) for *mcr-1* positive Enterobacteriaceae isolates.

Enterobacteriaceae isolates (<i>mcr-1</i> +)	Pentamidine MIC ($\mu\text{g/ml}$) (Mean)	Rifampin MIC ($\mu\text{g/ml}$) (Mean)	Synergy testing Time-kill assay Pentamidine +Rifampin (1×MIC)	Synergy testing Time-kill assay Pentamidine +Rifampin (½×MIC)
<i>E. coli</i> (#0346)	100	>32	−3.0 SYN	−4.8 SYN
<i>E. coli</i> (#0349)	200	>32	−1.0 ADD	−3.0 SYN
<i>E. coli</i> (#0350)	100	>32	−5.0 SYN	−4.0 SYN
<i>E. coli</i> (#0493)	200	>32	−1.0 ADD	−1.0 ADD
<i>E. coli</i> (#0494)	100	>32	−5.0 SYN	−2.0 SYN
<i>S. enteritidis</i> (#0496)	200	>32	−2.0 SYN	−5.0 SYN
<i>K. pneumoniae</i> (#0497)	400	32	−3.0 SYN	−3.0 SYN

SYN, synergy; ADD, additivity.

found in various parts of the USA. It can move from one bacterium to another, possibly making bacteria also resistant to the polymyxins, a last resort drug for multidrug-resistant Gram-negative infections. This increases the need for new therapeutic approaches. In 2017 Stokes et al showed potentiation of rifampin (RI) by pentamidine (PNT) against 1 isolate of *mcr-1*-positive *E. coli* using the checkerboard method. We evaluated the combination of PNT and RI against 7 *mcr-1*-positive Enterobacteriaceae isolates using time-kill assay (TKA). **Methods used** The seven clinically unique *mcr-1*-positive isolates (5 *E. coli*, 1 *Klebsiella pneumoniae* and 1 *Salmonella enteritidis*) were obtained from the CDC Antimicrobial Resistance Bank. MICs for PNT and RI were determined in triplicate by broth microdilution (mean value used). Synergy testing by TKA was performed using two different concentrations of PNT and RI: each drug at 1×MIC or at ½×MIC. Synergy was defined as $\geq 2 \log_{10}$ decrease in CFU/ml after 24 hour by the combination compared to the most potent agent alone; additivity, a 1 to $<2 \log_{10}$ decrease.

Summary of results See table 1.

Conclusions Synergy was demonstrated with PNT plus RI using ½×MIC against 6/7 *mcr-1* positive Enterobacteriaceae. This may enable the use of a lower amount of PNT and RIF for *mcr-1* positive bacteria. Further studies with additional *mcr-1* (as well as *mcr-2–5*) positive isolates, including other bacterial genera are needed. *In vitro* synergy may or may not correlate clinically.

615

IN VITRO SYNERGY OF FOSFOMYCIN PLUS DOXYCYCLINE AGAINST LINEZOLID AND VANCOMYCIN RESISTANT *ENTEROCOCCUS FAECIUM* USING A RAPID ETEST METHOD AND TIME-KILL ASSAY

HR Davis*, RM Brown, DS Ashcraft, GA Pankey. *Ochsner Clinic Foundation, New Orleans, LA*

10.1136/jim-2018-000974.621

Purpose of study Linezolid and vancomycin resistant *Enterococcus faecium* (LRVREF) is globally emerging as a nosocomial pathogen. In 2013, the CDC reported vancomycin resistant *E. faecium* (VREF) as a serious threat and projected it will account for 10 000 infections as well as 650 deaths each year.

VREF has also become resistant to linezolid, creating a need for the development of new therapeutic options. Combination therapy may be a means for treatment of LRVREF. Fosfomycin (FOS) has shown synergistic activity with daptomycin or amoxicillin against linezolid and FOS-susceptible VREF using time-kill assay (TKA) (Descourrouez et al. 2012). We investigate the interaction of FOS +doxycycline (DOX) against LRVREF (most isolates FOS-resistant) using Etest, in addition to TKA.

Methods used Twenty-four genetically and clinically unique LRVREF isolates were collected from 2002–2004. MICs for FOS and DOX were determined in triplicate by Etest and in addition, by broth microdilution for DOX. Synergy testing with DOX +FOS (1×MIC) was performed in triplicate by a MIC:MIC Etest method and read at 24 hour (mean value used). The summation fractional inhibitory concentration (ΣFIC) was calculated: synergy ≤ 0.5 ; additivity $>0.5–1$. Synergy testing was also performed by TKA. Synergy was defined as $\geq 2 \log_{10}$ decrease in CFU/ml after 24 hour by the combination compared to the most potent agent alone; additivity, a 1 to $<2 \log_{10}$ decrease; indifference, $<1 \log_{10}$ change.

Summary of results Etest MICs ($\mu\text{g/ml}$) were: DOX 0.094–16 (50% >4 ; non-susceptible) and FOS 64 to >1024 (no CLSI interpretive guidelines available). With Etest, DOX +FOS revealed synergy in 11/24 (46%) and additivity in 13/24 (54%) of isolates in 2 days. TKA showed synergy with 10/24 (42%) and additivity in 4/24 (17%) after 4 days. The remaining isolates showed indifference.

Conclusions Linezolid and vancomycin resistant *E. faecium* (LRVREF) is globally emerging as a nosocomial pathogen. In our study of 24 LRVREF isolates using fosfomycin +doxycycline, synergy was found in 46% (Etest) and 41% (time-kill assay). Further synergy testing with additional isolates and drug combinations should be performed. *In vitro* synergy may or may not be beneficial *in vivo*.

616

INTEGRASE STRAND TRANSFER INHIBITORS ARE ASSOCIATED WITH WEIGHT GAIN IN WOMEN

¹A Kerchberger*, ¹A Sheth, ¹CD Angert, ¹C Mehta, ¹N Summers, ¹I Ofotokun, ²W Team, ¹CD Lahiri. ¹Emory University, Atlanta, GA; ²WIHS, Baltimore, MD

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Purpose of study Integrase strand transfer inhibitor (INSTI)-based antiretroviral therapy (ART) is recommended as first line HIV therapy. Studies have suggested individuals who switch to INSTI-ART experience increase in body weight which may be more prominent in women. We evaluated the effect of INSTI use in HIV +women.

Methods used Data collected from 2008–2017 on HIV +women enrolled in the Women's Interagency HIV Study (WIHS) with viral load <1000 copies/mL on ART. Women who switched to or added INSTI to ART (SWAD) were compared to women who remained on non-INSTI ART (STAY). Outcomes included changes in body weight; body mass index (BMI); percentage body fat (PBF); body circumference measurements; blood pressure (BP); and incident diabetes mellitus (DM). Outcomes measured 6–12 months before and 6–18 months after INSTI switch/add in SWAD with comparable points in STAY. Baseline (BL) characteristics for groups were compared. Linear regression models compared change over time in outcomes by STAY/SWAD, adjusted for BL demographics and stratified by INSTI type (dolutegravir or raltegravir/elvitegravir).

Summary of results 1118 WIHS participants (884 STAY and 234 SWAD) followed for 2.0 (± 0.1) years. At BL, mean age 48.8 (± 8.8) years, 61% Black, and mean CD4 669 (± 294) cells/mm³. At BL, SWAD women were more likely to be on protease inhibitor-ART, but did not differ from STAY by demographics or body measurements. Compared to STAY, SWAD experienced 2.14 kg greater increase in weight, 0.78 kg/m² greater increase in BMI, 1.35% greater increase in PBF, and 2.05, 1.87, 0.58, and 0.98 cm greater increases in waist, hip, arm, and thigh circumference, respectively. SWAD women had 2.24 and 1.17 mmHg greater change in systolic and diastolic BP. New-onset DM occurred in 4.5% (n=8) SWAD and 2.2% (n=15) STAY, p=0.11. No differences in outcomes were observed by INSTI type.

Conclusions In a longitudinal study of HIV +women on ART, a switch to INSTI was associated with significant increases in body weight and measurements, body fat, and blood pressure compared to those on non-INSTI ART. Further research is needed for prevention and management of metabolic effects with INSTI use.

617 ESTIMATE OF THE EFFECTIVENESS OF INFLUENZA VACCINE AMONG CHILDREN FOR THE 2017–2018 SEASON

L Powell*, RE Begue. LSU, New Orleans, LA

10.1136/jim-2018-000974.623

Purpose of study The 2017–2018 flu season was one of the deadliest seasons in decades. According to the CDC, there were 180 pediatric deaths with approximately 80% of these occurring in children who did not receive the flu vaccine. Since the circulating flu strains change periodically, it is extremely important to determine the efficacy of the vaccine (VE) on an annual basis specifically in susceptible populations. A preliminary estimate by CDC early in the 2017–2018 season found a VE of 33% (95% CI: 24 to 41) for all and 44% (95% CI: 32 to 55) for children. A case-control test-negative design was implemented to estimate the VE of the influenza vaccine for 2017–2018.

Methods used Children 6 months to 17 years seen at Children's Hospital New Orleans with respiratory symptoms and tested for influenza during 2017–2018 were included. Age groups were divided 6 mon-1 year, 2–4 years, 5–8 years, 9–17 years. Each child's immunization status was verified via the Louisiana Immunization Registry (LINKS). Each child was considered vaccinated if they received ≥ 1 dose of an influenza vaccine ≥ 14 days before their flu like illness. Vaccine efficacy was estimated by comparing vaccination status of influenza-positive versus influenza-negative cases (VE=(1-OR) $\times 100$).

Summary of results 4825 children were included for the 2017–2018 season with an approximate equal distribution among age groups. Overall, 1001 children (21%) were vaccinated and 1069 (22%) tested positive for influenza. Children were four times more likely to test positive for Influenza A than Influenza B. Children 6 mon-1 year were more likely to be vaccinated (36%) while children 2–4 years were more likely to be influenza positive (26%). The overall vaccine effectiveness for the 2017–2018 season was found to be 44% (95% CI: 32 to 53); 45% for Influenza A (95% CI: 33 to 56) and 38% (95% CI: 11 to 57) for Influenza B.

Conclusions Our influenza VE estimates were similar to the ones reported by the CDC and similar to the ones reported for the past two seasons (40% and 48%, respectively). While lately conferring disappointingly low protection (VE <50%), influenza vaccine remains the best intervention to contain influenza at the populational level.

618 GENOMIC AND MESSAGE RNA LONGITUDINAL VIRAL DYNAMICS IN RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTED INFANTS

RH Tomlinson*, E Meals, L Harrison, J DeVincenzo. UTHSC, Mem, TN

10.1136/jim-2018-000974.624

Purpose of study RSV is the world's leading cause of lower respiratory tract infections in children. Approximately three percent of all U.S. infants (≤ 1 years of age) are hospitalized due to RSV, making it the most common cause of hospitalization in this age group. The true extent of RSV replication in humans has not been defined. We have previously determined that standard genomic PCR can detect virus in infants for a long period of time – greater than 1 month after they first show symptoms. Whether this genomic PCR detection of RSV represents continued, prolonged viral replication has never before been assessed.

Methods used Therefore, we developed a PCR assay to quantify RSV mRNA (message) of both RSV-A and RSV-B, the two RSV genotypes that infect humans. Genomic and message PCR of RSV was performed from the same aliquots of respiratory secretions in 96 well plates using the ABI 7500 FAST real-time PCR system, using the same standard curves. Specimens consisted of quantitatively collected nasal aspirates of infants initially hospitalized at Le Bonheur Children's Hospital in Memphis, TN and then followed longitudinally after discharge. We compared the quantity of message vs. genomic RSV over time in 9 subjects (5 RSV-A, 4 RSV-B).

Summary of results The message PCR assay in nasal aspirates showed good precision and reproducibility. Message was detectable throughout the time of persistence of genomic RSV positivity. The relative concentration of viral mRNA/genomicRNA correlated with time since infection onset (p<0.0001). Additionally, when genomic RSV load rebounded a concomitant rebound in message was consistently observed.

Conclusions Our data strongly suggests that RSV replication persists for prolonged periods of time in infants. This continuing active viral replication may be driving the prolonged symptoms associated with RSV infections. Our data also predicts the efficacy of antiviral treatments for RSV. Our message RSV PCR assay may also be valuable in measuring the effects of experimental antivirals that are currently entering clinical trials.

619 RIFAXIMIN VS NORFLOXACIN FOR THE PREVENTION OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH CIRRHOSIS: A META-ANALYSIS

C Rosero*, V Kohli, W Krolkowski, P Patel. ETSU, Johnson City, TN

10.1136/jim-2018-000974.625

Purpose of study Spontaneous bacterial peritonitis (SBP) is defined as the presence of infection in ascitic fluid without an evident intra-abdominal source. Its early recognition and

treatment reduces the morbidity and mortality in cirrhotic patients with ascites. Fluoroquinolones, including Ciprofloxacin and Norfloxacin, are widely used antibiotics for SBP prophylaxis. However, its extensive long-term use has increased the incidence of quinolone-resistant bacteria and they are associated with significant side effects. Rifaximin is a relatively safe antibiotic when compared to quinolones due to its low systemic absorption and effectiveness against enteral bacteria. This meta-analysis was conducted to evaluate the efficacy of Rifaximin vs Norfloxacin for the primary and secondary prevention of SBP in cirrhotic patients with ascites.

Methods used A systematic review was conducted using MEDLINE, Cochrane and ScienceDirect databases from inception through October 2018 to identify randomized controlled studies that evaluated the efficacy of Rifaximin vs Norfloxacin for primary or secondary prevention of SBP. The number of cases from each study were extracted and combined using fixed-effect, generic inverse variance method of DerSimonian and Laird.

Summary of results Four randomized controlled studies with a total of 542 patients on antibiotic prophylaxis for primary or secondary prevention of SBP (269 on Rifaximin and 273 on Norfloxacin) were enrolled. Compared with Norfloxacin, Rifaximin therapy was more effective for the secondary prevention of SBP with a pooled OR of 0.19 (95% CI, 0.08–0.45, $I^2=0$). There was no statistically significant difference between Rifaximin and Norfloxacin for primary prevention of SBP with a pooled OR of 0.61 (95% CI, 0.34–1.10, $I^2=0$). Six-month overall mortality rate was lower with Rifaximin therapy compared to Norfloxacin with a pooled OR of 0.47 (95% CI, 0.27–0.81, $I^2=0$).

Conclusions Secondary prevention of SBP and overall mortality rate were lower in patients treated with Rifaximin compared to Norfloxacin. However, primary prevention of SBP was similar between the two treatment options. Rifaximin can be considered as an alternative for the secondary prevention of SBP as it can also decrease the overall mortality risk.

620

THE HOSPITAL CURTAIN LEADING EDGE: A SOURCE OF INFECTION IN THE MEDICAL INTENSIVE CARE UNIT

¹L Brown*, ¹S Siddiqui, ²A McMullen, ²J Waller, ^{1,3}S Baer. ¹Medical College of Georgia, Augusta, GA; ²Augusta University, Augusta, GA; ³Augusta VA Medical Center, Augusta, GA

10.1136/jim-2018-000974.626

Purpose of study Hospital privacy curtains in Medical Intensive Care Unit (MICU) rooms are rarely cleaned or changed, and frequently touched by hospital staff without proper hand hygiene. Previous studies have suggested that the ‘leading edge’ of the curtain, characterized by the edge most frequently touched, plays a role in the hospital acquired infection (HAI) rate at many hospitals. To date, the ‘leading edge’ has only been arbitrarily defined. The aims of this study were to compare the bacterial load of the edge vs the middle of hospital curtains in the MICU, and determine the identity and distribution of pathogens colonizing the curtains.

Methods used Prospective observation was performed by recording touch location and frequency on MICU curtains in a 12 hour period. Each curtain consisted of 3 panels. Two 2.5 cm² sections of four areas (L and R edge, L and R middle) of each panel were sampled on the staff and patient sides of 8 curtains, and colony-forming units (CFU) were counted at

36 hours. Select colonies were sub-cultured for species identification. Mixed models on the CFU ranks were used to examine differences in medians between the four areas within each side of the curtain. A contrast to compare the median CFU on the edges to the middle areas was performed.

Summary of results Observation of staff revealed they touched the edge and middle of the curtains usually without hand hygiene. On the patient side of the curtain, median CFU for edges (11 CFU) was higher than median CFU for the middle (7 CFU) ($p=0.0366$). On the staff side, median CFU for edges (10.5 CFU) was higher than median CFU for the middle (7 CFU) ($p=0.0032$). While most identified bacteria were skin flora, several pathogens were detected, such as MSSA, MRSA, *A. baumannii*, and *E. faecium*. These pathogens were found mostly on the curtain edges.

Conclusions Hospital staff touch both the edge and middle of MICU curtains, often without hand hygiene. Bacterial load was significantly higher on the curtain edge than middle. Relevant pathogens such as MRSA, *Acinetobacter*, and *Enterococcus* were found. These results implicate hospital curtains as potential sources for HAI.

621

REDUCING OVERDIAGNOSIS AND TREATMENT OF PEDIATRIC URINARY TRACT INFECTIONS

J Bassett*, J Stultz, M Hofstetter, S Delozier, A Murphy, J Dreher, S Arnold. University of Tennessee Health Science Center, Memphis, TN

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Purpose of study Diagnosing pediatric urinary tract infections (UTI) requires urine cultures (UC) for which results are available days later. Consequently, emergency department (ED) providers must treat patients empirically. To reduce excessive antibiotic use, we aimed to assess and improve diagnostic accuracy of UTIs in the ER at the time of visit.

Methods used We included children 0–18 years diagnosed and treated in an urban, tertiary-care, Pediatric ED from 2014–2015 for uncomplicated, community-acquired UTI. We collected demographic, clinical, and laboratory data by chart review. We created a multivariable regression model with age, gender, urinalysis (UA), fever and dysuria to determine the strongest predictors of UTI, defined as >10 000 colony forming units/mL of pathogenic bacteria in UC. Each patient contributed a single episode of UTI. Patients without UC were excluded from analysis.

Summary of results Among 897 patients treated for UTI, 105 (12.6%) had no UC obtained; thus, 792 were included in this analysis. Of these, 408 (49.5%) had a UTI. Average age was 7.5 years $\pm$ 5.6. Most common presenting symptoms were dysuria (50.1%), fever (42.5%) and abdominal pain (36.1%). Most common exam findings were none (58.0%), fever (25.2%), and abdominal tenderness (14.3%). Leukocyte esterase (LE) 1+ or greater (odds ratio [OR] 3.1, 95% confidence interval [CI] 1.8–5.4), nitrites (OR 18.2, 95% CI 8.9 to 37.5) and >10 white blood cells (WBC) (OR 3.3, 95% CI 2.1 to 5.4) on UA independently increased odds of UTI. Patients >2 years had lower odds of UTI (OR 0.29, 95% CI 0.17 to 0.48). Fever and dysuria were not associated with UTI (both $p>0.15$). Requiring presence of one or more of LE 1+ or greater, nitrites, and WBC >10 on UA to diagnose UTI would reduce unnecessary treatment by 10.9% while missing 2.5%

of UTIs. A 16.9% reduction would be seen while missing only 4.0% if WBC>20 were used.

Conclusions Providers could improve diagnostic accuracy in patients >2 years by utilizing UA criteria of LE 1+ or higher, nitrites, or >10 WBCs rather than clinical features. Use of these criteria could significantly reduce empiric antibiotic use without compromising patient safety. External validation of these criteria is required.

Neurology and Neurobiology

Concurrent Session

2:00 PM

Friday, February 22, 2019

622 ANTIBODIES AGAINST VOLTAGE-GATED POTASSIUM CHANNELS AND WIDESPREAD INVOLVEMENT OF THE NERVOUS SYSTEM

AV Varma*, EC Mader, D Devier, R El-Abassi. *Louisiana State University Health Sciences Center School of Medicine New Orleans, New Orleans, LA*

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Introduction Antibodies against voltage-gated potassium channels (VGKC) have been implicated in the pathogenesis of Isaac syndrome, Morvan syndrome, and limbic encephalitis with faciobrachial dystonic seizures. Anti-VGKC antibodies are also detected in patients with other clinical phenotypes prompting clinicians to question the precise role these antibodies play in the pathogenesis of these neurological disorders.

Case report A previously healthy 65-year-old man presented with a several-month history of cognitive decline, diplopia, gait ataxia, and REM sleep behavior disorder (RBD). On examination, he had vertical nystagmus, dysarthria, myoclonic jerks, absent knee and ankle reflexes, bilateral Babinski sign, diminished vibratory and position sense, and positive Romberg sign. His muscle strength was normal and he had no signs of cerebellar dysfunction. Neuropsychological testing confirmed the presence of aphasia, visuospatial defects, and impairment in executive function. EEG was normal. Brain MRI showed gadolinium enhancement in both mesial temporal lobes consistent with limbic encephalitis. EMG/NCS revealed large-fiber axonal sensory polyneuropathy. Of the many laboratory tests performed, the only positive result was the high anti-VGKC antibody serum titer (0.29 nmol/L). Paraneoplastic workup was negative. Intravenous immunoglobulin, mycophenolate mofetil, and prednisone resulted in improvement of cognitive and language function and resolution of myoclonic jerks, choreoathetosis, nystagmus, and dysarthria. Although sensory ataxia and other neuropathic symptoms failed to resolve, these symptoms ceased to progress.

Conclusion This is the first report of anti-VGKC seropositivity in the setting of widespread nervous system dysfunction. Our patient had findings that indicate limbic encephalitis, involvement of neocortical, subcortical, and brainstem structures, and large-fiber sensory polyneuropathy. Symptom resolution or arrest with immunotherapy suggests a key role of anti-VGKC antibodies in the pathogenesis of our patient's central and peripheral nervous system disorders.

623 BENZODIAZEPINE-RESPONSIVE CATATONIA AND STATUS EPILEPTICUS

SH Rathore*, BJ Copeland, LA Branch, EC Mader. *LSUHSC, New Orleans, LA*

10.1136/jim-2018-000974.629

Introduction Historically, catatonia has been viewed as a syndrome that is exclusive to psychiatric disorders, particularly schizophrenia. It is now known that catatonia is more common in mood disorders than in schizophrenia. Moreover, catatonia has been described in various neurological and medical conditions, such as drug intoxication or withdrawal, metabolic disturbances, and inflammatory disorders. There are also rare reports of status epilepticus with catatonia as the presenting sign.

Case report A 26-year-old male with schizoaffective disorder was found unconscious and soaked in urine. On examination, he was noted to be awake but catatonic—with mutism, psychomotor retardation, waxy flexibility, and fixed limb postures. Blood tests showed leukocytosis, elevated creatine kinase, and mild hyperammonemia. Cerebrospinal fluid analysis was normal except for mildly elevated protein. Head CT and brain MRI were normal. Catatonia responded to intravenous lorazepam but recurred a few hours later. EEG recording during catatonia revealed bisynchronous high-voltage rhythmic delta activity consistent with nonconvulsive status epilepticus. Treatment consisted of levetiracetam, lacosamide, and on-demand lorazepam. Continuous EEG showed relapse of catatonia and status epilepticus, both of which were suppressed with 4 mg of lorazepam. Catatonia and status epilepticus resolved, and the patient was completely normal on the day of discharge.

Conclusion Our case underscores the importance of searching for an 'organic' cause of catatonia, even in patients with a past psychiatric diagnosis. In the absence of expert consensus, clinicians can use the delirium protocol as a tentative approach to catatonia, provided EEG is included in the initial workup. The parallel response of catatonia and status epilepticus to benzodiazepines suggests that enhanced GABAergic neurotransmission leads to inactivation of brain circuits that are pathologically activated during these seemingly unrelated paroxysmal disorders.

624 STRESS-INDUCED MITOCHONDRIAL DYSFUNCTION IN MICE WITH POST-TRAUMATIC STRESS DISORDER

¹GJ Preston*, ²T Emmerzaal, ¹F Kirdar, ³E Morava, ³T Kozicz. ¹Tulane University, New Orleans, LA; ²Radboud UMC, Nijmegen, Netherlands; ³Mayo Clinic, Rochester, MN

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Purpose of study Post-traumatic stress disorder (PTSD) is a debilitating psychiatric disorder induced by exposure to a traumatic event. Mitochondrial dysfunction has been increasingly implicated in several psychopathologies, including PTSD. We therefore investigated whether susceptibility to PTSD is associated with mitochondrial dysfunction using a novel paradigm in mice.

Methods used 48 wildtype male mice were exposed to an established PTSD-induction paradigm, and 7 PTSD-vulnerable and 16 PTSD-resilient animals were identified. The activities of the mitochondrial electron transport chain (ETC) complexes isolated from brain and muscle of PTSD-vulnerable and -

resilient animals, as well as 12 stress-naïve animals, were analyzed. Metabolomics was also performed in brain tissue and blood plasma. Mitochondrial DNA copy number in brain and blood was determined by qRT-PCR. Levels of the stress hormones corticosterone and FGF-21 in blood plasma were assayed by ELISA.

Summary of results Animals exposed to the PTSD-induction paradigm displayed significantly reduced brain mitochondrial capacity compared to stress-naïve animals, and PTSD-vulnerable animals displayed significantly reduced brain mitochondrial complex activity compared to PTSD-resilient animals. Both PTSD-vulnerable and -resilient animals showed significantly reduced mtDNA copy number in both brain and blood. PTSD-vulnerable animals also showed reduced short chain acyl-carnitines in the brain, and reduced free, short, and medium-chain acyl-carnitines in blood compared to stress-naïve animals. PTSD-vulnerable and -resilient animals also showed several additional metabolic biomarkers of mitochondrial dysfunction. While there was no difference in plasma concentration of CORT, PTSD-vulnerable animals showed significant reduction in the metabolic stress hormone FGF-21.

Conclusions Mitochondria play a central role in several physiologic processes involved in the pathophysiology of PTSD, including memory and learning, inflammation, and large-scale brain network activation/deactivation/switching. Our data indicate that traumatic event exposure may induce mitochondrial dysfunction in the brain and circulating lymphocytes, and that the severity of this dysfunction may predict PTSD-susceptibility.

625 VALIDATION OF AN AXONAL INJURY MODEL BY SCANNING ELECTRON MICROSCOPY IMAGING

^{1,2,3}AV Wilson*, ³VM Pozo Devoto. ¹Meharry Medical College, Nashville, TN; ²Mayo Clinic, Rochester, MN; ³St. Anne's University Hospital in Brno (FNUA), Brno, Czechia

10.1136/jim-2018-000974.631

Purpose of study Studies using different experimental settings have focused on the relationship between axonal injury and the effects on neuronal homeostasis and functionality. Axonal pathology is present in many neurodegenerative diseases, but there still is not a clear understanding of the molecular mechanisms involved in this process. Histopathology studies show that damage to axons typically appear as breaks in the axon (axotomy) or focal enlargements referred to as axonal swellings. We developed an *in vitro* model where a physical stress is applied to the axons in a time and force-controlled manner. One of the key novelties of our model is the possibility to image in real time changes in the axons during the injury.

Methods used We validated our model by assessing axonal changes generated by the physical injury. Briefly, human neurons were first differentiated from NSCs and seeded in the proximal chamber with their axons elongating through a series of parallel channels ending in the distal chamber. Perpendicularly to the axonal grid an additional channel goes from side to side of the chamber, connected to a syringe controlled by an electronical device, which sets the pressure of the syringe and ultimately controls the flow through the channel. After 90 s of a flow rate of 100 ul/min, chambers were fixed and processed for imaging in a

Scanning Electron Microscope. Images from axons across the region of injury were taken and morphometric analysis performed.

Summary of results As expected, our results show a significant increase in the number of enlargements per axon, as well as a significant decrease in the distance between adjacent enlargements. Surprisingly, enlargements size (length and width) remains unchanged when injured and control axons are compared.

Conclusions Validation of the physical stress system and the results obtained open novel paths to describe and understand the molecular events that are involved in axonal response to injury.

626 IVIG-RESPONSIVE HTLV-1 POLYRADICULONEURITIS WITH DELAYED PROGRESSION TO TROPICAL SPASTIC PARAPARESIS

D Chachkhiani*, M Soliman, EC Mader, R El-Abassi. Louisiana State University, Metairie, LA

10.1136/jim-2018-000974.632

Introduction Human T-lymphotropic virus type-1 (HTLV-1) is known for causing tropical spastic paraparesis, a myelopathy that mainly affects the thoracic cord. Other HTLV-1 associated syndromes, such as conus medullaris syndrome, polyradiculoneuritis, and myositis, are less common and often overlooked. We describe a case of HTLV-1 manifesting initially as cauda equina syndrome and, 3 years after disease onset, as tropical spastic paraparesis.

Case report A 50-year-old man presented with a 2 year history of impotence and saddle anesthesia followed by bilateral lower extremity numbness and weakness and gait difficulty. On examination, he was noted to be paraplegic with absent patellar and ankle reflexes, L5 to S3 sensory loss, and intact anal sphincter tone—findings that are consistent with a cauda equina syndrome. MRI of the spine was normal. NCS revealed severe sensorimotor polyneuropathy. Peripheral neuropathy workup was significant for elevated cerebrospinal fluid (CSF) protein. Anti-HTLV-1 antibodies were detected in blood but not in CSF. Plasma exchange was given and resulted in improved muscle strength. Follow-up NCS showed absent sensory and motor responses in the lower extremities and signs of acute on chronic denervation and reinnervation. A decision was made to treat him with scheduled intravenous immunoglobulin (IVIG) infusions. This arrested the progression of his symptoms and improved his muscle strength. Eventually, he was able to stand up and ambulate with a walker. Repeat HTLV-1 testing showed the same results: antibodies in blood but not in CSF. Three years from disease onset, he developed bilateral lower extremity spasticity, hyperreflexia, clonus, and Babinski sign despite continuous IVIG therapy. He has been receiving IVIG for over 3 years now.

Conclusion This is an elusive case of HTLV-1 infection, which presented as a cauda equina syndrome, and raised questions in regard to the detection, progression, and treatment of HTLV-1 infections with atypical phenotypes. Why are HTLV-1 antibodies present in blood but not in CSF? Is IVIG the treatment of choice for HTLV-1 polyradiculoneuritis? Although IVIG did not prevent disease progression, it appeared to have delayed the progression of disease from the neuropathic to the myelopathic phase.

627 THE RELATIONSHIP BETWEEN EXECUTIVE FUNCTION BRAIN CONNECTIVITY AND SOCIAL FUNCTIONING IN CHILDREN WITH AUTISM SPECTRUM DISORDER

H Bednarz*, R Kana. *University of AL at Bham, Birmingham, AL*

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Objective Executive function (EF) deficits are well documented in autism spectrum disorder (ASD). Recent work indicates that EF may be related to social impairment in ASD; however, the specific mechanism remains unclear. The goal of this study is to explore how behavioral and neuroimaging measures of EF are related to social functioning in a large sample of ASD and typically developing (TD) children.

Method Data were obtained from the ABIDE-II database. Social functioning and EF behavior were measured using parent raters: Social Responsiveness Scale (SRS), Behavior Rating Inventory of Executive Functioning (BRIEF). Final sample consisted of 109 ASD and 195 TD children (5–13 years). Hierarchical multiple regressions were used to examine the effect of BRIEF Index T-scores (Metacognition, MI; Behavioral Regulation, BRI) on SRS total and subscale T-scores in ASD. Hierarchical regression was also used to examine whether diagnostic category was a significant predictor of social functioning after controlling for EF. Bonferroni correction was applied ($p < 0.0071$). Using resting-state functional MRI data, ROI-to-ROI connectivity was computed between nodes of the EF network (left and right prefrontal cortex; left and right posterior parietal cortex). Average EF network connectivity was computed per subject. Hierarchical multiple regression was used to examine the effect of EF functional brain connectivity on SRS total T-scores in ASD.

Results Among ASD participants, MI ($\beta = 0.40$, $p < 0.001$) and BRI ($\beta = 0.50$, $p < 0.001$) were statistically significant predictors of SRS Total scores (Change $R^2 = 0.37$, $F(2, 103) = 35.19$, $p < 0.001$). Diagnostic category remained a significant predictor of social functioning after controlling for EF (Change $R^2 = 0.09$, $F(1, 297) = 203.48$, $p < 0.001$). Average connectivity of the frontal-parietal EF brain network was not a significant predictor of overall social functioning.

Conclusions While EF influences multiple domains of social functioning in ASD, EF does not entirely account for ASD-TD differences in social function. The neural mechanisms of how EF influences social functioning remain unclear. Future work will examine additional neural measures of EF as it relates to social functioning. Funding source: TL1TR001418.

628 INFANTILE INTRACTABLE SEIZURES, SODIUM CHANNEL DUPLICATIONS, AND THE VAGUS NERVE STIMULATOR DEVICE

¹SL Nelson*, ²B Gerstein. ¹Tulane University School of Medicine, Metairie, LA; ²Tulane University, New Orleans, LA

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Case report Genetic mutations can result in severe forms of epilepsy, especially channelopathies. Genetic testing can be valuable in determining prognosis and guiding therapy decisions. We report here an infant who presented with intractable seizures who had sodium channel duplications, and ultimately

placement of a VNS (vagus nerve stimulation) device is what controlled her seizures.

Term infant female with no complications of the pregnancy or delivery, who began having seizures on the first day of life. She was admitted to the NICU, where brain MRI and routine labs were normal. She required multiple doses of lorazepam as well as levetiracetam and phenobarbital for refractory seizures. Once discharged, she was readmitted for status epilepticus multiple times over the next two months despite increasing doses of levetiracetam and phenobarbital, and the addition of clonazepam and topiramate. Video EEG monitoring demonstrated very frequent electroclinical seizures despite being on four anti-epileptic medications at therapeutic doses. CSF neurotransmitters and amino acids, and other metabolic testing, were also negative. Chromosomal microarray and epilepsy panel revealed duplication of SCN2A and SCN3A, which encode subunits of voltage-gated sodium channels essential for proper neuronal function, and thus would be pathogenic. At the age of 2.5 months old, a VNS was placed to control her seizures. Within 24 hours there was a marked reduction in seizure frequency, and by 2 weeks post VNS placement, the patient was almost seizure free. She has achieved incredible benefit from the VNS, and now is only on levetiracetam and remains seizure free. Although she initially had global developmental delay diagnosed at 5 months of age, she has continued to make developmental progress in all areas.

To our knowledge, this patient is the youngest child to receive the VNS device. Additionally, she is the only patient we are aware of with duplication of these sodium channel genes resulting in intractable epilepsy. This case has several important points: genetic testing is an essential part of evaluating children with epilepsy; VNS should be considered for children with intractable epilepsy, even infants.

629 SYSTEMATIC REVIEW OF MESENCHYMAL STEM CELL TREATMENT OF SENSORINEURAL HEARING LOSS

M Willis*, K Chorath, N Morton-Gonzaba, A Moreira. *University of Texas Health San Antonio, San Antonio, TX*

10.1136/jim-2018-000974.635

Purpose of study The purpose of this study is to review experimental studies mimicking SNHL to: i) determine the effects of mesenchymal stem cells (MSCs) on functional hearing, and ii) identify current research gaps and/or limitations to optimize stem cell therapies in future human trials.

Methods used Two investigators independently conducted a systematic search of randomized and non-randomized pre-clinical trials. The primary outcome was functional hearing. The protocol was registered through Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES) and adhered to Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) guidelines. Continuous data was expressed as mean $\pm$ SEM and categorical data was expressed as a percentage. A p -value < 0.05 indicated statistical significance.

Summary of results A total of 11 studies met inclusion criteria. Most studies used rodent animal models (90%). The ages of the animals varied, where six (55%) studies used animals ≤ 8 weeks of age and five (45%) studies with ages 9–12 weeks.

Source of MSCs varied (bone marrow, umbilical cord, adipose tissue, placental cells, and olfactory tissue). The method of delivery included local administration (45%), as well as systemic administration into the peritoneum or intravenous route. Two primary hearing tests were measured: ABR (81%), DPOAE (36%). Despite variability between studies, early analysis of primary outcomes demonstrates improved functional hearing after MSC treatment. Meta-analysis and meta-regression analysis are currently ongoing.

Conclusions Regenerative medicine shows promising potential in treating SNHL. This systematic review calls attention to limitations of the literature, including variability in animal models, MSC characteristics, administration routes, as well as measures of hearing function. Future experimental studies should standardize methods to increase success in clinical trials.

630 COMPLEX DECISION-MAKING IN THE MANAGEMENT OF ISCHEMIC STROKE SECONDARY TO INFECTIVE ENDOCARDITIS

P Pachariyanon*, S Thakolwiboon, R Winn. *Texas Tech University Health Science Center, Lubbock, TX*

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Case report Acute ischemic stroke (AIS) is a devastating complication of infective endocarditis (IE). The management is very challenging. Herein, we demonstrate a case of IE complicated by AIS and evidence-based decisions of management.

A 28-year-old right-handed Caucasian man presented with an acute onset of right hemiparesis for 4 hours, fever, and a history of intravenous drug use. Physical examination revealed multiple Janeway lesions and a 'to-and-fro' murmur along parasternal border. Global aphasia, right homonymous hemianopsia, and right hemiparesis were found. His initial National Institutes of Health (NIHSS) Stroke Scale was 13. Non-contrast computed tomography (CT) of the head was unremarkable. CT angiography demonstrated complete occlusion of the left middle cerebral artery (MCA). Intravenous (IV) tissue plasminogen activator was not given because of the suspicion of IE. The risk of hemorrhagic transformation in IE is much higher than general population. Complete reperfusion was achieved after mechanical thrombectomy. Transesophageal echocardiogram (TEE) showed 2 large vegetations on the aortic valve with severe aortic regurgitation. The patient was empirically treated with IV vancomycin and cefepime.

After blood cultures grew methicillin-susceptible *Staphylococcus aureus* (MSSA), antibiotics were de-escalated to IV nafcillin and oral rifampicin. Aortic valve replacement was performed on day 11 of admission as the recent studies demonstrated the association between early surgery and favorable outcome. A bioprosthetic valve was used to avoid anticoagulation. The risk of intracerebral hemorrhage (ICH) with anticoagulation is highly elevated in IE. The patient clinically improved after surgery. Then, aspirin was started. The patient was discharged to a rehabilitation hospital on day 19 of admission.

The decision making in this situation should be based on a balance of the risk of exacerbation of neurological injury by ICH or worsening cerebral ischemia during surgery and of the benefit from treatment. More evidence supporting the decision analysis will be presented.

631 N-METHYL-D-ASPARTATE-RECEPTOR ENCEPHALOPATHY IN A WOMAN WITH ANTI-THYROID PEROXIDASE ANTIBODIES AND A PAROTID PLEOMORPHIC ADENOMA

KY Sitterley*, T von Kleist, B Bagert. *Ochsner Clinical School, Metairie, LA*

10.1136/jim-2018-000974.637

Purpose of study Anti-N-methyl-d-aspartate-receptor encephalitis is an autoimmune disorder that was first described in 2007. It can cause severe neurological and psychiatric symptoms, and patients are often misdiagnosed as having a primary psychiatric disorder. This is an important differential diagnosis of psychosis, as it can be treated with the appropriate therapy.

Methods used Literature search and patient case analysis.

Summary of results

Case presentation A 42-year-old woman with a history of hypothyroidism presented for evaluation of weakness and possible seizures. Six months prior she complained of a headache, and neuroimaging showed a small right frontal FLAIR hyperintensity. Workup was largely unremarkable, and she improved with steroids. She then developed psychiatric symptoms and had four admissions to separate inpatient psychiatric facilities. She was tried on various antipsychotic medications and mood stabilizers with no improvement and lost 30 lbs over three months.

Neuroimaging was stable, and serum and cerebrospinal fluid were positive for thyroid peroxidase (TPO) and N-methyl-d-aspartate (NMDA)-receptor antibodies. She was treated with a combination of intravenous immunoglobulin, high dose steroids and rituximab. A PET scan revealed a parotid mass, which was resected and determined to be a pleomorphic adenoma.

Conclusions This case demonstrates a typical presentation of NMDA-R encephalitis, as well as the challenges and delays to diagnosis. Symptoms vary and are often psychiatric, which make these patients difficult to diagnose clinically and therefore require careful and thorough investigations. We must continue to be inquisitive and challenge our diagnosis when a clinical picture is not congruent, since an accurate diagnosis is imperative in guiding appropriate treatment.

632 EMERGENCE OF STATUS EPILEPTICUS DURING MIDBRAIN EXTENSION OF BITHALAMIC INFARCTION

V Losada*. *LSUHSC, New Orleans, LA*

10.1136/jim-2018-000974.638

Introduction Early-onset seizure occurs in 3% to 33% of acute strokes, most of which are hemorrhagic. It is rather uncommon for an acute ischemic stroke to manifest early with seizure but, when it does, it is almost always associated with hemispheric infarction. Even more uncommon is early-onset seizure during an acute thalamic and/or midbrain stroke due to top of the basilar artery occlusion. We describe a patient who manifested refractory status epilepticus during midbrain extension of acute bithalamic infarction.

Case report A 64-year-old woman with a cardiac defibrillator and an old stroke presented with profound somnolence. Head CT showed right frontal encephalomalacia consistent with an old stroke. Repeat CT 24 hours later revealed acute infarcts in both thalami. CT angiography showed possible artery of Percheron occlusion. Continuous EEG (cEEG) on days 2 and

3 showed bihemispheric slowing and no epileptiform activity. Methylphenidate was started on day 3 resulting in increased level of alertness. She became hypersomnolent again on day 11. She also manifested bilateral clonic seizures and a left third nerve palsy. Head CT on day 12 showed extension of bithalamic infarcts to the midbrain. EEG revealed epileptiform activity in the form of bianterior rhythmic delta and sharp activity with dramatic response to Ativan challenge. cEEG showed bihemispheric cortical hypersynchrony, i.e. nonconvulsive status epilepticus, which was only partially controlled with lorazepam, levetiracetam, and phenytoin. Complete resolution of seizures was finally achieved after 3 weeks when ethosuximide and valproate were added to the antiepileptic regimen.

Conclusion There are some reports of seizure/status epilepticus in the setting of acute thalamic/midbrain infarction. Our case is unique in that cEEG allowed us to: (1) exclude an epileptic disturbance during bithalamic infarction, (2) detect status epilepticus as it emerged during midbrain infarction, and (3) follow the course of status epilepticus over 3 weeks during which various antiepileptic drugs were administered. Our observations support the key role of the brainstem reticular formation in initiating, maintaining, and terminating generalized seizures. It also implies that an impairment in midbrain and thalamic network function may be responsible for seizure refractoriness.

Nutrition & Dietary Supplements

Concurrent Session

2:00 PM

Friday, February 22, 2019

633 SEX DIFFERENCES IN THE TRANSITION PHASE OF NUTRITION IN ELBW INFANTS

¹P Alur*, ¹R Kalikkot, ¹M Johnson, ¹M Meeks, ¹K Hart, ¹J Desai, ¹S Presley, ²N Hussain. ¹University of Mississippi Medical Center, Brandon, MS; ²University of Health Sciences, Farmington, CT

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Purpose of study We evaluated the sex differences in the effect of calories (C) and protein (P) on weight gain during the transition phase (TP).

Methods used A retrospective review of ELBW infants born from 2014–16 was performed at a level 4 NICU. Those with NEC, short bowel, or chromosomal anomalies were excluded. TP was defined as the period when the infant's enteral feeds were increased from 30–120 ml/kg/day as parenteral nutrition (PN) was weaned. Effect of sex and C and P on change in weight percentiles (wt.pc) from the beginning of TP and end of TP was analyzed. All ELBW infants were started on 100 ml/kg/d and 4 g/kg/d (goal) of protein in PN after birth. Dextrose and lipids in PN were advanced as tolerated. Enteral nutrition was started with breast milk and advanced by 10–20 ml/kg/d as tolerated.

Summary of results Total C intake significantly ($p=0.026$) correlated with a decrease in wt.pc for the whole group. On sex-specific analysis, total C intake significantly correlated with a

Patient Characteristics			
Demographics	Male (36)	Female (60)	P value
Gest.Age	26.4 ± 1.7	26.2 ± 1.7	0.52
B.weight (grams)	855 ± 110	786 ± 153	0.02
Wt. Centile before T-Phase	21 ± 15	23 ± 17	0.58
Wt.Centile After T-phase	21 ± 13	22 ± 15	0.64
CLD	54%	57%	0.75
Postnatal steroids	25.70%	25.40%	0.97
PDA	45.70%	50.80%	0.63
Duration of T.phase	9.7 ± 3.5	9.2 ± 3.5	0.47
DOL BW regained	8.7 ± 6.3	8.3 ± 5.6	0.74
Feed vol fortified to 24 cal	95 ± 36	91 ± 33	0.58
Nutrition			
Mean Calories	102 ± 7	102 ± 8	0.83
Mean Protein g/kg	3.7 ± 0.5	3.8 ± 0.5	0.3
Calories-Wt.centile change	-0.57		0.32
Calories-Wt.centile change		-1.08	0.03

Abstract 633 Figure 1

decrease in wt.pc only in girls (regression $p=0.03$). P did not correlate with wt.pc or sex. C & P intake was similar in both sexes (figure 1). However, girls lost 5 centiles versus boys gained 0.4 in head circumference during TP ($p=0.08$). The demographics and pre-TP growth percentiles were similar in both sexes.

Conclusions Despite similar intake of C and P during TP, there was a significant decrease in wt.pc only in girls. Large prospective studies may help us understand if ELBW girls need higher calories or have a higher metabolic rate.

634 SERIAL ULTRASOUND AND BREASTMILK MACRONUTRIENT ANALYSIS ARE FEASIBLE AND DEMONSTRATE DIFFERENCES IN CALORIC INTAKE AND BODY COMPOSITION IN VLBW INFANTS

CB Ramirez*, R Jacob, J Gelfond, DC McCurnin, CL Blanco. University of Texas Health San Antonio, Boerne, TX

10.1136/jim-2018-000974.640

Purpose of study Extrauterine growth restriction affects over 50% of very low birth weight (VLBW) infants. The purpose of this study is to assess the utility of new technology [ultrasound (US) and milk analyzer] to predict infant BC and to assess the effect of mom's own milk (MOM) on BC via dual energy x-ray absorptiometry (DXA).

Methods used Singletons weighing ≤ 1500 g on an exclusive human milk diet were enrolled. At 7 days (d) of age and every 14d fat and muscle measurements were obtained via US at four different body sites. The interclass correlation coefficient (ICC) for US was performed on a subset of patients. At 36 weeks post-menstrual age (PMA) BC via DXA was performed. Milk macronutrient analysis was performed weekly with a near infrared analyzer.

Summary of results Thirty-four infants were enrolled with a mean GA 28.4 ± 2.4 weeks, BW 1108 ± 285 , and CRIB score median of 7.5 (IQR 5–11.25). A total of 860 US measurements were performed serially regardless of ventilator support. The ICC demonstrated good reliability ($R_{20.93}=\text{abdomen}$, $0.79=\text{subscapula}$, $0.67=\text{arm}$, and $0.91=\text{thigh}$, $p<0.05$). The%

fat growth overtime using linear mixed effect models by US demonstrated growth on each site with an increasing trend as %MOM intake increased ($p=0.06$). The measured enteral caloric intake was 12, 10, 3 and 10 kcal/kg/day lower than the presumed caloric intake at 7,14,21 and 28d respectively. Lower measured caloric intake at 21 days trended towards a lower fat-free mass at 36 weeks PMA ($p=0.06$) with odds of 12.7 (0.8–197, $p=0.06$) after adjusting for CRIB score. There was no correlation between %MOM intake during the first 4 weeks of life and %BF by DXA at 36 weeks PMA. The caloric concentrations measured were 15% and 11% lower in unfortified MOM vs donor milk at 14d and 28 DOL respectively, $p=0.01$; however, the caloric intake, growth velocity and %BF by DXA was similar.

Conclusions VLBW infants exclusively feeding human milk have differences between measured and presumed caloric intake that do not translate into poor growth via US, growth velocity or %fat by DXA. Ultrasound in 4 body sites can reliably measure fat/lean mass overtime in VLBW infants and is a promising tool to assess/optimize growth in sick preterm infants.

635

A PREOPERATIVE STANDARDIZED FEEDING PROTOCOL EMPHASIZING HUMAN MILK TO IMPROVE OUTCOMES IN INFANTS WITH DUCTAL-DEPENDENT CONGENITAL HEART DISEASE

^{1,2}J Kataria-Hale, ^{1,2,5} Osborne, ^{1,2}D Roddy, ^{1,2}AB Hair. ¹Baylor College of Medicine, Houston, TX; ²Texas Children's Hospital, Houston, TX

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Purpose of study To evaluate the postoperative outcomes of infants with ductal-dependent congenital heart disease (CHD) after implementation of a preoperative standardized feeding protocol that emphasizes the use of human milk.

Methods used This is a prospective quasi-experimental study whereby neonates with ductal-dependent CHD requiring prostaglandin therapy were enrolled in a standardized feeding protocol emphasizing human milk use. The neonates were prospectively followed throughout their hospitalization to document protocol adherence, rates of human milk use, and postoperative outcomes. The prospective data was compared to a retrospective cohort prior to implementation of the protocol.

Summary of results After implementation of the feeding protocol, the proportion of infants fed before surgery was significantly higher ($p=0.043$) after the intervention (21/24=87.5%) compared to before the intervention (363/546=66.5%). The proportion of infants receiving formula after the intervention (1/21=4.8%) was significantly lower ($p<0.001$) compared to after the intervention (151/363=41.6%). The average number of days to full feeds postoperatively was 8.5 ± 6.1 days before the intervention versus 9.5 ± 5.7 after the intervention ($p=0.258$). Since implementation of the feeding protocol, 20/24 patients received oral care with maternal colostrum prior to starting feeds. There was one case of necrotizing enterocolitis prior to surgery.

Conclusions Despite the fear of feeding neonates with ductal-dependent CHD prior to surgery, our data suggest that, since implementation of a standardized preoperative feeding protocol, a significantly higher proportion of infants were fed prior

to surgery compared to pre-implementation of the protocol. With an emphasis on human milk in the feeding protocol, we found that formula use was significantly lower compared to pre-implementation of the protocol. As a result of the protocol, most infants received oral care with mother's colostrum prior to receiving enteral feeds- a practice that was not standard of care until implementation of the protocol. Although the data do not suggest a difference in number of days to achieve full feeds between the two cohorts, the data collection is ongoing.

636

WHEN TOO MUCH OF A GOOD THING BECOMES HARMFUL?

N Mehta*, M Germain, L Quiel. White River Health System, Batesville, AR

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Case report Dietary supplements are used for optimizing one's well-being and requires monitoring.

A 71-year-old female with history of hypertension and hypothyroidism was admitted for AMS, AKI, atrial fibrillation, and abnormal electrolytes. Patient's son noted that the patient consumed 30+ dietary supplements (DS) daily. Creatinine was elevated (6.2 mg/dL) from baseline (0.8 mg/dL). Patient was compliant with her antihypertensive (hydrochlorothiazide, valsartan, and lisinopril) and hypothyroidism (levothyroxine) medications. Hours after admission, patient became anuric. Dialysis was initiated. Her kidney function improved while hospitalized, but required dialysis on discharge.

DS usage has increased to ~70% of adults over the age of 60.¹ A recent study found only 5% of patients taking supplements had every supplement discussed/documented during PCP visits² highlighting the passive management of DS. DS are marketed as 'natural' which is perceived as safe.³ However, supplements including St. John's Wort, Echinacea, Chromium, and Glucosamine (all of which our patient consumed) have been associated with AKI.⁴ Our patient's borderline selenium toxicity likely altered selenoproteins contributing to kidney failure.⁵

Supplements are treated differently than pharmaceutical drugs.⁶ The FDA requires safety/efficacy documentation prior to market entry for drugs, but DS are not held to the same standard.³ Dietary Supplements Health and Education Act allow DS to be regulated as food not 'drugs' with minimal oversight from the FDA.³ FDA can remove DS from the market if it provides a danger to public health.⁶ By law, pharmaceutical companies are required to meet quality standards established by United States Pharmacopeia (USP), whereas manufacturers of DS are only required to exceed USP standards if the manufacturer reports following USP standards.⁶ Simply, DS do not have to be a certain quality.

In conclusion, the usage of DS warrants careful monitoring to ensure that maximizing one's well-being does not become deleterious.

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637

KRATOM INDUCED HEPATOTOXICITY AND THE ROLE OF N-ACETYL CYSTEINEP Desai*, K Ramachandra, M Shah. *Upstate Medical University, Syracuse, NY*

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Case report Kratom has recently gained significant popularity in the western world as an herbal supplement for alcohol and opioid withdrawal, chronic pain, and recreation. Multiple cases of fatalities associated with Kratom use have been reported from various mechanisms, most commonly from respiratory depression from the combined use of Kratom and opioids. Rarely, Kratom has been found to cause acute liver damage including acute hepatic failure.

A 36-year-old Caucasian lady was transferred to our tertiary care center for management of peri-nephric abscess. On arrival, she was found to have elevated ALT (592), AST (1482), and total bilirubin (2.4). She had a history of only mild alcohol use (few beers per week) and occasional acetaminophen use (<10 gm/week). Viral hepatitis panel and RUQ ultrasound were unremarkable. After her AST and ALT increased to more than double the initial levels within a few hours, poison center recommended starting NAC administration empirically. Her liver enzymes improved to ALT<300 and AST<1000. After her acetaminophen level was found to be negative, NAC was stopped. Within 6 hours, the levels started increasing again peaking at ALT>3800 and AST>12000 and NAC was restarted. At this time, a family member reported that the patient was abusing Kratom concoctions for recreational use since few weeks. The patient was diagnosed with drug-induced hepatitis secondary to Kratom abuse. Her liver enzymes gradually improved with continuous administration of NAC.

Kratom (*Mitragyna Speciosa*) is a plant that has been used in traditional medicines in tropical countries. It contains multiple alkaloids including mitragynine, which is a partial agonist at Mu opioid receptors. Kratom is also a potent inhibitor of some of the CYP450 enzymes which have resulted in deaths from an opioid overdose from toxic accumulation of metabolites with combined use. Between 2011 and 2017, the FDA reported 44 kratom-related deaths in the United States. It is believed that due to prolonged cytochrome inhibition, Kratom can cause glutathione overconsumption and ultimately depletion (similar to acetaminophen toxicity). The resolution of hepatic injury in our patient using NAC, along with similar case reports from others, indicate a promising role of NAC in acute hepatic injury caused by Kratom.

638

EVALUATION OF SUBCLINICAL MAGNESIUM DEFICIENCY IN POSTMENOPAUSAL WOMEN¹RB Costello*, ²F Nielsen, ¹A Rosanoff, ³RJ Elin. ¹Center for Magnesium Education and Research, Leesburg, VA; ²USDA, Grand Forks, ND; ³University of Louisville, Louisville, KY

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Purpose of study Controlled metabolic ward studies provide guidance for the determination of status indications for individuals who may be at risk of magnesium (Mg) deficiency. Low serum Mg along with decreased dietary intake of Mg may incur increased risk for a number of chronic diseases. The objective of this study was to evaluate the risk profile of

Abstract 638 Table 1

Measure (n=645)	Mean±SD	Range
Serum Mg (mg/dL)	1.99±0.18	1.6–2.4
Serum Ca (mg/dL)	9.33±0.37	8.2–10.6
Ca/Mg ratio	4.71±0.42	3.8–6.0
QTc msec.	0.419±0.02	0.319–0.476

women participating in the USDA Mg depletion studies as reflected by their serum Mg and calcium (Ca) concentrations and EKG parameters.

Methods used Data from three USDA depletion-repletion studies in healthy postmenopausal women (n=41) were analyzed for occurrence of a serum Mg level <2.1 mg/dL with or without QT interval changes on the EKG during the study period, consuming a depletion diet between 104 to 146 mg Mg/day lasting from 72 to 93 days. The serum Ca/Mg ratio was also evaluated.

Summary of results Forty-one healthy women submitted a total of 645 serum measures throughout the entire study period paired with an EKG QT measure (mean of 5 complexes/reading) corrected for heart rate (QTc). Serum Mg was <2.1 mg/dL on 406/645 (63%) of time points during the study. A borderline QTc (>0.450 msec) or greater was evident on 46/645 (7%) EKG tracings. Within a subgroup of 12 women, who displayed both a serum Mg <2.1 mg/dL (mean 1.88 mg/dL) and prolonged QTc (mean 0.457 msec), 6/12 women (50%) did so at one time point and 4/12 (33%) displayed a low serum Mg with a prolonged QTc on two or more time points (depletion and/or repletion phases). There was a nonsignificant inverse correlation ($r^2=-0.34$; $p=0.08$) between serum Mg and the QTc. The mean Ca/Mg ratio was increased at 4.92. Four women in this study developed cardiac arrhythmias.

Conclusions A serum Mg level in the lower part of the reference interval may have a negative impact on normal physiology. Clinicians may find it useful to evaluate both a serum Mg along with EKG data in individuals with established chronic disease or risk factors.

639

A MULTI-DISCIPLINARY APPROACH TO IMPROVING NUTRITION IN PATIENTS WITH CYSTIC FIBROSISA Mathew*, N Mehdi, S Palle. *OU Children's Hospital, Oklahoma City, OK*

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Purpose of study In Cystic Fibrosis (CF), better early childhood nutrition is associated with better height growth, lung function and improved survival into adulthood. In order to improve the nutritional status, we assessed the level of malnutrition in our CF population and identified barriers to their nutritional care

Methods used Our CF dietician assessed nutritional status of the kids who presented to the pulmonary clinic for routine CF follow-up over a year based on their body mass index (BMI) or weight-for-length (WFL) percentiles. Additionally, the pulmonary and psychosocial status of patients with a BMI or WFL less than the 50th percentile were individually analyzed to identify specific barriers to their nutritional improvement. In addition to receiving a comprehensive nutritional plan from

the dietician, our center has started utilizing the services of gastroenterology as part of developing innovative gastroenterology specialty training (DIGEST) initiative from CF foundation from July 2016

Summary of results On review of 165 CF kids, 35% had a BMI or WFL less than the 50th percentile. In this sub-optimal weight population, the average FEV1 was 90.5%, in comparison to an FEV1 of 90.6% among our entire CF population. In addition to medical reasons, we identified major psychosocial barriers like lack of patient/family education related to nutrition in CF, adherence to enteral therapy like poor compliance secondary to a two-household status and refusal of tube feeds due to enteral feeds impacting quality of life at school and home. In order to address these concerns effectively, we adopted a CF multidisciplinary approach where we added a full time psychologist and social worker in addition to pulmonologist, RD, gastroenterologist, nurse, pharmacist and respiratory therapist. Moreover, the potential need for supplemental nutrition will be addressed with families from the onset of care in order to accommodate families to its potential need in future.

Conclusions Due to the direct correlation between nutritional status and pulmonary function in CF patients, our center analyzed the GI and nutritional needs of our CF population and developed a multidisciplinary approach to addressing these concerns. In a year, we will review this approach in our CF population to assess the impact of improved nutritional status on pulmonary function and survival.

640 KWASHIORKOR AND VITAMIN DEFICIENCY IN AUTISM SPECTRUM DISORDER

^{1,2}B Casey, ^{1,2}D Nguyen, ^{1,2}A McKernan, ^{1,2}B Desselle, ^{1,2}C Sandlin. ¹LSUHSCNO, New Orleans, LA; ²Children's Hospital of New Orleans, New Orleans, LA

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Case report Kwashiorkor is an edematous malnutrition which results in peripheral pitting edema, marked muscle atrophy, and micronutrient deficiency. It is usually seen in resource limited countries. Despite the rarity of malnutrition in the United States, research shows a strong correlation with Autism Spectrum Disorder (ASD) and sensory sensitivity, with picky diets noted in many children with ASD and concern for potential undernutrition. However, there is conflicting data on nutritional adequacy when comparing children with and without ASD. We discuss a case of a 13-year-old male with Kwashiorkor and Vitamin Deficiency secondary to sensory feeding issues in ASD.

A 13-year-old male with ASD presented to the Pediatric ICU with a 2 day history of difficulty seeing and abdominal, lumbar, and bilateral lower extremity swelling. History was significant for sensory feeding issues with a diet limited to potato chips, goldfish crackers, and cupcakes. Initial labs revealed a microcytic anemia, hypoalbuminemia, hypoproteinemia, direct hyperbilirubinemia, and coagulopathy. A CT Chest/Abdomen demonstrated bilateral pleural effusions and abdominal ascites. There was a pericardial effusion and diminished left ventricular diastolic function on echocardiogram. The patient's Vitamin A level was low, and his ophthalmologic exam revealed Xerophthalmia of the left eye with conjunctival and corneal involvement. Vitamins A, D,

and K were replaced, and nasogastric feeds were initiated. Ultimately, the patient's clinical findings and labs normalized with proper nutritional replenishment. He was discharged with feeding team follow-up and plans for gastrostomy tube placement.

The patient had multiple severe lab abnormalities, edema, and acute vision changes suggesting chronic nutritional deficit. This level of malnutrition is rare in developed nations with nutritionally rich food availability; however, lack of available resources and inadequate follow-up likely contributed to a delay in this patient's diagnosis and management. His case highlights the importance of having a high index of suspicion for vitamin deficiencies and a poor nutritional status in children with ASD and sensory feeding issues.

641 LOW VITAMIN K STATUS IS ASSOCIATED WITH MARKERS OF DIABETES RISK AND VISCERAL ADIPOSITY IN OVERWEIGHT CHILDREN

U Chandra*, CF Williams, M Fain, M Brown, R Bassali, C Davis, NK Pollock. *Medical College of Georgia, Augusta University, Augusta, GA*

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Purpose of study Although animal studies suggest that vitamin K status may impact diabetes risk and the type of fat accumulation, the human data are scant and equivocal. This study investigated associations of vitamin K status with risk of prediabetes and measures of insulin resistance and total and central adiposity in 348 overweight children aged 8–11 years (60% female, 68% black).

Methods used Fasting blood samples of glucose and insulin were collected to determine homeostasis model assessment of insulin resistance (HOMA-IR) and to identify prediabetes. Using additional fasting sera, total osteocalcin (OC) and uncarboxylated OC (ucOC) were assessed to determine vitamin K status based on percentage ucOC [%ucOC = (ucOC/total OC) × 100] as follows: sufficient, <20%; insufficient, 20%–50%; and deficient, >50% (elevated levels of %ucOC are indicative of poorer vitamin K status). Percentage body fat (%BF) and visceral adipose tissue (VAT) were measured by dual-energy X-ray absorptiometry and magnetic resonance imaging, respectively.

Summary of results Overall prevalence of vitamin K insufficiency and deficiency were 70% and 10%, respectively, and 33% had prediabetes. Multinomial logistic regression, adjusting for sex, race, and %BF, revealed that compared to the vitamin K sufficient group, the odds ratio for presence of prediabetes was 3.2 (95% CI: 1.3 to 7.7). In further analyses with multiple linear regression adjusting for sex and race, HOMA-IR ($\beta=0.13$) and VAT ($\beta=0.12$) were associated with %ucOC (both $p<0.05$). No association was found between %ucOC and %BF.

Conclusions These data suggest that suboptimal vitamin K status is prevalent in overweight children, particularly those with prediabetes. Given that poorer vitamin K status was associated with insulin resistance and visceral adiposity, vitamin K trials are needed to determine whether improving vitamin K status is effective in delaying progression of insulin resistance and diabetes in pediatric populations at high risk of developing diabetes in adulthood.

Perinatal Medicine I

Concurrent Session

2:00 PM

Friday, February 22, 2019

642

ABSENCE OF SURFACTANT PROTEIN A LEADS TO A DECREASE IN RETINAL VASCULARIZATION IN NEONATAL MICE¹J Kung, ²J Wren, ²C Georgescu, ¹F Bhatti*. ¹University of Oklahoma Health Sciences Center, Oklahoma City, OK; ²Oklahoma Medical Research Foundation, Oklahoma City, OK

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Purpose of study Retinopathy of prematurity (ROP) is the leading cause of visual impairment in children and is impacted by inflammation. Surfactant protein A (SP-A) is an important immune modulator and is deficient in preterm infants. We previously showed that global lack of Surfactant Protein A (SP-A) is associated with neovascularization in the mouse oxygen induced retinopathy model. We hypothesize that lack of SP-A reduces physiological retinal vascularization and investigate the signaling pathways that may be responsible.

Methods used We compared the retinal vascular phenotype of wild type (SP-A^{+/+}, WT) and SP-A^{-/-} mice at ages P4, P6, P8 and P10. Whole retinas were flat mounted and blood vessels visualized by immunohistochemistry (IHC) with antibodies against CD31. Rate of vascularization, vascular density, length and number of tip cells at the vascular front were quantified using image analysis software. Differential gene expression of samples from SP-A^{-/-} and WT whole retina tissues was evaluated using RNA sequencing. Data quality was checked, sequences aligned to genome, differential expression values calculated with DEseq, then Gene Ontology and pathway enrichment analyses performed.

Summary of results Differences in vascular phenotype were only observed at P6. Rate of vascularization was significantly reduced in SP-A^{-/-} vs. WT (64% vs 73%). Length of tip cells was 1.6-fold greater in SP-A^{-/-} vs. WT. There was no difference in vascular density or total number of tip cells. RNASeq showed 1134 genes that were differentially expressed at P6 between WT and SP-A^{-/-}. A subset of differentially expressed genes mapped to signaling pathways and transcription regulation that control the cell cycle progression and cytoskeleton-dependent functions such as actin polymerization or microtubule formation. Of note, no differences were observed in expression of vascular endothelial growth factor genes, which are commonly implicated in ROP.

Conclusions These initial findings can explain the observed phenotype of elongated tip cells and decreased rate of retinal vascularization. We are working to determine the underlying mechanisms of these observed differences.

643

INFLAMMATORY MONOCYTES ARE MOBILIZED IN INFANTS WITH TYPE 1 RETINOPATHY OF PREMATURITY

B Stansfield*. Augusta University, Augusta, GA

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Purpose of study Retinopathy of prematurity (ROP) is the pathologic consequence of delayed retinal vascular development coupled with exposure to relative hyperoxia and inflammatory processes. Monocytes are key mediators of inflammation, and emerging evidence suggests that monocyte-derived macrophages are abundant in retinas during the neovascular phase of the oxygen-induced retinopathy model and promote retinal neovascularization. Despite a strong clinical rationale and supportive animal data, human studies implicating specific inflammatory cells has not been performed. The purpose of this study was to examine monocyte subpopulations in infants with/without Type 1 ROP.

Methods used We identified 4 patients with Type 1 ROP, as defined in the ETROP study, and 4 controls without Type 1 ROP matched for birthweight, gestational age, and postmenstrual age. Informed consent was obtained and peripheral blood was obtained in coordination with routine laboratory tests on the same day for matched subjects. Mononuclear cells were isolated using Ficoll-Paque Plus. Cells were washed, incubated with Fc Blocking Reagent, and labeled with the following fluorochrome-labeled antibodies: CD45-APC; HLA-DR5-PC5; CD14-FITC; and CD16-PE. Samples were run on a Beckman Coulter FC500 at Augusta University Medical Center. The percent of total CD16 + and intermediate CD14 ++ CD16 + monocyte, the putative pro-inflammatory monocyte population, were compared between the matched subjects and total cohorts.

Summary of results Subjects with Type 1 ROP had increased total CD16 + and intermediate CD14 ++ CD16 + monocytes in their peripheral blood compared to matched controls without ROP. As a cohort, subjects with Type 1 ROP exhibited a 33% increase in total CD16 + monocytes (p=0.001) and 45% increase in intermediate CD14 ++ CD16 + (p=0.001) monocytes in their peripheral blood compared to the control cohort.

Conclusions At the time of intervention for Type 1 ROP, we demonstrate that pro-inflammatory CD16 + monocytes, particularly CD14 ++ CD16 + intermediate monocytes, are much more mobilized in infants with Type 1 ROP than in matched controls. These data provide a compelling rationale for a prospective longitudinal examination of monocyte subpopulations as a potential biomarker for Type 1 ROP and may enable early identification of infants who go on to develop severe ROP requiring intervention.

644

THE THIOREDOXIN REDUCTASE INHIBITOR AURANOFIN SUPPRESSES IL-1 β PRODUCTION IN LIPOPOLYSACCHARIDE-TREATED ALVEOLAR MACROPHAGES

A Freeman*, S Wall, R Li, K Dunigan, Q Li, TE Tipple. University of Alabama at Birmingham, Birmingham, AL

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Purpose of study Inflammation driven by alveolar macrophage IL-1 β production significantly contributes to the development of acute lung injury (ALI) and bronchopulmonary dysplasia (BPD). Our lab has established that thioredoxin reductase-1 (TXNRD1) inhibition is protective in murine models of ALI and BPD, primarily driven by the transcription factor nuclear factor (erythroid-derived 2)-like 2 (Nrf2) activation. These studies tested the hypothesis that TXNRD1 inhibition

decreases IL-1 β production and increases Nrf2 dependent antioxidants in alveolar macrophages.

Methods used Immortalized murine alveolar macrophages (MH-S) were cultured in the presence or absence of 0.05 μ g/ml lipopolysaccharide (LPS) and/or 0.5 μ M auranofin (AFN). AFN inhibited TXNRD1 activity by 90% and was associated with increased nuclear Nrf2 accumulation.

Summary of results Within 2 hour, IL-1 β mRNA levels, assessed by qRT-PCR, were 200-fold greater in LPS-treated MH-S cells than in vehicle-treated cells. In contrast, IL-1 β mRNA levels were increased by 100-fold in LPS-treated cells cultured in the presence of AFN. When compared to control-treated cells, IL-1 β protein levels, assessed by ELISA at 6 hour, were 18-fold greater in LPS-treated cells but only 10-fold greater in LPS +AFN cells. Levels of glutathione (GSH), a key intracellular antioxidant, measured at 24 hour by Tietze recycling assay, were 1.4-fold greater in LPS-treated MH-S cells when compared to controls. In the presence of AFN, LPS treatment increased GSH levels by 2.5-fold.

Conclusions Our novel data indicate that TXNRD1 inhibition attenuates LPS mediated increases in IL-1 β in alveolar macrophages. We speculate that attenuated IL-1 β expression and enhanced endogenous antioxidant responses contributes to improved outcomes in our murine models of ALI and BPD.

645

EXOSOME PROFILES FOR NORMAL AND COMPLICATED PREGNANCIES – A LONGITUDINAL STUDY

^{1,2}A Nakahara*, ^{1,2}O Elfeky, ¹C Garvey, ²D Guanzon, ¹S Longo, ^{1,2,3}C Salomon. ¹Ochsner Baptist Hospital, New Orleans, LA; ²Exosome Biology Laboratory, Centre for Clinical Diagnostics, UQ Centre for Clinical Research, Royal Brisbane and Women's Hospital, Faculty of Medicine and Biomedical Sciences, The University of Queensland, Brisbane, Australia; ³Faculty of Pharmacy, University of Concepción, Concepción, Chile

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Purpose of study Exosomes are small nanovesicles which play a key role in cell-to-cell communication during pregnancy by transferring bioactive molecules to other cells and modifying their biological functions. Little is known about the changes in the concentration of circulating exosomes throughout gestation in normal and complicated pregnancies.

Methods used A prospective cohort of patients was recruited during pregnancy and retrospectively stratified based on normal (n=30), gestational diabetes mellitus (GDM) (n=10) and preeclampsia (PE) pregnancy outcomes (n=15). Total exosomes and specific placental-derived exosomes (PdE) were determined by Nanoparticle Tracking Analysis using quantum dots coupled with CD63 or PLAP antibodies. Linear mixed modelling was performed on normalized total and PdE across gestation using the lme4 package in R. Using likelihood ratio tests, statistically significant differences were found in exosome concentration across gestation.

Summary of results Significant factors contributing to variations in total and PdE were gestational age and pregnancy outcomes (ANOVA, $p < 0.05$). Post-hoc analyses established that PdE concentrations increased during gestation in normal, GDM and PE pregnancies. The increase was significantly greater in GDM and PE compared with normal pregnancies. Our linear mixed modelling analysis showed that PdE increased ~2.1 fold in PE and GDM compared to normal throughout gestation. Interestingly, maternal BMI, glucose

concentrations and fetal weight significantly affect the concentration of PdE across gestation.

Conclusions This study provides evidence of the changes exosomes present in maternal circulation across gestation, suggesting that exosomes may be involved in maternal metabolic adaptation to pregnancy. Further, exosomes can be an early predictor of adverse outcomes, including GDM and PE.

646

INTRANASAL DELIVERY OF MESENCHYMAL STEM CELLS RESTORES LUNG DEVELOPMENT IN EXPERIMENTAL BRONCHOPULMONARY DYSPLASIA

¹A Moreira*, ¹C Winter, ¹L Winter, ¹M Jones, ¹K Quim, ¹M Noronha, ¹M Porter, ¹A Corral, ¹Y Alayli, ¹J Joy, ¹T Seno, ²P Hornsby, ³J Hsieh, ¹SB Mustafa. ¹UT Health Science Center-San Antonio, San Antonio, TX; ²UT Health San Antonio, San Antonio, TX; ³UT San Antonio, San Antonio, TX

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Purpose of study The therapeutic potential of mesenchymal stem cells (MSCs) has been established in animal models of lung injury. Most studies administer these novel agents intravenously or intratracheally. We hypothesized that intranasal delivery of MSCs was feasible and effective in restoring lung alveolarization and vasculogenesis in a rat model mimicking neonatal lung disease.

Methods used Human umbilical cord cells were isolated and characterized to meet the minimum criteria for MSCs. In a hyperoxia-induced rat model of bronchopulmonary dysplasia (BPD), MSCs (500,000 cells/20 μ L) were administered intranasally on days 4, 10, and 20. On day 21, animals underwent a forced swim test followed by necropsy. Lung slides were stained with hematoxylin and eosin stain (Alveolarization), von Willebrand factor (Vasculogenesis), Masson's trichrome (Fibrosis), and α -SMA (Muscularization). Lung lysates from each group (Control, BPD, and BPD+MSC) were analyzed with a rat cytokine array kit.

Summary of results Newborn rats exposed to hyperoxia demonstrated the characteristic arrest in alveolar growth and decrease in lung vasculature. Intranasal delivery of MSCs was well tolerated, migrated to the lungs, and fully restored alveolarization and vascularization. Hyperoxia-exposed animals had a 41% increase in medial wall thickness compared to animals housed in 21% O₂. MSCs reduced pulmonary artery medial wall thickness by 29%. Protein lysate from the BPD+MSC group had increased expression of VEGF, HGF, FGF, MMP2, Neprilysin, and VCAM-1. Growth velocity and exercise tolerance did not differ among groups.

Conclusions Intranasal delivery of MSCs can be safely deliv-

Abstract 646 Figure 1

ered to the lungs and provides a noninvasive and effective approach to current cell-based approaches for treating lung disease. The beneficial effects of MSCs can be attributed to their expression of pro-angiogenic and immunomodulatory factors.

647

THE ROLE OF HEME IN A MURINE MODEL OF BRONCHOPULMONARY DYSPLASIA

H Wongprasert*, C Ren, Q Li, TL Summerlin, B Halloran, J Oh, R Patel, TE Tipple, T Jilling. UAB, Birmingham, AL

10.1136/jim-2018-000974.653

Purpose of study Cell-free heme is pro-oxidant and cytotoxic, causing cellular oxidant injury and inflammation. Heme oxygenase 1 (HO-1), which is inducible by heme, is the key enzyme of intracellular heme catabolism. HO-1 plays a protective role in the neonatal murine lung against hyperoxia-induced abnormal lung development, an animal model for bronchopulmonary dysplasia (BPD). Hemopexin (HPX) is a heme-binding plasma protein that delivers heme for cellular uptake, but its potential protective role in hyperoxia has not been studied. Objective: To test the hypothesis that cell-free heme contributes to abnormal lung development in hyperoxia-exposed neonatal mice and that treatment with HPX protects from the deleterious effects of hyperoxia.

Methods used Newborn C57BL/6 mice on postnatal day 4 (P4) were administered either intramuscular (IM) injections of saline (vehicle control), HPX, or HPX plus aurothioglucose (ATG, a HO-1 inducer). Mice were then exposed to either 21% (room air) or 85% oxygen (hyperoxia) from P4–14 to induce lung injury. At P6, 8, and 10, HPX administration was repeated in the treatment groups. Weights were monitored and dams were switched daily. Lung morphology, lung tissue mRNA, plasma heme, and pro-inflammatory cytokines were assessed at P14.

Summary of results Gene expression analysis revealed hyperoxia increased mRNA levels for genes involved in inflammation such as CXCL1 (KC/GRO) (10.0 ± 1.9 fold) and PTGS2 (COX2) (3.6 ± 1.1 fold) and in fibrosis, such as TGF β 2 (3.7 ± 0.7 fold) and ACTA2 (2.8 ± 0.7 fold) (all $p < 0.05$; ANOVA $n = 4$). ELISA analysis demonstrated hyperoxia also elevated plasma IL-6. Mean linear intercept (MLI; inversely correlated with alveolar development) was increased from 40.1 ± 1.1 μ m (room air) to 69.2 ± 1.1 μ m (hyperoxia) in vehicle control group. Administration of HPX alone or HPX plus ATG did not show protective effect on alveolar development, inflammatory gene expression, or plasma IL-6 levels. Circulating heme was not significantly different between room air and hyperoxia-exposed P14 mice.

Conclusions Cell-free heme was not increased in hyperoxia exposure, even though pro-inflammatory signaling in both lungs and plasma were increased. Treatments with either IM hemopexin alone or combined with ATG failed to attenuate alveolar injury in hyperoxia-exposed neonatal mice.

648

ELECTIVE HIGH-FREQUENCY JET VENTILATION VERSUS CONVENTIONAL MECHANICAL VENTILATION IN PERIVIAL PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME

R Phaltas*, F Eyal, O Jha, R Bhat. University of South Alabama, Mobile, AL

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Purpose of study Early elective high-frequency jet ventilation (HFJV) strategy improves short-term respiratory outcomes in preterm infants with respiratory distress syndrome but associated with increased risk for perinatal brain injury. As periviable infants are most susceptible for adverse respiratory outcomes, early elective HFJV strategy compared to

conventional mechanical ventilation (CMV) strategy may improve respiratory outcomes, and if optimal lung volume strategy is used, even may alleviate the adverse impact on short-term neurological outcomes.

Methods used In this retrospective, 1:1 matched case-control study, a total of 74 periviable preterm infants ($22^{0/7}$ – $23^{6/7}$ weeks or birth weight < 500 grams), born between 2013 and 2017 were included. Infants who received CMV were included control group ($n = 37$), while infants who received elective HFJV were included in the intervention (case) group ($n = 37$). A total number of days alive and off assisted or mechanical ventilation during first 28 days postnatal age and percentage changes in the lung volume from baseline during the first postnatal week as estimated by chest x-ray planimetry were the primary outcome measures.

Summary of results Use of elective HFJV strategy compared to CMV strategy was associated with an increase in number of days alive and off assisted ventilation during first 28 days of postnatal age after the adjustment for all the potential confounders identified based on the univariate analyses [adjusted mean difference of +3.8 days favoring elective HFJV with 95% confidence interval (CI) of 1.1–6.5, $p = 0.006$]. Adjusted mean (95% CI) percentage changes in the lung volumes from baseline did not differ between elective HFJV and elective CMV groups ($p = 0.68$). Use of elective HFJV strategy was associated with a trend towards reduction in death or need for assisted ventilation by postnatal day 28 [adjusted odds ratio (aOR) 0.3, 95% CI 0.1 to 1.0, $p = 0.05$], but not associated with higher odds of severe intraventricular hemorrhage (aOR 2.2, 95% CI 0.2 to 18.2, $p = 0.47$).

Conclusions Use of elective HFJV strategy was associated with an improvement in short-term respiratory outcomes without increasing the risks for lung hyperinflation and perinatal brain injury in periviable infants.

649

THE EFFECT OF UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS IN AN *IN-VITRO* MODEL OF BRONCHOPULMONARY DYSPLASIA

J Joy, D McDaniel, C Winter, SB Mustafa, A Moreira*. UT Health Science Center-San Antonio, San Antonio, TX

10.1136/jim-2018-000974.655

Purpose of study Umbilical cord-derived mesenchymal stem cells (UC-MSCs) may serve as potential therapeutic agents for BPD. UC-MSCs have higher proliferative abilities, longer lifespan, and secrete greater amounts of regenerative factors when compared to adult tissue-derived MSCs. The purpose of this study was to investigate the effects of UC-MSCs in an *in-vitro* model of hydrogen peroxide-induced BPD.

Methods used MSCs derived from human UC Wharton's jelly met the criteria for MSCs per the International Society for Cellular Therapy. Rat lung epithelial cells (RLE-6) were used to model the lung epithelium. RLE-6 cells were separated as follows:

- Control (grown at standard cell conditions),
- Injured (100 μ M H_2O_2 for 1 hour), and
- Treated (100 μ M H_2O_2 for 1 hour + 50% UC-MSC conditioned media).

Experiments included cell proliferation, wound healing, production of extracellular reactive oxygen species, RNA expression of caspase-6 and superoxide dismutase-2 (SOD-2).

Summary of results Compared to Control, RLE-6 proliferation after H₂O₂ injury to the cells decreased by 51% versus a decrease of 4% in the Treated group ($p < 0.05$). Four hours after creating a wound in RLE-6 cells, Control group had healed by 14% while the Injured group reached 33% closure and the Treated group had 48% closure ($p < 0.05$). H₂O₂ increased oxidant injury by 1.7-fold whereas the Treated group decreased oxidant injury to 0.5-fold of Control ($p < 0.05$). Caspase-6 mRNA expression increased after injury and was lower in treated cells. SOD-2 expression was similar in all groups. Protein analyses are currently ongoing.

Conclusions UC-MSCs may potentially improve alveolar epithelial cell proliferation, wound healing, and abate oxidant injury. Further studies will optimize the concentration of UC-MSC conditioned media and examine mitochondrial function.

650

IS EXCESSIVE WEIGHT LOSS DURING THE FIRST MONTH AFTER BIRTH A USEFUL PREDICTOR OF POOR LINEAR GROWTH AT 36 WEEKS IN PRETERM INFANTS WITH BIRTHWEIGHT <1250 GRAMS?

H Wongprasert, DM Homrich, AA Salas*. *University of Alabama at Birmingham, Birmingham, AL*

10.1136/jim-2018-000974.656

Purpose of study Weight loss due to contraction of extracellular fluid and transient nutritional deficits during the first month after birth could have a significant impact on growth outcomes of preterm infants at term-equivalent age. The main goal of this prospective cohort study was to determine the association between excessive weight loss during the first month after birth and length at 36 weeks of postmenstrual age (PMA) in preterm infants.

Methods used We prospectively collected anthropometric data in preterm infants with birthweight less than 1250 g. Excessive weight loss was defined as a decline in weight-for-age z score greater than -0.8 by postnatal day 28. Physiologic weight loss was defined as a decline in weight-for-age z score less than or equal to -0.8 by postnatal day 28. The primary outcome was length Z-score at 36 weeks PMA or hospital discharge (whichever occurred first).

Summary of results We assessed growth at 36 weeks PMA or hospital discharge in 70 infants (mean birthweight: 912 g, median gestational age: 28 weeks). Forty-five infants had excessive weight loss by postnatal day 28. In an analysis adjusted for birthweight, gestational age, sex, race, and weight Z-score at birth, excessive weight loss by postnatal day 28 was not associated with lower length-for-age Z-scores at 36 weeks PMA (mean difference between groups: 0.3; R^2 : 0.75; $p = 0.14$).

Conclusions Excessive weight loss in the first month after birth is a poor predictor of unfavorable linear growth in preterm infants.

651

A COMPARISON OF NON-INVASIVE VENTILATION METHODS USED TO PREVENT ENDOTRACHEAL INTUBATION DUE TO APNEA IN INFANTS LESS THAN 30 WEEKS GESTATIONAL AGE

CC Beaulieu, B Duyka, AM Khan*. *University of Texas Health Science Center at Houston, Houston, TX*

10.1136/jim-2018-000974.657

Purpose of study Apnea of prematurity is an almost universal problem in premature infants. It can be controlled through the use of caffeine; however, some patient's apneic events may be severe enough to require endotracheal intubation and invasive mechanical ventilation.

Non-invasive ventilation is another tool used in an attempt to reduce apneic events in preterm infants. When applying different modes of non-invasive ventilation, small studies have shown that nasal intermittent positive pressure ventilation (NIPPV) is more effective in reducing apneic events when compared to nasal continuous positive airway pressure (NCPAP).

This proposed study is to determine whether NIPPV reduces the need for endotracheal intubation in infants who fail NCPAP secondary to apnea.

Methods used We enrolled 13 infants born less than 30 weeks gestational age with recurring apneic events refractory to standard of care methods including maximum caffeine therapy and NCPAP of 6 or greater. Infants were randomized to either NIPPV ($n = 7$) or continued NCPAP ($n = 6$). The subjects were followed for 28 days from randomization or until their second required intubation within the 28 day period, which was considered a failure of the intervention. The primary outcome was the frequency of endotracheal intubation due to apnea. This was conducted as a pilot study in order to estimate the sample size for a subsequent definitive trial.

Summary of results There was no significant difference in birth weight, gestational age, weight at enrollment or corrected gestational age at enrollment between the two groups. Of the 7 subjects on NIPPV, 3 did not require intubation due to apnea as compared with 1 out of 6 on NCPAP. In regards to intervention failures, 1 out of 7 infants on NIPPV required two intubations as compared with 2 out of 6 on NCPAP.

Conclusions The preliminary data suggests no conclusive evidence that NIPPV prevents intubation due to apnea as compared with NCPAP. This is an incomplete data set with continued patient enrollment; therefore, conclusions are subject to change. NIPPV may be useful to try prior to intubation given that no additional harm has been observed. A larger, more definitive study needs to be performed.

652

A NOVEL THREE DIMENSION MOTION CAPTURE TECHNOLOGY TO EVALUATE HUMAN PERFORMANCE DURING SIMULATED NEONATAL RESUSCITATION

TT Alexander*, L Wilson, C Dionne, BA Shah. *University of Oklahoma, Oklahoma City, OK*

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Purpose of study Human factors remain understudied with limited understanding of how it can be used to optimize neonatal resuscitation. The objective of this study is to utilize three-dimension motion capture technology to study human performance of chest compressions (CCs) during simulated neonatal resuscitation.

Methods used This is a pilot study of 5 health care providers trained in the Neonatal Resuscitation Program (NRP). Each participant performed 3:1 chest compression to ventilation ratio (C:V) over a 20 min simulation. 99 reflective marker positions were measured via the Qualisys motion capture system 120 times per second to evaluate the force, rate and

depth of CCs. Participants were also asked to rate their perceived exertion using the Borg Rating of Perceived Exertion scale at two minute intervals.

Summary of results Overall for each participant the force, depth and time period between each chest compression remained stable throughout the simulation. The exception being that one participant had increasing force applied with increasing variability as the simulation progressed. There was a substantial variability between participants for all measurements. While force required to depress the chest to 1/3 of the anteroposterior (AP) diameter was measured to be 80 n, a range among participants was 30.5 to 153.1 n. The depth of CC in mm had a range of 12 mm to 42 mm among participants with 1/3 of the AP diameter measured at 35 mm. Every participant rated their perceived exertion as increasing throughout the simulation.

Abstract 652 Figure 1

Conclusions We have demonstrated that the three dimensional motion capture technology is a reliable and innovative way to evaluate the human performance during simulated neonatal resuscitation.

Pulmonary and Critical Care

Concurrent Session

2:00 PM

Friday, February 22, 2019

653

ANTIOXIDANTS IMPROVE LUNG IMMUNITY AS WELL AS T-CELL PROLIFERATION AND ACTIVATION PROFILES IN HIV-1 IMMUNE NON-RESPONDERS

¹M Ahmed*, ^{1,2}SK Cribbs, ¹BS Staitieh, ¹L Brown, ¹M Paiardini, ¹C King, ^{1,2}V Marconi, ^{1,2}D Guidot. ¹Emory University, Atlanta, GA; ²Atlanta VA, Decatur, GA

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Purpose of study HIV-1 immune non-responders are at increased risk for lung infections. Alveolar macrophages (AM) can be infected by HIV-1. We have previously shown that HIV-1 replication within AM impairs phagocytic function, that HIV-1 is associated with zinc and glutathione deficiency leading to oxidative stress, and that *in vitro* supplementation of zinc and antioxidants improves phagocytic function. We therefore hypothesized that dietary zinc and antioxidant S-adenosylmethionine would enhance AM immune function in immune non-responders.

Methods used In a prospective study, HIV-1 immune non-responders were given zinc (30 mg) and S-adenosylmethionine (1600 mg) daily for 12 months; a subgroup continued treatment for 24 months. All subjects underwent bronchoalveolar lavage and blood sampling pre- and post-treatment. Immunologic parameters were analyzed by flow cytometry. AM phagocytic index was measured by fluorescence microscopy using FITC-labeled *S. aureus*. AM Proviral DNA was measured using the Abbott RealTime HIV-1 Assay (Abbott Molecular Inc.).

Summary of results We enrolled 20 HIV-1 infected subjects (mean CD4 count=245 cells/ μ l, undetectable viral load) and 11 continued the intervention for 24 months. A significant increase in mean CD4 counts was seen after 12 months of treatment (326 cells/ μ l, $p<0.01$). There were significant reductions in the frequencies of CD4 ($p<0.01$) and CD8 ($p=0.03$) T cell proliferation, as assessed by Ki-67 expression that persisted for at least 2 years. There were significant reductions in the frequencies of CD4 ($p<0.01$) and CD8 ($p<0.01$) T cells expressing activation markers (HLA-DR and CD38) after 24 months of treatment. In a sub-group of 10 subjects, AM phagocytosis increased with treatment ($p<0.01$). HIV-1 proviral DNA was detected in AMs from 7/20 subjects; 3/7 were negative after 12 months of treatment.

Conclusions In HIV-1 infected immune non-responders on antiretroviral therapy, dietary supplementation with zinc and S-adenosylmethionine reduced T cell proliferation and activation, and improved AM phagocytosis. We speculate that these responses could help reduce the risk of lung infections in HIV-1 immune non-responders.

654 ALCOHOL INDUCES TGF β THROUGH SUPPRESSION OF MIR-1946A

V Sueblinvong*. Emory University, Atlanta, GA

10.1136/jim-2018-000974.660

Purpose of study We previously showed that chronic alcohol ingestion promotes fibroproliferative disrepair following bleomycin-induced acute lung injury in a mouse model and that is associated with exaggerated constitutive and injury-provoked expression of TGF β . Importantly, the aberrant expression of TGF β has been identified as a proximal event that mediates the 'alcoholic lung' phenotype. However, the mechanisms by which alcohol induces TGF β 1 has not been identified. Several microRNAs (miR) have been shown to directly target TGF β . Using an *in silico* analysis, we identified that miR-1946a is predicted to directly bind to the 3' untranslated region of the TGF β mRNA and thereby inhibit its transcription. We hypothesize that alcohol-mediated miR-1946a expression leads to an induction of TGF β expression.

Methods used Mouse primary lung fibroblasts (PLFs) were cultured $\pm$ alcohol (60 mM) for 24–48 hours, miR-1946a expression was quantified. In parallel, PLFs were cultured with miR-1946a mimic, miR-1946a inhibitor, or appropriate controls in the presence or absence of alcohol, then assessed for TGF β gene and protein expression. Lastly, PLFs were transfected with the vector containing TGF β 3'UTR (or control clone) tagged with the luciferase reporter and miR-1946a mimic (or negative mimic), then analyzed for luciferase activity.

Summary of results Alcohol suppressed the PLFs expression of miR-1946a. Treatment of PLFs with miR-1946a mimic suppressed alcohol-induced TGF β expression while miR-1946a inhibitor treatment led to an induction of TGF β expression. Lastly, miR-1946a mimic suppressed TGF β 3'UTR luciferase activity.

Conclusions These data suggest that miR-1946a modulates TGF β expression likely through direct interaction with TGF β 3'UTR. These findings identify a novel mechanism by which alcohol induces TGF β in the lung which would help us design therapeutic or preventative tools for alcoholic patients with or at risk of acute lung injury.

655 PSEUDOMONAS AERUGINOSA INFECTION ATTENUATES EXPRESSION OF CRITICAL GENES RESPONSIBLE FOR MITOCHONDRIAL BIOGENESIS AND ANTI-OXIDANT DEFENSE IN THE LUNG EPITHELIUM

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

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Purpose of study *P. aeruginosa* (PA) causes pulmonary infections in susceptible patients. The lung epithelium is the first defense against microbial invasion, but PA infection induces epithelial dysfunction. Within lung epithelial cells, the intricate regulation of cellular bioenergetics, anti-oxidant defense, and mitochondrial (mt) biogenesis are critical for the proper function of the epithelial barrier. The key genes responsible for these processes include PGC-1 α , TFAM, Nrf2, and Sirt3. AMPK acts as a central regulator of these genes to promote mt health during times of stress and mt damage. We have previously shown that bacterial molecules inhibit mt

respiration and biogenesis, and induce reactive oxygen species in host lung epithelial cells. The purpose of this study was to determine if PA infection attenuates expression of these genes *in vivo* and if therapy targeting the activation of these pathways can prevent bacterial invasion.

Methods used For *in vitro* experiments, BEAS-2B lung epithelial cells were infected with PA strain, PAO1, (MOI 1, 16 hrs). For transmigration studies, CALU-3 cells grown on transwells to allow formation of the epithelial barrier were treated with 1 mM metformin or 20 μ M resveratrol for 24 hours prior to apical infection with PAO1 (MOI 1, 6 hours). The basolateral media was then collected and cultured to quantify colony-forming units (cfu). For *in vivo* experiments, 3 month old male C57BL/6 mice (n=9) were infected with PAO1 (10⁸cfu, intranasal) or PBS control for 24 hours and then sacrificed. Quantitative PCR (QPCR) was used to quantify gene expression normalized to the endogenous control, GAPDH.

Summary of results PAO1 infection significantly attenuated expression of PGC-1 α , TFAM, Nrf2, and Sirt3 *in vitro* and *in vivo*. Pre-treatment with metformin or resveratrol, two drugs that are known to activate AMPK, significantly decreased bacterial invasion.

Conclusions PA infection attenuates key pathways responsible for the cellular maintenance of mt health. Pharmacologic AMPK activation decreased bacterial invasion across the epithelial barrier and may provide a complementary approach in the treatment of PA infection.

656 TRANSCRIPTIONAL AND POSTTRANSCRIPTIONAL MECHANISMS CONTRIBUTE TO HYPOXIA-INDUCED PINK1 LOSS AND MITOPHAGY DERANGEMENTS IN PULMONARY ARTERY SMOOTH MUSCLE CELLS

^{1,2}T Murphy, ^{1,2}D Green*. ¹Emory University, Decatur, GA; ²Atlanta VA Medical Center, Decatur, GA

10.1136/jim-2018-000974.662

Purpose of study In pulmonary hypertension (PH), pulmonary artery smooth muscle cells (PASMCs) characteristically proliferate and resist apoptosis signals. In our recent report, we determined that loss of mitophagy initiator protein, PTEN-induced putative kinase-1 (PINK1) recapitulated this proliferative PASMC phenotype *in vitro*, and stimulated vascular remodeling and right ventricular hypertrophy *in vivo*. The objectives of this investigation are to define the mechanisms that regulate PINK1 in hypoxic conditions and to determine the consequences of PINK1 alterations on mitophagy in hypoxic HPASMCs.

Methods used HPASMC proliferation was assessed using an automated cell counter. Luciferase reporter assays containing the PINK1 3'UTR (NM 032409) were conducted using miR mimics to overexpress miR-27a and miR-516a. HPASMCs were transfected with PPAR γ - or PINK1-carrying adenoviruses to investigate their therapeutic effects. *In vivo* hypoxia-exposure studies were conducted by placing C57BL/6J mice in cages in room air or in a hypoxia chamber (10% O₂) for three weeks.

Summary of results Mitophagy was reduced in hypoxic conditions and rescued by PINK1 overexpression. Using a PINK1 3' UTR luciferase reporter assay, we demonstrated that gain of miR-27a and miR-516a function suppresses PINK1 luciferase, whereas loss of miR-27a and miR-516a function

attenuates hypoxia-induced HPASMC proliferation. We identified cAMP response element-binding protein (CREB) as a novel transcriptional regulator of PINK1. Depleting CREB with siRNA significantly reduced PINK1 expression. Stimulation of PINK1 by PPAR γ likely occurs through indirect mechanisms that inhibit miR-27a and derepress PINK1.

Conclusions In the current study, we determined that mechanisms by which PINK1 levels are reduced by hypoxia involve the loss of transcriptional regulator (CREB) and gain of post-transcriptional regulators (miR-27a and miR-516a) that influence PINK1 expression. Using adenovirus constructs to overexpress PPAR γ or PINK1 augmented mitophagy, inhibited miR-27a expression, and blunted HPASMC hyperproliferation in hypoxic conditions. Collectively, these findings broaden our understanding of PINK1 regulation in hypoxic conditions and demonstrate that PINK1 is a promising therapeutic target in PH.

657 INVESTIGATING THE SAFETY AND OPIOID SPARING EFFECTS OF A SCHEDULED REGIMEN OF ACETAMINOPHEN AND NONSTEROIDAL ANTI-INFLAMMATORY DRUG IN POSTOPERATIVE PEDIATRIC CARDIAC SURGERY PATIENTS

¹K Passmore*, ^{1,2}R Mehta, ³J Waller. ¹Medical College of Georgia, Augusta, GA; ²Children's Hospital of Georgia, Augusta, GA; ³Augusta University, Augusta, GA

10.1136/jim-2018-000974.663

Purpose of study Opioids are currently the first-line agents for postoperative pain management, despite their significant side effects. Evidence is increasing for safer alternatives to opioids, however those alternatives are used sparingly in pediatric patients recovering from congenital heart disease (CHD) surgery. The purpose of this study was to examine if a scheduled regimen of Acetaminophen and nonsteroidal anti-inflammatory drug (NSAID) during the first 48 postoperative hours decreases the need for opioid analgesia and the number of opioid-related adverse effects.

Methods used Patients admitted to the pediatric intensive care unit at Children's Hospital of Georgia post-CHD surgery from January 2012 – March 2018 were retrospectively recruited. Patient medical records were reviewed for durations of opioid and alternative analgesia usage and any instances of adverse effects. Many patients were given Lortab (Hydrocodone-Acetaminophen combination) to fulfill the scheduled regimen of Acetaminophen, which prompted further investigation of non-Lortab opioid usage. These outcomes were compared between 120 patients who received the Acetaminophen-NSAID regimen and 100 who did not. Statistical analysis included chi-square test, two-sample t-test, Fisher's Exact test, and Wilcoxon Rank Sum test using an alpha level of 0.05.

Summary of results The mean length of stay ($p=0.0072$), number of days of overall opioid usage ($p=0.136$), and number of days of non-Lortab opioid usage ($p=0.0068$) were lower in patients receiving the scheduled regimen of Acetaminophen-NSAID. There was no significant difference in occurrences of constipation, hypotension, rash, and pruritus between the two groups.

Conclusions Our data indicates that a scheduled regimen of Acetaminophen and NSAID may decrease length of stay and a dependence on opioid analgesia, but not decrease the number of opioid-related adverse effects. This study highlights the

need for prospective randomized controlled trials that evaluate the efficacy of non-opioid alternatives for pain management in pediatric post-CHD surgery patients.

658 THE ACCURACY OF THE BROSELOW TAPE IN OVERWEIGHT AND OBESE PATIENTS

R Davie*, S Hao, R Mehta. Medical College of Georgia, Augusta, GA

10.1136/jim-2018-000974.664

Purpose of study The Broselow Tape is a color-coded tape that uses height to predict weight-based dosage of medications and equipment sizes in order to safely treat pediatric patients in medical emergencies. The rise of childhood obesity in the United States, with a prevalence of 18.5% in 2016, has brought up recent concerns for underestimation of weight using the Broselow Tape. This study aims to determine the accuracy of the Broselow Tape among pediatric patients with a body mass index (BMI) greater than the 85th percentile. It was hypothesized that the predicted weight needed adjustment by at least color zone for obese and overweight patients in order to provide adequate medication during emergency.

Methods used A retrospective chart review was performed using the electronic medical records at Augusta University's Children's Hospital of Georgia, between May 2015- March 2018. Subjects were placed into groups according to the CDC guidelines of BMI percentile categories: underweight, normal, overweight, obese. Heights and weights were recorded and compared to predicted Broselow Tape weight. SAS 9.4 was used for all statistical analyses with an alpha level of 0.05 to assess statistical significance.

Summary of results Percent of true classification and misclassification of body weight zones was calculated for each BMI percentile category. Results showed that the overall accuracy of the Broselow Tape decreases as BMI percentile increases. Only 13% of overweight patients' weights were accurately measured while 83% were underestimated by one zone and 4% were underestimated by two zones. For obese patients' weights, 71% were underestimated by one zone, 23% were underestimated by two zones and 5% were underestimated by three or more zones.

Conclusions The Broselow Tape underestimated the weights of both overweight and obese patients, suggesting the need for adjustment of the length-based dosing zones for patients above the 85th percentile. These findings support the 2017 Broselow Tape guideline of adjusting by at least one zone for obese patients. However, an adjustment of two zones may be necessary for obese patients. In the future, a prospective study is needed to test this methodology during emergencies.

659 SERIAL ARGININE AND CITRULLINE LEVELS AND NITRIC OXIDE PRODUCTION IN PRETERM INFANTS WHILE WEANING OFF TOTAL PARENTERAL NUTRITION

M Honhar*, VD Modi, A Qasim, S Jain. University of Texas Medical Branch, Galveston, TX

10.1136/jim-2018-000974.665

Purpose of study Decreased levels of L-arginine (Arg) and L-citrulline (Cit) are associated with BPD associated pulmonary hypertension (BPD-PH) due to decreased production of Nitric Oxide (NO) (measured by urinary nitrates NO₃). TPN

contains a significant amount of L-arginine (1 mg/1 mL) to metabolize ammonia via urea cycle. Breast milk and formula has very low levels of Arg. We aimed to measure the effect of weaning TPN on serial Arg, Cit and urinary NO₃ in pre-term infants (PI).

Methods used PI ≤ 30 wks of gestation and ≤ 1500 g were included in the study (n=7). PI with congenital anomalies (except PDA or ASD) and necrotizing enterocolitis were excluded. Blood and urine levels of Arg and Cit were measured at 1, 3, 7, 14 and 21 days by liquid chromatography and mass spectrometry (LC-MS/MS); urinary NO₃ was measured via gas chromatographic-mass spectrometer. LC-MS/MS chromatogram of amino acids was quantified prior to use.

Summary of results Serial plasma Arg, Cit, and urinary NO₃ at all time points gradually decrease as TPN intake was going down and enteral intake was going up (figure 1). We also found that urinary and serum Arg and Cit levels were not significantly different.

Abstract 659 Figure 1 A,C: Arg; B,D: Cit in plasma and urine

Conclusions The time-dependent changes over a 3 week period after weaning from an Arg containing TPN diet showed that the plasma and urine Arg levels gradually decrease with time while the levels of Cit remain relatively unchanged. The urinary NO₃ also decreased over time. We speculate, this drop in Arg levels in PI after discontinuation of TPN can be a potential risk factor for predisposing them to develop BPD-PH. This pilot study helps to find a possible area of intervention that can effectively change the course and outcome of PI at risk for developing BPD-PH.

660 UTILITY OF CARDIAC EVALUATION IN PATIENTS HOSPITALIZED FOR ASTHMA

R Parlar-Chun*, K Kakarala, M Singh, R Traweck. *MGovern Medical School, Houston, TX*

10.1136/jim-2018-000974.666

Purpose of study Along with respiratory symptoms, patients with acute asthma exacerbations may also have concurrent cardiac symptoms such as tachycardia, chest pain, and blood pressure abnormalities. Some clinicians obtain EKGs, ECHOs, or serial cardiac enzymes to evaluate. We identified patients who obtained this work up and describe their outcomes to see the utility of this testing in this population.

Methods used Patients aged 4 to 17 years admitted with ICD codes for asthma exacerbation from 1/1/2012 to 12/31/2016 were identified. Those that obtained an EKG, ECHO, or

cardiac enzymes were analyzed. Patients were grouped into cardiac complications including tachycardia, arrhythmias, blood pressure abnormalities, syncope, and chest pain.

Summary of results Out of 1296 patients, 77 (6%) received cardiac work up including 65 EKGs, 27 ECHOs, and 18 cardiac enzymes. The most common reasons for cardiac workup were chest pain (32%), blood pressure abnormalities (14%), tachycardia (10%), arrhythmia (8%), and syncope (8%).

Aside from sinus tachycardia (66%), the most common EKG findings were nonspecific T wave (20%), nonspecific ST segment (18%), and T wave inversion (18%). 4 out of 27 who received ECHOs had abnormalities: 2 with hypertrophic cardiomyopathy, 1 vascular ring, and 1 with evidence of pulmonary hypertension.

All patients with EKGs obtained for tachycardia had insignificant results and resolution of tachycardia on discharge. No patients with chest pain with cardiac enzymes drawn had evidence of cardiac ischemia. There were 2 cases of SVT, 2 PVCs, and 2 with irregular rhythm. None had evidence of arrhythmias on discharge. Diastolic hypotension (DhTN) was found in 10 out of the 11 blood pressure abnormalities. There was mixed efficacy of fluid bolus to correct DhTN. All DhTN resolved on discharge. Besides one new diagnosis of HCM, no other cardiac etiology was found in patients that presented with syncope.

Conclusions While cardiac complications such as chest pain, tachycardia, diastolic hypotension, arrhythmias, and syncope are seen in patients admitted for asthma exacerbations, they are rarely a result of underlying cardiac disease. EKGs, ECHOs, and cardiac enzymes should have a minimal role in the management of the hospitalized asthmatic patient.

661

HIV-RELATED VIRAL PROTEIN EXPOSURE IMPAIRS ALVEOLAR MACROPHAGE MITOCHONDRIAL FUNCTION

¹N Smirnova*, ^{1,2}S Yeligar, ¹M Ahmed, ¹X Fan, ^{1,2}D Guidot, ¹BS Staitieh. ¹Emory University, Atlanta, GA; ²Atlanta VA, Decatur, GA

10.1136/jim-2018-000974.667

Purpose of study Persons living with HIV (PLWH) suffer from increased rates of bacterial pneumonia. We have described a number of defects in the alveolar macrophage (AM), the resident innate immune effector of the lung, that likely contribute to that risk. Using an HIV-1 transgenic rat model to simulate the intrapulmonary conditions of PLWH, we previously determined that impaired mitochondrial bioenergetics underlie a number of key defects in AM function. We therefore designed a series of experiments to determine the mechanism by which HIV-viral protein exposure impairs mitochondrial function.

Methods used AMs obtained by whole lung lavage from HIV-1 transgenic rats and their wild-type littermates were stained with MitoTracker Orange to assess mitochondrial biomass. In parallel, AMs were stained with an antibody to glucose-regulated protein 75 (Grp75) and analyzed by fluorescence microscopy. A rat alveolar macrophage cell line (NR8383) was treated with the HIV-related viral protein Tat and expression of Dynamin-1-like protein (Drp1) and voltage-dependent anion channel (VDAC) were assessed by qRT-PCR.

Summary of results Mitochondrial biomass was significantly decreased in HIV transgenic rat AMs. VDAC expression was decreased by immunofluorescence in transgenic rat AMs as

well. Gene expression of Drp1 and VDAC were both decreased in NR8383 cells exposed to Tat.

Conclusions HIV-related viral protein effects on AM mitochondria are myriad. Chronic exposure to viral proteins, as in the HIV transgenic rat model, significantly reduces the number of baseline mitochondria. Accordingly, those same cells have reduced levels of Grp75, another indication of reduced biomass. Treatment with Tat decreased gene expression of both Drp1 and VDAC, implying defects in both mitochondrial fission and membrane potential, respectively. Although these findings require confirmation in PLWH, they support our underlying contention that enhancing mitochondrial function may offer a fruitful therapeutic avenue for these vulnerable individuals.

Renal, Electrolyte and Hypertension I

Concurrent Session

2:00 PM

Friday, February 22, 2019

662 GLOMERULAR CAPILLARY WALL SHEAR STRESS IN THE DIABETIC RAT: A MODELING STUDY

O Richfield*. Tulane University, New Orleans, LA

10.1136/jim-2018-000974.668

Purpose of study Diabetes mellitus (DM) reduces renal blood flow autoregulation efficiency, increasing glomerular pressure (ΔP) and afferent plasma flow (Q_a), which is assumed to increase glomerular capillary wall shear stress (SS). However, the actual magnitudes of SS in the glomerular capillaries have not been estimated in DM. In response to increased SS, endothelial cells release growth factors associated with glomerulopathy. Using mathematical models, we estimated the change in SS on the glomerular capillary walls to determine the extent of mechanical insult to the glomerulus in DM.

Methods used We developed a mathematical model of blood flow through an anatomically-accurate rat glomerular capillary network. Individual capillary filtration rates and wall SS were calculated based on values of Q_a , ΔP and single nephron GFR (SNGFR) obtained from micropuncture studies. To validate mechanical predictions of our model, we compared our calculated SS magnitudes to results from intravital imaging studies of blood flow in rat glomeruli. To calculate SS magnitudes in the rat glomerulus in DM, we performed simulations with parameters obtained from a previous micropuncture study using rats with streptozotocin induced Type I DM. In this study, DM markedly increased Q_a and ΔP and reduced the filtration coefficient (K_f) such that filtration fraction (FF) remained constant.

Summary of results Using the calibration parameters, our model's calculated mean glomerular capillary wall SS was within 5% of the mean SS predicted using intravital imaging. Using parameters from micropuncture experiments, our model predicted a 76.4% rise in glomerular capillary wall SS in the diabetic rat over control, approximately equal to the percent increase in Q_a . While an increased ΔP in isolation slightly

reduces mean shear stress by increasing filtered volume, the reduction in K_f attenuated this effect.

Conclusions We have developed and validated an anatomically-accurate mathematical model of glomerular filtration for use in predicting functional and mechanical results of varied ΔP , Q_a and K_f . Using this model, we demonstrated that there is a significant rise in SS on glomerular capillary endothelial cells in DM, which may play a significant role in the progression of glomerulopathy. Further studies will consider the change of glomerular capillary diameter for more accurate modeling of SS on the capillary walls.

663

MICE LACKING INNER MEDULLARY UREA TRANSPORTERS HAVE REDUCED RENAL FIBROSIS FOLLOWING UNILATERAL URETERAL OBSTRUCTION

F Rianto*, CL Ellis, XH Wang, JD Klein, JM Sands. Emory University School of Medicine, Atlanta, GA

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Purpose of study Low protein diets reduce the progression of chronic kidney disease (CKD) and, in theory, CKD-related renal fibrosis, possibly due to restricted urea levels. Unilateral ureteral obstruction (UO) in rodents results in fibrogenic responses such as increased capillary macrophages, pro-fibrogenic proteins, interstitial matrix, myofibroblasts, etc. We hypothesized that the urea transporters contribute to the development of renal fibrosis in UO mice. We used UO mice receiving a maximal urea load to investigate contributions of urea transporter to renal fibrosis.

Methods used C57Bl6 mice±genetic ablation of UT-A1 and UT-A3 urea transporters (UT-A1/A3 KO mice) underwent UO surgery as follows: the retroperitoneal area was opened, left kidney exteriorized, proximal ureter ligated, kidney replaced and the incision closed. Four days after surgery mice were changed to a high (40%) protein diet for 10 further days. Mice were killed and obstructed kidneys were collected for protein and histochemical analysis.

Summary of results TGF- β was increased in both WT and UT-A1/A3 KO mice with UO (359% and 424% respectively). WT mice with UO showed a significant 268% increase in α -SMA vs mice without UO. In contrast, UT-A1/A3 KO mice with UO showed no significant change in α -SMA vs unobstructed UT-A1/A3 KO mice. Vimentin, another marker of fibrosis, was significantly increased 647% by UO (vs no UO). Vimentin in UO-UT-A1/A3 KO mice was not significantly different from UT-A1/A3 KO mice without UO. H and E staining revealed infiltration of inflammatory cells in both UO WT mice and UO UT-A1/A3 KO mice. Trichrome staining showed higher collagen levels in UO WT mice vs UO UT-A1/A3 KO mice. Immunohistochemical staining for α -SMA and vimentin revealed higher levels in UO WT mice vs UO UT-A1/A3 KO mice.

Conclusions These data suggest that urea transporters do not prevent inflammation caused by UO. However, the development of fibrosis in UO mice fed a high protein diet is attenuated by the absence of urea transporter suggesting that urea reabsorption by urea transporters contributes to renal fibrosis. If urea transport inhibitors replicate the effects of genetic knock out, they may represent a promising future therapy.

664

SURVEY OF MIGRANT DIALYSIS PATIENTS DISCLOSES A MAJORITY WITH PARAQUAT OR OTHER AGROCHEMICAL EXPOSURE: A POTENTIAL ETIOLOGY FOR MESOAMERICAN NEPHROPATHY

¹MW Holliday*, ¹Q Li, ¹J Dominguez, ²E Bustamante, ¹I Espina, ¹M Shah, ¹S Anumudu, ¹A Awan, ¹D Sheikh-Hamad. ¹Baylor College of Medicine, Houston, TX; ²Harris Health System, Houston, TX

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Purpose of study Mesoamerican Nephropathy (MeN) is a form of chronic kidney disease of unknown etiology (CKDu) that is devastating communities of agricultural workers in Mexico and Central America. Although linked to heat exposure/dehydration, infection, heavy metals and agrochemicals, MeN has no clearly defined etiology. We report an expanded survey of migrants with MeN in our safety-net dialysis unit and identified paraquat and well water as possible culprits. Based on the survey, we hypothesized that repetitive exposure of mice to sub-toxic doses of paraquat would result in chronic kidney disease with pathology similar to MeN.

Methods used Of 155 patients screened for MeN, 48 matched the inclusion criteria and were surveyed. Exclusion criteria included known cause or evidence of primary or secondary renal disease. C57BL/6J mice received ten weekly intraperitoneal injections of low-dose paraquat or vehicle. Serum creatinine and 24 hour urine CrCl and protein were measured. Organs were immunostained for collagen, T-cells and macrophages.

Summary of results Patients were 39±10 (range 22–60) years old and 96% male. 27 (56%) were from Mexico, 16 (33%) from El Salvador, with remainder from Guatemala and Honduras. 33 (69%) patients had worked in agriculture for an average of 10±6 years. 13 (27%) patients reported use of Gramoxone (paraquat) specifically, while 28 (58%) patients reported use of agrochemicals. 29 (60%) consumed well water. Paraquat-treated mice exhibited decreased creatinine clearance and increased renal interstitial collagen deposition and inflammatory cells.

Conclusions The majority of migrants from Mexico and Central America with CKDu in our dialysis unit reported prior exposure to Gramoxone or other agrochemicals. Well water was the predominate water source. Sub-toxic doses of paraquat administered to mice weekly for 10 weeks induced renal insufficiency with increased interstitial fibrosis and inflammation, establishing chronic exposure to paraquat as a potential mediator of renal disease. Given our results, further investigation into the role of paraquat and other agrochemicals in the pathogenesis of CKDu is warranted.

665

ANGIOTENSIN II BIPHASICALLY REGULATES CELL DIFFERENTIATION IN INDUCED PLURIPOTENT STEM CELL-DERIVED HUMAN KIDNEY ORGANIDS

SM Yanofsky*, CM Dugas, A Katsurada, SS El-Dahr, Z Saifudeen, R Satou. Tulane University School of Medicine, New Orleans, LA

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Purpose of study Recent advancements in growth of induced pluripotent stem cell (iPS)-derived human organoids have implications for future regenerative medicine, and impact

work on renal disease models and pharmacological studies. Ongoing efforts to improve kidney organoid technology face obstacles in refining renal structural development to better model structural nuances in human renal tissue. Although angiotensin II (Ang II), a hormone in the renin-angiotensin system (RAS), is essential to nephrogenesis, effects of Ang II on kidney organoid development have not been established. Thus, we investigated effects of Ang II on growth of renal structures in kidney organoids.

Methods used Human iPS-derived kidney organoids were induced for 18 days by Dr. Little's protocol. We first established using digital PCR that all RAS components are expressed in the organoids. Ang II type 1 receptor (AT1R) was highly expressed early in development, at day 0, whereas Ang II type 2 receptor (AT2R) expression peaked at day 5 and then decreased. Accordingly, organoids were treated with 100 nM Ang II in either the early phase (day 0–5, Ang II-E) or the middle phase (day 5–10, Ang II-M), and compared with untreated organoids (control).

Summary of results Immunohistochemical staining with cell type markers indicated that podocytes, renal proximal tubules, and distal tubules were formed in the organoids on day 10. Ang II-E decreased levels of a renal tubule marker gene (CDH16: 0.32 ± 0.05 , ratio to the control), whereas Ang II-M did not alter CDH16 levels. Levels of markers for proximal tubules and distal tubules also showed a decreasing trend by Ang II-E. In contrast, Ang II-M increased levels of markers for podocytes (PODXL: 1.41 ± 0.16 , MAFB: 1.66 ± 0.09). In addition, levels of a marker for ureteric tip were augmented by Ang II-M. Ang II-E did not affect the differentiation to podocytes and ureteric tip. Results of flow cytometry supported these results that Ang II-E inhibits development of tubules, and Ang II-M enhances podocyte formation.

Conclusions Ang II exerts biphasic effects on epithelial cell differentiation in the renal organoids, providing a novel strategy to establish human kidney organoids.

666

UPREGULATION OF A UREA TRANSPORTER IN UREMIC HEART IS LINKED TO CARDIAC FIBROSIS

A Kuma*, XH Wang, JD Klein, JM Sands. Emory University, Atlanta, GA

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Purpose of study Chronic kidney disease (CKD) induces hypertension and retention of water, urea and salt within the body. These are strongly associated with the cardiovascular disease known as uremic cardiomyopathy, which shows characteristics of interstitial fibrosis and hypertrophy. In kidney, the urea transporter (UT) is necessary to concentrate urine, but its function in heart is not well known. We hypothesized that UT is associated with uremic heart, and investigated the role of UT in CKD mice heart.

Methods used CKD models were produced by 5/6 nephrectomy in C57BL6 mice, which subsequently received 0.45%–1.0% NaCl water for 8 weeks. In some groups, mice were treated with dimethylthiourea (DMTU) delivered by minipumps to inhibit UT-A. Protein expression levels were detected by western blot. Blood pressure (BP) was monitored by tail cuff. Collagen deposition was detected by Masson Trichrome staining.

Summary of results BUN was 28.1 mg/dL (sham) and 56.7 mg/dL (CKD) ($p<0.01$) proving success of the CKD model. Both systolic and diastolic BP was increased in CKD mice; SBP: 132 mmHg (CKD) vs 107 mmHg (sham); DBP: 59 mmHg (CKD) vs 53 mmHg (sham). Inhibition of UT-A prevented CKD-induced increases in SBP and DBP (SBP: 119 mmHg and DBP: 55 mmHg). The heart to body weight ratio was increased in CKD mice (7.18 mg/g (CKD) vs 4.73 mg/g (sham); $p<0.05$). Cardiac fibrosis was confirmed by Masson's Trichrome staining in CKD mice and the ratio of collagen to total area was 0.04% (sham) and 0.9% (CKD), $p<0.02$. The protein abundance of UT-A was increased 1.6-fold in CKD vs sham mice hearts. The pro-fibrosis marker, vimentin, was increased in CKD mice vs. sham mice assayed by immunohistology. The endothelial-mesenchymal transition (EMT) related protein, 14-3-3 γ , was also increased 1.5-fold in the hearts of CKD mice compared with shams. There was a correlation of protein expression levels between UT-A and 14-3-3 γ in CKD hearts ($R^2=0.6656$, $p=0.025$).

Conclusions The upregulation of UT-A in uremic heart was related with increased vimentin protein, suggesting increased cardiac fibrosis in CKD mice. The increased 14-3-3 γ offers a possible mechanism for the UT-A-related cardiac fibrosis in uremic mice. Inhibition UT-A attenuated CKD-induced hypertension.

667

ACTIVATION OF PRORENIN RECEPTOR (PRR) STIMULATES PRODUCTION OF TNF α AND IL-6 IN MURINE MACROPHAGES

¹B Visniauskas*, ¹SL Crabtree, ^{1,2}JV Castro, ^{1,3}M Acosta, ¹A Curnow, ^{1,4}MC Prieto. ¹Tulane University, New Orleans, LA; ²Universidad Industrial de Santander, Bucaramanga, Colombia; ³Louisiana State University, New Orleans, LA; ⁴Tulane Hypertension and Renal Center of Excellence, New Orleans, LA

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Purpose of study The prorenin receptor (PRR), a component of the renin angiotensin system (RAS) is expressed in several tissues, including kidney and immune cells. In human lymphocytes and monocytes, PRR activation stimulates ERK1/2 pathway and release of cytokines and cyclooxygenase 2 (COX-2). However, whether PRR contributes to the production of inflammatory cytokines in the macrophages is unknown. The aim of the study is to test the hypothesis that PRR activation in macrophages increases the production of inflammatory cytokines.

Methods used C57BL/J male mice were IP injected with 3.8% of thioglycollate medium to isolate peritoneal macrophages after 72 hours of injection. Then, isolated macrophages were cultured and stimulated them with prorenin (10^{-7} mmol/L) for 6, 12, 24 and 48 hours. The expression of PRR in macrophages was assessed by immunofluorescence, flow cytometry, and Western blotting. Secretion of cytokines, TNF α and IL-6 by macrophages were measured in the extracellular media using multiplex ELISA (Meso Scale Discovery).

Summary of results We found that PRR was co-localized with CD68 in mature macrophages and that 96% of isolated macrophages expressed positive PRR. Interestingly, prorenin treatment of macrophages induced the production of TNF α and

IL-6 after 6 hours and remained increasing up to 48 hours (max peak) in the murine isolated macrophages.

Conclusions Activation of PRR increases the production of TNF- α and IL-6 in mouse macrophages. The data support the concept of PRR stimulation by its agonist prorenin, contributes to inflammatory responses in macrophages. Ongoing studies are pursuing to demonstrate that PRR activation in inflammatory cells play a critical role in the development of salt-sensitive hypertension.

668

IMPACT OF PORTAL PULMONARY HYPERTENSION IN THE COURSE OF HEPATORENAL ACUTE KIDNEY INJURY

¹M Rivera*, ¹J Velez, ²AE Mohammed. ¹University of Queensland, New Orleans, LA; ²Ochsner's Center for Outcomes and Health Services Research, New Orleans, LA

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Purpose of study Porto-pulmonary hypertension is prevalent in cirrhotic patients. However its impact on outcomes of acute kidney injury (AKI) and cirrhosis has not been previously studied. We hypothesized that echocardiographic evidence of pulmonary hypertension affects the interplay between change in mean arterial pressure (MAP) and course of hepatorenal AKI during vasoconstrictor therapy as well as overall renal outcome.

Methods used We conducted a prospective observational study of hospitalized patients with AKI stage ≥ 2 and cirrhosis over 4 months. Daily MAP and serum creatinine (sCr) values were collected, as well as pulmonary arterial pressure (PAP) estimated by echocardiography at the time of AKI. Patients were divided into PAP tertiles: 1st ≤ 30 , 2nd 31–40, 3rd > 40 mmHg. Daily change in MAP (Δ MAP) and daily change in sCr (Δ sCr) from baseline were computed. Renal outcome chosen was need for renal replacement therapy (RRT).

Summary of results Among 52 patients, 19 (37%) were female, mean age was 56 (range 25–75). Baseline values were median MAP 76 (IQR 71–84) mmHg, median sCr 2.3 (IQR 1.7–3.7) mg/dL, median serum albumin 2.3 (IQR 1.8–3) g/dL and median total bilirubin 4.1 (IQR 1.8–27.2) mg/dL. A significant inverse correlation was found between Δ MAP and Δ sCr on the following day ($r=-0.20$, $p=0.0003$) throughout the course of AKI. PAP was obtained in 36 patients. The correlation between Δ MAP and Δ sCr within each PAP tertile were: ≤ 30 : $r=0.08$ ($p=0.37$), 31–40: $r=-0.36$ ($p=0.002$) and > 40 : $r=-0.40$ ($p=0.0006$). Thus, as PAP increases, a negative correlation between Δ MAP and Δ sCr on the following day strengthens. Furthermore, there was a trend for an increased need for RRT within those in the highest tertile of PAP (need for RRT: 28.6%, 33%, and 70%, for the 1st, 2nd, and 3rd tertiles, respectively ($p=0.0511$, chi-square for trend).

Conclusions Cirrhotic patients with more severe pulmonary hypertension exhibit a significantly stronger negative correlation between Δ MAP and Δ sCr, suggesting that those with higher PAP may display increased sensitivity to improved kidney function upon optimization of MAP with vasoconstrictors. Moreover, higher PAP is associated with greater need for RRT, adding complexity to the pathogenesis of hepatorenal AKI.

Correction: Fecal incontinence in children with ADHD, before and after ADHD treatment: the role of stimulant medication

L McCann. Fecal incontinence in children with ADHD, before and after ADHD treatment: the role of stimulant medication. *J Investig Med* 2019;**67**:587. doi: 10.1136/jim-2018-000974.597

The co-author list for this abstract is: A Ponnambalam, University of South Alabama, Mobile, AL

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Correction: *Serial arginine and citrulline levels and nitric oxide production in preterm Infants while weaning off total Parenteral nutrition*

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The correct author order should read: Honhar M, Modi VD, Qasim A, Herring J, Jain S. University of Texas Medical Branch, Galveston, TX.

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