1 CYTOKINE AIRWAY RESPONSES TO ACUTE RHINOVIRUS INFECTION AND RESPIRATORY MORBIDITY IN SEVERE PREMATURE CHILDREN

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Purpose of Study: Rhinovirus (RV) has been strongly linked to the pathogenesis of asthma in children. Prematurity is a risk factor for severe RV infection in early life, but is unknown if RV elicits pro-asthmatic airway cytokine responses in premature infants. This study investigated if young children born severely premature (<32 weeks gestation) exhibit airway secretion of Th2/Th17 cytokines during natural RV infections and if RV-induced Th2/Th17 responses are linked to more respiratory morbidity in premature children during the first two years of life.

Methods Used: We measured Th2/Th17 nasal airway cytokines in a retrospective cohort of young children aged 0-2 years with PCR-confirmed RV infection or non-detectable virus. Protein levels of IL-4, IL-13, TSLP and IL-17 were determined with multiplex magnetic bead immunoassays. Demographic and clinical variables were obtained by electronic medical record (EMR) review.

Summary of Results: The study comprised 214 children born full term (n=108), pre-term (n=44) or severely premature (n=62). Natural RV infection in severely premature children was associated with elevated airway secretion of Th2 (IL-4 and IL-13) and Th17 (IL-17) cytokines, particularly in subjects with history of bronchopulmonary dysplasia. Severely premature children with high RV-induced airway IL-4 had recurrent respiratory hospitalizations (median 3.65 hospital; IQR 2.8-4.8) and were more likely to have at least one pediatric intensive care unit admission during the first two years of life (OR 8.72; 95% CI 1.3-58.7; p<0.02).

Conclusions: Severely premature children have increased airway secretion of Th2/Th17 cytokines during RV infections, which is associated with more respiratory morbidity in the first two years of life.

2 IN VIVO EVIDENCE IN A XENOGRAFT MODEL FOR ASTHMATIC EPITHELIUM DRIVING AIRWAY REMODELING

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Purpose of Study: We recently showed that regeneration of asthmatic-derived epithelium in vitro induces basolateral secretion of TGF-β1. We hypothesized that epithelial regeneration in asthma induces underlying matrix fibrosis. The goal of this study was to mechanistically dissect the cause/effect relationship between epithelial repair processes and airway remodeling in an in vivo model.

Methods Used: Human airway epithelial cells from asthmatic and non-asthmatic donors (n=5 per group, donor age range 17 - 68 years) were seeded into decellularized tracheas harvested from Fisher 344 rats. Tracheas were ligated to a sterile tubing cassette at both ends and implanted subcutaneously in the flanks of athymic nude mice. Grafts were flushed bi-weekly with Ham’s F12 and harvested at 2, 4, or 6 weeks for tissue histology, fibrillar collagen deposition by multiphoton microscopy, and TGFβ1 activation by immunofluorescence.

Summary of Results: Grafted epithelial cells generate a differentiated epithelium containing basal, ciliated, and mucus expressing cells as confirmed by histology. By 4 weeks post-engraftment, asthmatic-derived epithelia showed increased mucus production, decreased numbers of ciliated cells, and decreased E-cadherin expression compared to non-asthmatic controls. While there was no evidence of matrix remodeling in acellular xenografts, grafts seeded with asthmatic-derived epithelial cells had 3 times as much fibrillar collagen at 6 weeks post-engraftment as non-asthmatic grafts. This was accompanied by a >2-fold induction of matrix TGFβ1 [with evidence of pSMAD3 activity] in asthmatic grafts at 4 weeks (positive pixels/total field pixels = 0.12±0.001 vs. 0.05±0.001; p=0.003) and 6 weeks (0.09±0.02 vs. 0.04±0.01; p=0.044) post-engraftment.

Conclusions: These results support our hypothesis that epithelial regeneration in asthma induces underlying matrix fibrosis in vivo. In addition, these data demonstrate the utility of this xenograft model in the effort to mechanistically dissect the cause/effect relationship between airway epithelial repair and fibrosis in the lung.

3 VASCULAR INFLAMMATION IN THE AORTA IS RELATED TO CORONARY PLAQUE BURDEN IN PSORIASIS

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Purpose of Study: Psoriasis, a chronic inflammatory skin disease, is associated with increased vascular inflammation (VI) by [18F]-fluorodeoxyglucose (FDG) PET/CT. Psoriasis also increases the risk of myocardial infarction, which may be due to inflammatory, lipid-rich coronary plaque. Whether VI in the aorta is related to coronary plaque burden is not known and is a critical step in understanding local effects of vascular inflammation. Therefore, we aimed to probe the relationship between VI by FDG PET-CT and coronary plaque burden by quantitative CT angiography in a well-phenotyped psoriasis cohort.

Methods Used: Psoriasis patients (N=67) and healthy controls (N=21) underwent coronary CT angiography (Toshiba 320 slice) and FDG PET-CT imaging (Siemens Biograph). Coronary plaque was assessed using QAngio CT (Medis, The Netherlands). Total burden (TB), dense calcium burden (DCB), and non-calcified burden (NCB) plaque indices were calculated by dividing total vessel plaque volume by total vessel length. VI was assessed using dedicated image analysis software (Phillips Healthcare). Target-to-background Ratio (TBR) was calculated as the ratio of arterial and venous standardized uptake values (SUV). Cardiometabolic parameters including lipid particles, HDL efflux, and homeostatic model assessment-insulin resistance (HOMA-IR) were also assessed.

Summary of Results: The population had a low Framingham Risk Score (median 4%, IQR 2%–7%) but had high VI (1.82 ± 1.68 in psoriasis vs healthy controls, respectively; p<0.001). In univariate regression, an increase in aortic VI was associated with an increase in coronary TB (β=0.80, p<0.001) and NCB (β=0.71, p<0.001) even after adjustment for cardiovascular risk factors (β=0.56, p=0.02; β=0.47, p=0.02, respectively). Both VI and coronary plaque burden were associated with HDL function (β=−0.57, p<0.001; β=−0.89, p<0.002, respectively) and HOMA-IR with VI (β=−0.04, p<0.001).

Conclusions: We show that VI is increased in PSO and that this VI is associated with coronary plaque burden. Vascular inflammation in the aorta therefore may be a strong surrogate marker for subclinical atherosclerosis.
IMMUNOSUPPRESSIVE DRUGS MYCOPHENOLEATE MOFETIL AND CYCLOSPORIN A: DISPARATE EFFECTS ON Atherosclerotic LIPID ACCUMULATION IN THP-1 HUMAN MACROPHAGES

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Purpose of Study: Systemic Lupus Erythematosus (SLE) patients have a 5 to 9-fold increase in incidence of coronary heart disease (CHD) compared to those of the same age with no SLE, and similar risk factors. Clinical observations indicate that statins are ineffective in preventing atherosclerosis progression in SLE. Renal transplant recipients also exhibit elevated CHD risk. Mycophenolate mofetil and cyclosporin A (CsA) are immunosuppressive agents currently used for the treatment of SLE and in transplant recipients. Mycophenolic acid (MPA), the active form of mycophenolate mofetil, has been reported to improve inflammation and lipid metabolism. Here, we compare the effect of MPA and CsA on the expression of proteins involved in cholesterol influx and lipid accumulation in naïve THP-1 human macrophages.

Methods Used: THP-1 macrophages (105/ml) were incubated 24h and 48h in: media (control); CsA (1 μg/ml); MPA (1 μg/ml). After incubation, total RNA and protein were isolated. Message levels of the scavenger receptors CD36, LOX1, SRA1 and CXCL16 were measured using Real Time PCR. All mRNA expression was normalized to GAPDH. 

Summary of Results: CsA significantly increased expression of the main scavenger receptors responsible for oxLDL uptake: CD36, SRA1 and LOX1 (1.45±0.04, 1.67±0.07 and 1.37±0.1, respectively) vs. control untreated cells set at 1. In contrast, MPA decreased expression of CD36, SRA1 and LOX1 to 0.75±0.03, 0.6±0.08 and 0.75±0.09, respectively. Expression of CXCL16 was not changed. Consequently, CsA increased FCF by 18%; and MPA decreased FCF by 25% vs. untreated.

Conclusions: In contrast to CsA, which promotes oxLDL accumulation in THP-1 macrophages, MPA decreased atherogenic cholesterol influx proteins and reduced lipid accumulation. This may influence drug choice in high CVD risk SLE and renal transplant patients.

CHARACTERISTICS OF AFRICAN AMERICAN CHILDREN WITH INADEQUATE CALCIUM INTAKE

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Our study sample was comprised of 150 healthy 5–9 year old AA children with and without fractures originally enrolled in a study to evaluate fracture risk. The study was conducted at a large urban pediatric academic center in Washington, DC. Measurements included BMI, dietary intake (BLOCK Kids 8-17 Food Frequency Questionnaire), BMD and body composition (DXA scan), and serum 25-hydroxyvitamin D level. Our data analysis used descriptive statistics to compare children that met the RDA for calcium intake (adequate intake) to children that did not meet this RDA (inadequate intake).

Summary of Results: The analysis included 148 children; of these, 115 children (77.7%) had inadequate dietary intake of calcium. Inadequate intake of calcium was significantly associated with male gender (84% vs 69%; p=0.04), parental education beyond high school level (77% vs 50%, p=0.01), obesity [BMI= 95th percentile] [24% vs 6%, p < 0.01], less total weekly servings of milk [5.5 (±4.7) vs 12.6 (±8.1), p<0.01] and less daily servings of dairy products [1.2 (±0.7) vs 3.0 (±1.1), p<0.03]. There was a trend toward an association with vitamin D deficiency [serum 25-hydroxyvitamin D level <20 ng/mL] [42% vs 34%, p=0.07]. There were no statistically significant associations between inadequate calcium intake and age, total body BMD, lumbar spine BMD, or bone mineral content (BMC).

Conclusions: In our study population, the majority of 5-9 year old AA children did not meet the RDA for calcium intake. This dietary deficiency was significantly more prevalent in boys, children with higher parental education levels, and obese children and may reflect lower consumption of dairy products. Our results suggest that inadequate intake may be associated with potential negative effects on BMI and vitamin D status, but not BMD or BMC.

THE IMPACT OF PERINEURAL INVASION IN PATIENTS WITH ESOPHAGEAL ADENOCARCINOMA TREATED WITH ESOPHAGECTOMY

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Purpose of Study: Once thought to be a passive process, emerging evidence suggests perineural invasion is associated with reciprocal signaling between tumor and nerve cells. The presence of perineural invasion is an established marker of poor outcome in several types of malignancy yet its role in esophageal cancer has not been clearly elucidated. The objective of this study was to examine the prognostic significance of perineural invasion in patients with esophageal adenocarcinoma treated with esophagectomy.

Methods Used: We conducted a retrospective study of patients with esophageal adenocarcinoma treated with primary surgical resection. We analyzed the relationship between the presence of perineural invasion and overall survival and recurrence-free survival. Kaplan-Meier survival curves were constructed and differences were evaluated with the log rank test.

Summary of Results: We evaluated a total of 128 patients (95 men) with adenocarcinoma of the esophagus. Of these patients, 63 (49%) were positive for the presence of perineural invasion. Our analysis demonstrated the stratum of subjects with perineural invasion had significantly worse overall survival (p < 0.0001) and recurrence-free survival (p < 0.0001) relative to the group without perineural invasion. The probability of 3-year overall survival for the cohort with no perineural invasion was 63% (95% CI: 52%-78%) compared to 28% (95% CI: 18%-44%) for the cohort with invasion present (p < 0.0001) (Figure).

Conclusions: The presence of perineural invasion was associated with significantly worse outcomes in a retrospective cohort of esophageal adenocarcinoma patients following surgical resection. These data suggest that perineural invasion may be a valuable marker of tumor biology that can be utilized for prognostic and therapeutic purposes. Further follow-up and larger studies are required to confirm these findings.

8
SERUM IGF1 AND INSULIN RESISTANCE: HEPATIC STEATOSIS AND METABOLIC SYNDROME

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Purpose of Study: Insulin resistance can cause elevated serum free fatty acids which often leads to hepatic steatosis or dyslipidemia of the metabolic syndrome. Serum free fatty acids can also suppress growth hormone (GH) response to physiologic stimuli. To investigate the downstream effects of these observations, we examined measures identified with insulin resistance and related these to IGF1 levels.

Methods Used: Data from third national health and nutrition examination survey were analyzed. Men and women over 20 years old with body mass measures, hepatic ultrasound results, and laboratory values including serum IGF1 and IGF binding protein-3 (IGFBP-3) levels were studied. Metabolic syndrome criteria was defined by NCEP/ATP III. Participants who had homeostatic model assessment (HOMA) values greater than the 75th percentile were classified with insulin resistance.

Summary of Results: The Bone Health (BH) cohort included healthy African American children aged 5 to 9 years. The Muscle and Bone (MB) cohort included healthy college aged participants. Dual energy x-ray absorptiometry scans were obtained using the Hologic QDR Discovery A Densitometer. Genotyping was performed using the Taqman allele discrimination assay.

The Bone Health (BH) cohort included healthy African American children aged 5 to 9 years. The Muscle and Bone (MB) cohort included healthy college aged participants. Dual energy x-ray absorptiometry scans were obtained using the Hologic QDR Discovery A Densitometer. Genotyping was performed using the Taqman allele discrimination assay.

Conclusions: Serum IGF1 and IGF1 binding to IGFBP-3 indicates that the low IGF1 is not caused by decreased binding proteins. Whether hepatic steatosis and metabolic syndrome are suppressing IGF1 or low IGF1 from an alternative etiology is promoting insulin resistance remains to be determined.

9
GENETIC VARIATION IN NEUROMEDIN U INFLUENCES LEAN BODY MASS AND BONE MORPHOMETRY IN MEN

Elizabeth A. Hedges1, Courtney A. Sprouse2, Heather Gordish-Dressman3, Leticia M. Ryan3, Michael Liu1, Zachary Kendrick1, Elizabeth Dominic1, Jacqueline McKesey4, Eric Hoffman5, Joseph M. Devaney5, Laura L. Tosi4, 1The George Washington University School of Medicine and Health Sciences, Washington, DC, United States; 2Children’s National Medical Center, Washington, DC, United States; 3Johns Hopkins School of Medicine, Baltimore, MD, United States; 4Georgetown University School of Medicine, Washington, DC, United States and 5Children’s Research Institute, Children’s National Medical Center, Washington, DC, United States.

Purpose of Study: Noreumedin U (NMU) is a highly conserved hypothalamic neuropeptide that regulates energy homeostasis and bone formation by acting on the osteoblast beta-2-adrenergic receptor. Understanding genetic differences in NMU may be important for maximizing childhood bone development and preventing osteoporosis.

Methods Used: The Bone Health (BH) cohort included healthy African American children aged 5 to 9 years. The Muscle and Bone (MB) cohort included healthy college aged participants. Dual energy x-ray absorptiometry scans were obtained using the Hologic QDR Discovery A Densitometer. Genotyping was performed using the Taqman allele discrimination assay.

Summary of Results: MB: Total body BMD, lumbar bone mineral density, total body BMC, and lumbar BMC were significantly associated with variations in rs6827359. Variations in rs12500837 were found to be significantly associated with lean mass in males.

Conclusions: Osteoporosis is the most common bone disorder in the western world and is a significant cause for morbidity and mortality. We have demonstrated that variations in the NMU gene are associated with better BMD and BMC primarily in men. Further exploration into how these genetic variants influence bone development may be important for maximizing bone health.
EFFECT OF METABOLIC SUBSTANCES ON INTERMITTENTLY ANOXIC PERIPHERAL NERVE
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Purpose of Study: Polyneuropathy can be caused by diabetes mellitus, alcohol abuse, HIV infection, and autoimmune disorders. Ischemia is an important contributor to nerve damage by inducing an anoxic environment. To better understand how the peripheral nerve functions during oxidative stress, we determined how different metabolic substrates affect the nerve action potential (NAP) during anoxia and subsequent recovery.

Methods Used: We extracted sciatic nerves from Sprague-Dawley rats and placed them in perfusion chambers containing 1 of 7 metabolic substrates: glucose, fructose, galactose, sorbitol, lactate, acetate, and β-hydroxybutyrate. The nerve perfusion alternated from an oxygenated-to-anoxic solution every 90 minutes. The nerve was stimulated every 4 seconds and the NAP was recorded and digitized. We then increased the concentration of each substrate tenfold and repeated the experiment.

Summary of Results: The NAP disappeared during anoxia and recovered when oxygenated in each condition. Repeated anoxia episodes the NAP amplitude decreased. The NAP amplitude remained above 20% of its baseline amplitude when the nerve was perfused with 5.5mM glucose, 5.5mM fructose, 55mM fructose, 5.5mM galactose, 5.5mM lactate, and 55mM lactate. The amplitude dropped to less than 20% of its baseline when perfused with 55mM glucose, 5.5mM sorbitol, 5.5mM galactose, 55mM galactose, 5.5mM acetate, 55mM acetate, 5.5mM β-hydroxybutyrate, and 55mM β-hydroxybutyrate.

Conclusions: These results indicate that hyperglycemia has a negative effect on NAP amplitude preservation, while a high level of sorbitol has a positive effect on NAP amplitude during anoxic episodes. This apparent beneficial effect of sorbitol on nerve function is interesting because the accumulation of intracellular sorbitol is a possible mechanism of diabetic nerve injury. Acetate and β-hydroxybutyrate have no positive effect on the peripheral NAP amplitude during intermittent anoxia. This indicates that the intermittently anoxic nerve may be benefitting from metabolism upstream to the point at which acetate and β-hydroxybutyrate enter the TCA cycle. By further understanding the effect of metabolic substrates on the stressed peripheral nerve, we are opening the way toward mitigating nerve injury.

MP1
DO CLASSICALLY ACTIVATED M1 MACROPHAGES DISPLAY PRO-ATHEROGENIC CHANGES IN CHOLESTEROL TRANSPORT PROTEINS?
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Purpose of Study: Classically activated M1 macrophages produce inflammatory cytokines that trigger acute inflammation. Over-abundance of M1 macrophages is linked to atherosclerosis. Balanced flow of cholesterol into and out of the macrophage is necessary to avoid lipid overload and atheroma development. ATP binding cassette transporters (ABC) A1 and ABCG1 facilitate cholesterol removal and constitute a first line of defense against atherosclerosis. Scavenger receptors: CD36, SR-A1, LOX1 and CXCL16 are responsible for modified lipid uptake. We explore changes in expression of these proteins upon polarization of THP-1 human macrophages to the M1 phenotype.

Methods Used: THP-1 monocytes were differentiated to the non-polarized phenotype (M0) by 100nM PMA, followed by incubation with 20 ng/ml interferon-γ, 100 ng/ml LPS to obtain M1 macrophages. Phenotypes were confirmed via QRT-PCR and by flow cytometry. Expression of cholesterol transport proteins was analyzed by QRT-PCR and confirmed by Western blot.

Summary of Results: The M1 subset of macrophages display reduced expression of ABCA1 (54±5.2%) (P<0.001, n=3), but not ABCG1 (90±6%) as compared to M0 set at 100%. Expression of CXCL16 in M1 macrophages was 3 times higher than in M0 (P<0.001, n=3), level of CD36 and SR-A1 were not significantly affected while LOX1 mRNA level was significantly reduced (54±0.4%) vs. M0 (P<0.001, n=3) (Fig 1). Gene expression analysis was confirmed by Western blot.

Conclusions: This study identifies two major changes in the expression of cholesterol transport proteins — reduction of ABCA1 level and augmentation of CXCL16 expression. These changes may contribute to the pro-atherogenic profile for M1 macrophages.

MP2
PERIOPERATIVE MANAGEMENT OF CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES (CIEDS): AN ANALYSIS OF ADHERENCE TO GUIDELINES
Eric J. Berkowitz1, Aledrin Elton1, Arber Kodra1, Kabir Bhasin1, Neil L. Coplan1, Cardiovascular Medicine, Lenox Hill Hospital, New York, NY, United States.

Purpose of Study: Pacemakers and AICDs (CIEDs) are susceptible to electromagnetic interference when monopolar electrosurgery is used in close proximity to the device. Serious complications include inhibition of appropriate pacemaker therapy and/or delivery of inappropriate tachyarrhythmia therapy. The highest risk occurs with the use of monopolar electrosurgery above the umbilicus. Current recommendations state that all patients with CIEDs should optimally be evaluated by a member of the patient’s CIED team prior to the day of surgery, and if this is not done then a consultation should be obtained from any available CIED team. The team should provide guidance on perioperative CIED management.

Methods Used: All patients over the age of 18 with a CIED who underwent surgery were included to determine whether preoperative evaluation was done and recommendations made.

Summary of Results: 50 consecutive patients with CIEDs going to the operating room were enrolled (mean age 71.8±14 years). Of these 50 patients, 64% (32/50) had preoperative evaluation, with 50% (16/32) being evaluated by their own CIED team, on the team prior to the day of surgery. Reprogramming or magnet use occurred in 68.5% (22/32) of those patients evaluated. 88% (44/50) of surgeries were performed using monopolar electrosurgery and 64% (32/50) of surgeries were above the umbilicus. Highest risk surgeries, which include a combination of above the umbilicus and monopolar electrosurgery, were performed in 62% (31/50) of the patients. Of these patients, 68.8% (22/31) had a preoperative evaluation. Of the patients that did not have a preoperative evaluation, 50% (9/18) underwent surgery that poses the highest risk for perioperative complications.

Conclusions: Of the 50 patients with implantable cardiac devices, 36% (18/50) did not have preoperative evaluation by a CIED team, which fails to comply with current HRS guidelines. Additionally, 50% (16/32) of the
patients that were evaluated did not have the optimal preoperative evaluation by their own CIED team. Failure to comply with current guidelines may pose an unnecessary risk for patients with CIEDs during the perioperative period.

MP3
DIAGNOSTIC CARDIAC FELLOWS: DO THEY INCREASE RADIATION EXPOSURE AND PROCEDURAL TIMES
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Purpose of Study: Prior studies have shown increased radiation exposure on diagnostic cardiac procedures performed by cardiology fellows. We compared radiation exposure parameters during cardiac catheterization (CC) procedures performed by fellows and attendings in a community hospital without surgical backup.

Methods Used: We retrospectively reviewed medical records of 661 patients who underwent cardiac catheterization from January 2012 to February 2013. Fluoroscopy time, total kerrma area product (KAP), cumulative dose area product (DAP) and diagnostic start and end times were compared between second and third-year fellows and attendings. A t-test was run to determine whether the mean differences in exposure parameters were statistically significant.

Summary of Results: The attendings had lower exposure parameters except in mean fluoroscopy time. The mean total kerrma area product and cumulative DAP were statistically significant different when comparing fellows to attendings. Table 1 contains the results of the Independent Samples T-Test.

Conclusions: There was no significant difference in procedural times between fellows and attendings. We found a significant increase in total kerrma area product (KAP) and cumulative dose area product (DAP) during a cardiac catheterization procedure performed by a diagnostic fellow. Concordant with current literature, the participation of diagnostic fellows during CC procedures adds additional risk of radiation exposure to the patient.

<table>
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<tr>
<th>Fluoroscopy Times (min)</th>
<th>Patients (n)</th>
<th>Mean ± Std. Deviation</th>
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<tr>
<td>Follow</td>
<td>330</td>
<td>7.07 ± 5.056</td>
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<tr>
<td>Attending</td>
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<td>Total Kerrma Area Product (kg)</td>
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<tr>
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<tr>
<td>Attending</td>
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TABLE 1. Independent Samples T-Test

MP4
A GENETIC VARIANT IN THE GAMMA GLUTAMYL CARBOXYLASE GENE AFFECTS BONE QUALITY IN A PEDIATRIC AFRICAN AMERICAN COHORT
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Purpose of Study: To explore whether a single nucleotide polymorphism (SNP), recently demonstrated to be associated with bone mineral density in the general population (rs996644), located in the GGCX gene is associated with bone mineral density and bone mineral content in a population of 5-9 year old African American children.

Methods Used: The Bone Health cohort included 142 African-American children (ages 5 to 9) with measures of bone quality collected using dual energy X-ray absorptiometry (DXA). Measures collected included total body bone mineral density (BMD) minus head (tBMD), lumbar BMD (lBMD), total body mineral content (BMC) minus head (tBMC), and lumbar BMC (lBMC). The tBMD, tBMC, and lBMD z-scores were calculated from raw DXA BMD values.

We genotyped the SNP in the cohort using a TaqMan allelic discrimination assay. Hardy-Weinberg equilibrium was validated for the GGCX SNP. Associations between SNPs and phenotypes were tested using ANOVA on z-scores and ANCOVA on all other phenotypes. The ANCOVA models included covariates of age and gender. All analyses used the dominant genetic model.

Summary of Results: A significant association was discovered between tBMD z-score and genotype (GA/GG [n = 59]: -0.507 ± 0.120; AA [n = 38]: -0.111 ± 0.151; p = 0.04). The association approached statistical significance with tBMC (GA/GG [n = 75]: 942 ± 19 g; AA [n = 43]: 999 ± 25 g; p = 0.07) and lBMD z-score (GA/GG [n = 76]: 0.013 ± 0.122; AA [n = 44]: 0.362 ± 0.160; p = 0.08).

Conclusions: Our preliminary findings suggest that a single nucleotide variant in the GGCX gene may be associated with bone mineral density in a pediatric African American cohort. Whether this association holds up in larger studies remains to be determined. However, the results of this study are consistent with previous studies that have shown a genetic effect on bone mineral density in other populations.
MP7

CHARACTERIZATION OF NASAL AIRWAY MICROBIOTA DURING RHINOVIRUS INFECTION IN FULL TERM AND IN PREMATURNE INFANTS

Geovanny F. Perez1,2, Marcos Perez-Losada2, Krishna Pancham1, Shehla Noon1

Purpose of Study: Differences in nasal airway microbial communities are present in premature (PM) children after birth. It is unclear if these differences persist during infancy and if they change in response to viral respiratory infections. Rhinovirus (RV), the most common cause of acute respiratory infections, is to understand fetal outcome for women with PFO related stroke. The purpose of this study is to understand fetal outcome for women with PFO related stroke during pregnancy. The overall admission rate was 22%. After adjustment for covariates, hospitalization for acute asthma was not associated with aggregate number of recent visits with fever (aOR 0.96, 95% CI 0.91-1.02) or aggregate number of recent visits for acute asthma (aOR 0.10, 95% CI 0.09-1.02). Transfer status (aOR 8.4, 95% CI 6.56-10.80), high asthma severity (aOR 3.9, 95% CI 3.30-4.58) and private insurance status (aOR 1.3, 95% CI 1.04-1.61) were associated with hospitalization.

Conclusions: Surveillance of ED visits for fever and asthma was not associated with hospitalization for acute asthma in this population. Previously reported associations between acute asthma and season may not be expressed in terms of local burden of fever and acute asthma; alternatively, such associations may be related to ED visits but not hospitalization.

Methods Used: Retrospective analysis of patients, ages 1-17 years, with acute asthma, seen at two urban pediatric EDs between 1/2011-12/2012, residing in the District of Columbia. Two surveillance variables for local burden of febrile illness and asthma were created from all ED visits (n=240474) during the study period. Multivariable regression analyses were performed to determine associations between surveillance variables and individual risk of hospitalization. Covariates included asthma severity, race, insurance, transfer status, gender, and age.

Summary of Results: 5246 patients were included in the analyses; mean age of 5.7 years (SD 4), 39% female, 89% non-Hispanic Black, 86% public insurance, 7% transferred from an outside hospital. The overall admission rate was 22%. After adjustment for covariates, hospitalization for acute asthma was not associated with aggregate number of recent visits with fever (aOR 0.96, 95% CI 0.69-1.33) or aggregate number of recent visits for acute asthma (aOR 1.0, 95% CI 0.98-1.02). Transfer status (aOR 8.4, 95% CI 6.56-10.80), high asthma severity (aOR 3.9, 95% CI 3.30-4.58) and private insurance status (aOR 1.3, 95% CI 1.04-1.61) were associated with hospitalization.

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Conclusions: Surveillance of ED visits for fever and asthma was not associated with hospitalization for acute asthma in this population. Previously reported associations between acute asthma and season may not be expressed in terms of local burden of fever and acute asthma; alternatively, such associations may be related to ED visits but not hospitalization.
vitamin D status. Girls with fractures significantly more likely to report a prior fracture [7/32 (21.9%) vs 2/44 (4.5%), p = 0.04]. Girls with fractures had significantly less weekly hours of outdoor play than boys [13.6 ± (6.8) vs 18.3 ± (6.7), p = 0.01]. In comparison to girls, boys were less likely to meet the Recommended Dietary Allowance for calcium intake (8/42 (19.0%) vs 13/32 (40.6%), p = 0.04).

Conclusions: In our study population of AA children with fractures, gender differences were observed in factors associated with bone health. Girls had significantly less outdoor play and were more likely to have a previous fracture whereas boys were less likely to meet guidelines for calcium intake. These results suggest that bone health promotion in children should encourage physical activity in girls and optimization of calcium intake in boys.

MP10 PATHOSCOPE: INTEGRATING MICROBIOME CHARACTERIZATION AND HOST GENE EXPRESSION IN PEDIATRIC ASTHMA

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Purpose of Study: Emerging next-generation sequencing (NGS) technologies have revolutionized the collection of genomic data for applications in clinical settings. However, to make the most of these new data, new methodologies that can accommodate large volumes of genomic data from different sources (DNaseq and RNAseq) in a computationally efficient manner need to be applied. Here we present a new statistical framework to accurately and quickly analyze host and microbial NGS reads for microbiome characterization and transcript differential expression, and apply it to the study of pediatric asthma.

Methods Used: The newly developed bioinformatic platform, PathoScope, can map host and microbial NGS reads to databases of known target genomes, transcriptomes and amplicons. PathoScope can discriminate between closely related strains of microbes with very low genome coverage, while assessing differential expression of genes from both host and microbiota. We applied PathoScope to the analysis of RNA-Seq data from nasal epithelial cells in 14 children and adolescents (8 asthmatic and 6 healthy controls) enrolled in the AsthMap Project. We used an Illumina HiSeq 2500 platform to generate an average of 41.4 million single-end 100bp reads per sample (host and microbiome) after rRNA depletion.

Summary of Results: PathoScope revealed significant differences in the metagenomic composition of the nasal microbiomes of asthmatic and healthy patients. Moraxella catarrhalis was identified as the predominant microbe in 5 of the 8 asthmatic patients and was 5.6 times more abundant in cases than controls. Subsequent transcriptomic RNAseq analysis showed a strong host immune response to M. catarrhalis in 4 of the 5 asthmatic patients identified in our metagenomic analysis, but not response was detected in the healthy controls.

Conclusions: Our approach not only characterizes microbiomes from genomic data, but can also distinguish pathogens from commensals by determining if the host is mounting an immune response against specific infectious agents. Our results expand previous studies suggesting that M. catarrhalis is one of the driving factors of pediatric asthma.

MP11 OBESITY DERIVED ADIPOCYTE EXOSOMES ALTER TGFβ SIGNALING GENE EXPRESSION IN LUNG EPITHELIUM

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Purpose of Study: Adipose tissue is one of the driving factors of pediatric asthma. M. catarrhalis is one of the driving factors of pediatric asthma.

Methods Used: We hypothesized that obese adipocytes shed exosomes with miRNAs that upregulate expression of TGFβ in the lung. Using airway fibroblasts (important in subepithelial fibrosis), we aimed to define a mechanism how obesity impacts fibrosis. We hypothesized that obese visceral exosomes activate TGFβ signaling in asthmatic airway fibroblasts.

Methods Used: We isolated obese visceral exosomes (n=4) (previously preserved with Affymetrix miRNA 3.0 arrays) and co-incubated these exosomes with non-asthmatic and asthmatic fibroblasts (from endobronchial biopsy tissue)(n = 1) for 24 hours. Fibroblasts were profiled for mRNA expression. We generated miRNA-mRNA interaction treemaps using miR TarVis (visual analytics tool for integration of microRNA-mRNA profiles with microRNA target prediction algorithms). qRT-PCR was used for confirmation.

Summary of Results: PKH126-labeled exosomal uptake showed exosomal proteins in fibroblasts. Using miR TarVis, we identified 238 miRNA-mRNA pairs for obese visceral exosomes and non-asthmatic fibroblasts and 241 miRNA-mRNA pairs for asthmatic fibroblasts. ACVR2B and ZNF236 were in both datasets. ACVR2B (activin receptor, type IIB, myostatin and TGFβ receptor) was downregulated in non-asthmatic fibroblasts (fold change (FC) = 1.18, p = 0.01), and upregulated in asthmatic fibroblasts (FC = 1.31, p = 0.02). Obese visceral exosomal miRNAs targeting ACVR2B in non-asthmatic fibroblasts were upregulated (i.e., let-7 (FC = 1.35, p = 0.02) and miR-27a (FC = 1.12, p = 0.03)) and downregulated in asthmatic fibroblasts (miR-148 (FC = 1.25, p = 0.02), miR-27a (FC = 1.38, p = 0.01), miR-148B (FC = 2.22, p = 0.01), miR-182 (FC = 2.05, p = 0.01), and miR-192 (FC = 1.55, p = 0.01). qRT-PCR confirmed ACVR2B downregulation in non-asthmatics (FC = 0.26 [95% confidence interval=0.26, 0.78]) and upregulation in asthmatics (FC = 3.21 [3.21, 6.72]).

Conclusions: Obese visceral exosomes regulate mRNA expression of ACVR2B, a TGFβ receptor by downregulating ACVR2B in non-asthmatic fibroblasts and upregulating ACVR2B in asthmatic fibroblasts. This suggests that obese exosomes regulate airway fibroblast gene expression and that fibroblasts respond depend on disease.

MP13 LUPUS: AN UNUSUAL PRESENTATION

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Purpose of Study: Diffuse alveolar hemorrhage (DAH) is a rare presentation of systemic lupus erythematosus (SLE). We will discuss a patient with SLE presenting with DAH. Early diagnosis and appropriate treatment can improve outcomes.

Methods Used: 50 year old male presented with one day of chest tightness, epistaxis, hemoptysis, and respiratory distress. On physical exam there was frank bloody sputum, right sided creckles, and tachycardia. Rapid clinical deterioration required orotrachial intubation and mechanical ventilation.

Laboratory tests showed: hemoglobin: 7.6, creatinine: 2.5. Urinalysis showed hematuria. 24 hour urine protein was 4010 mg. Screening for P-ANCA, C-ANCA, anti-glomerular basement membrane, anti-cardiolipin were negative. He had a positive nuclear antibody, anti-smith, anti-RNP, anti-chromatin IgG and low C3 and C4.

Chest radiography showed bilateral central opacities. Computed tomography of the chest showed extensive bilateral airspace disease, suggestive of pulmonary hemorrhage. Bronchoalveolar lavage became progressively hemorrhagic after each aliquot. A renal biopsy showed class 5 lupus nephritis.

He was treated with pulse solo-medrol, followed by prednisone taper, cyclophosphamide, and plasma exchanges. Patient was extubated after 9 days, and discharged after 19 days in stable condition.

Summary of Results: Diffuse alveolar hemorrhage is a very rare presentation of SLE, with mortality rates reported as high as 70-90%. SLE should be considered in those presenting with DAH, since delay in therapy may cause a rapid deterioration of the patient.

The etiology of DAH includes: autoimmune diseases, pulmonary infections, cardiac disorders, coagulation disorders, anticogulant drugs, idiopathic pulmonary hemosiderosis, crack cocaine inhalation, PTU, amiodarone, and methotrexate.

Our patient meets the criteria for diagnosis of SLE according to the American College of Rheumatology. He has 4/11 criteria including lymphopenia, anti-ANA, Anti-Smith, low complementemia and renal biopsy consistent with class 5 lupus nephritis.

Conclusions: The diagnosis of SLE is illusive when DAH is the presenting symptom. Since early diagnosis and appropriate institution of treatment improves outcome, it is important to keep SLE in mind as an etiology of DAH. High dose glucocorticoids, cyclophosphamide and plasmapheresis therapy resulted in rapid improvement of respiratory function in our patient.

12 MITOTIC ASYNCHRONY INDUCES A PRO-INFLAMMATORY STATE IN AIRWAY EPITHELUM

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Purpose of Study: Mitotic behaviors are likely important for restoring homeostasis in lung diseases with epithelial injury. We recently proposed that regenerative asynchrony in tissue may underlie chronic inflammation and fibrosis, where immune cell infiltration is secondary to pro-inflammatory cross-talk among asynchronously repairing adjacent tissues. Building on our previous finding that regenerative asynchrony is associated with pro-inflammatory/fibrotic cytokine secretion, here we provide proof of cause-and-effect.

Methods Used: In vitro experiments were performed wherein airway epithelial cells were mitotically asynchronous due to disease state (i.e. asthma) and then resynchronized via capture of the G1/S checkpoint via two-hour daily pulse exposure to dexamethasone, simvastatin, or aphidicolin. Further experiments utilized a novel method we developed for inducing mitotic asynchrony in normal progenitors. Induced asynchronous populations were used to elucidate if TGF-β1 plays a role in resynchronization of normal progenitors.

Summary of Results: Upon mechanical injury, human asthmatic airway epithelial mitosis was asynchronous relative to normal epithelia. Mitotic capture increased the percentage of progenitors in G1. Resynchronization in the proliferating asthmatic epithelia reduced basolateral TGF-β1 secretion. We next examined whether inducing mitotic asynchrony in normal epithelial cells would result in TGF-β1 secretion. These samples showed moderate asynchronous at 6 and 12 hours that resolved spontaneously by 24 hours. Induced populations showed elevated TGF-β1 secretion at 12 hours compared to either cell population in isolation. Regulation of TGF-β1 is being investigated as a possible mechanism for synchronization.

Conclusions: We used a series of mitotic experiments wherein airway epithelial mitosis was desynchronized and resynchronized via G1/S checkpoint manipulation. Cumulative analysis shows mitotic synchrony is the homeostatic state in normal progenitors. Induced asynchronous populations showed moderate TGF-β1 secretion at 6 and 12 hours that resolved spontaneously by 24 hours. This finding establishes rationale for targeting progenitor cell mitotic behavior rather than immune-mediated inflammation in fibrotic disease.

13 YOUNG CHILDREN WITH HISTORY OF PREMATURITY HAVE IMPAIRED AIRWAY ANTIVIRAL IFNγ RESPONSES TO HUMAN METAPNEUMOVIRUS COMPARED TO RESPIRATORY SYNCTYIAL VIRUS.

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Purpose of Study: Human metapneumovirus (HMPV) is a recently discovered respiratory pathogen of the family Paramyxoviridae, and phylogenically
related to Respiratory Syncytial Virus (RSV). It is known that premature children are at high risk of severe RSV and HMPV infections but the nature of the human antiviral airway immune responses of HMPV infections in premature children is understudied.

Methods Used: Nasal airway secretions were collected from children <3 years during acute respiratory illnesses using standard nasal lavage technique. Clinical and demographic variables comprised gestational age in weeks, age, gender and ethnicity and were obtained by reviewing electronic medical records in our institution. Nasal samples were analyzed by PCR to identify RSV and HMPV and then for protein levels of IFNγ, CCL5 and IL-10 along with an expected elevation in Th1 (IFNγ)/Th2 (IL-4) ratios and HMPV-infected premature children do not exhibit increased Th1 (IFNγ)/Th2 (IL-4) ratios or elevated nasal airway secretion of IFNγ, CCL5 and IL-10 relative to uninfected controls.

Conclusions: Our study is the first to highlight that premature infants have defective IFNγ, CCL5/RANTES and IL-10 airway responses during HMPV infection and provides novel insights about the potential underlying mechanism by which HMPV causes severe respiratory disease in young individuals with history of prematurity.

14 VITAMIN D REPLETION REDUCES ADIPOSE TISSUE FIBROSIS AND IMPROVES INSULIN SENSITIVITY IN OBESER INSULIN-RESISTANT HUMANS

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Purpose of Study: Adipose tissue fibrosis may contribute to insulin resistance and inflammation in obesity, which in turn plays a major role in the pathogenesis of diabetes. Vitamin D (VitD) has been shown to reduce fibrosis in hepatic and renal tissues by inhibiting pro-fibrotic processes and collagen synthesis. We hypothesized that VitD repletion could reduce adipose fibrosis and improve insulin sensitivity.

Methods Used: Two step euglycemic, hyperinsulinemic clamp studies were performed in 9 obese, insulin resistant subjects (7M, age 43 ± 4 yr, BMI 33.6 ± 1.4 kg/m2 and HOMA-IR 5.1 ± 0.7), before and after normalizing VitD levels (>30ng/ml) with oral vitamin D3. 6-6 deuterated-glucose was infused with 38 and 37% decreased expression of TNFα, IL-6, iNOS and PAI-1 by adipose tissue fibrosis, with 38 and 37% decreased expression of TNFα and PAI-1 in whole fat and 67, 57 and 34% decreased expression of IL-6, iNOS and PAI-1 by adipose macrophages (all p<0.05). These findings were associated with 34% greater ability of insulin to suppress endogenous glucose production (p = 0.03); glucose uptake was unaffected.

FIGURE 1. Collagen immunofluorescence in Adipose Tissue.

Conclusions: Thus, VitD repletion reduced adipose tissue fibrosis in concert with improved hepatic insulin sensitivity and reduced inflammation in obese humans. Correcting VitD deficiency in obese insulin-resistant individuals could have considerable metabolic benefit.

15 ROLE OF ADENOSINE A2A AND A3 RECEPTORS IN MACROPHAGE POLARIZATION: LINK BETWEEN INFLAMMATION AND LIQUID ACCUMULATION

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Purpose of Study: Macrophages are key players in inflammation and atherosclerosis. Macrophages within atherosclerotic lesions attain two distinct functional phenotypes, M1 (pro-inflammatory) and M2 (immunosuppressive). They express surface receptors of different subtypes for the endogenous autacoid adenosine, which are crucial in an anti-inflammatory response. This study examines expression of adenosine receptors in THP-1 human macrophages upon differentiation to M1 and M2 subtypes in connection with lipid accumulation and foam cell formation (FCF).

Methods Used: THP-1 human monocyes were differentiated to a non-polarized phenotype (M0) with 20 ng/ml interferon-γ and 10 ng/ml LPS to obtain M1 or 20 ng/ml IL-4 to obtain M2 subtypes. Phenotypes were confirmed by QRT-PCR and flow cytometry. Expression of adenosine receptors, A1, A2A, A2B and A3 was performed in 9 obese, insulin resistant subjects (7M, age 43 ± 4 yr, BMI 25.1 ± 0.9 kg/m2) participated in two study protocols in random order over 3 years (SAL) or morphine (MOR; 0.1 mg/kg/min), separated by a 120-minute break (all euglycemic). On day 2 subjects underwent stepped hypoglycemic clamps (nadir 60mg/dL) with evaluation of counterregulation, endogenous glucose production (EGP, using 6.6-D2-glucose), and hypoglycemic symptoms.

Conclusions: Thus, VitD repletion reduced adipose tissue fibrosis in concert with improved hepatic insulin sensitivity and reduced inflammation in obese humans. Correcting VitD deficiency in obese insulin-resistant individuals could have considerable metabolic benefit.

16 HYPOGLYCEMIC COUNTERREGULATION IN HUMANS IS IMPAIRED BY OPIOID RECEPTOR ACTIVATION

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Purpose of Study: Although intensive glycemic control improves outcomes in type 1 diabetes mellitus (T1DM), iatrogenic hypoglycemia limits its attainment. Recurrent and/or antecedent hypoglycemia causes hypoglycemia-associated autonomic failure (HAAF), characterized by blunting of the sympathoadrenal responses to hypoglycemia and hypoglycemia unawareness. Opioid receptor blockade is associated with prevention of experimentally-induced HAAF in nondiabetic and T1DM subjects, but it has not been established whether opioid receptor activation induces HAAF in humans.

Methods Used: Twelve healthy, non-diabetic subjects (7M, age 32.3 ± 2.2 yr, BMI 25.1 ± 0.9 kg/m2) participated in two study protocols in random order over 2 consecutive days. Day 1 involved two 120-minute infusions of either saline (SAL) or morphine (MOR; 0.1mg/kg/min), separated by a 120-minute break (all euglycemic). On day 2 subjects underwent stepped hypoglycemic clamps (nadir 60mg/dL) with evaluation of counterregulation, endogenous glucose production (EGP, using 6.6-D2-glucose), and hypoglycemic symptoms.
SUMMARY OF RESULTS: Compared with saline, MOR induced a blunted epithelium response (Figure 1: SAL = 419 ± 20 vs MOR = 293 ± 16 pg/mL, p = 0.012), a blunted growth hormone response (SAL = 15 ± 4 vs MOR = 10 ± 3 ng/mL, p = 0.005) and fewer hypoglycemia-associated symptoms on day 2 (p = 0.012).

CONCLUSIONS: These findings demonstrate the first time in humans that opioid receptor activation induces some of the clinical and biochemical features of HAAF, suggesting novel pharmacologic approaches for preventing hypoglycemia and safer intensive glycemic control in T1DM.

PLASMA AND TISSUE MICRORNA PATTERNS DISCRIMINATE MALIGNANCY IN PATIENTS WITH BENIGN OVARIAN MASSES: ENRICHMENT ANALYSIS OF GENETIC PATHWAYS

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PURPOSE OF STUDY: Over 75% of women diagnosed with ovarian cancer are diagnosed at stage III. Treatment typically includes surgical debulking followed by chemotherapy; however, only 20% of ovarian cancers are cured. Surgical workup of suspicious pelvic mass reveals cancer in a minority of patients. To check if differential microRNAs (miRNAs) in plasma and tissue rules out ovarian cancer in patients with pelvic masses

METHODS USED: We analyzed pre-surgical plasma and available corresponding tissue samples from 42 women diagnosed with high grade serous ovarian cancer, 36 women diagnosed with a benign neoplasm and 23 women with no known disease. miRNA profiling: miRNA profiling profiles were generated using Illumina’s Whole Genome Gene Expression DASL HT assay according to manufacturer’s instructions. Intensity data was imported into GenomeStudio for expression analysis. Two-sample t-test was used for all 2-sample comparison and ANOVA followed by Tukey HSD post-hoc test to compare the miRs mean differences. All tests were 2-tailed and results with a p < 0.05 were considered statistically significant.

SUMMARY OF RESULTS: In preoperative plasma: levels of miR-106b, -126-3p, -150, -17, -20a and -92a were 2-4 times higher in benign versus cancer p = 0.005; miRNA and mRNA expression between cancer vs benign revealed 21 miRNAs met our criteria for significance: 14 were up-regulated in cancer and 7 were down regulated in cancer p < 0.005.

CONCLUSIONS: MiR-106b, miR-126, miR-150, miR-17, miR-20a, and miR-92a had increased expression in benign presurgical plasma from that of cancer subjects adj. P < 0.02. One of these miRs, 126-3p, has higher 5 fold higher expression in benign vs primary tissue (p = 1.1 E-12) and 4x higher expression in benign vs cancerous plasma (p = 6.1E-5), suggesting the source of this miRNA is ovarian tissue. MiRNAs (106b and 17-5p) were higher in cancerous than benign tissue but lower expression in cancerous vs. benign plasma (p < 0.5). This suggests that the source of these miRNAs is not ovarian in origin.

PCA cancer vs benign samples showed eight miRNAs (APP, CDK2, CUL3, ELAVL1, FN1, Nrf1, SUM02 and UBC) and 2 miRNAs (miR-506 and miR-548c) were chosen 100% of the time in each dataset.

TABLE 1. Test Characteristics of Asthma Score in Predicting Admission for Acute Asthma

POSITIVE PREDICTIVE VALUES OF POSITIVE D-DIMER LEVELS IN VENOUS THROMBOEMBOLIC EVENTS DIAGNOSED BY CT ANGIOGRAPHY, VENOUS DUPLEX, AND V/Q SCAN

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PURPOSE OF STUDY: Diagnostic studies for pulmonary embolism (PE) and deep vein thrombosis (DVT) consist of computed tomography angiogram (CTA), venous duplex and ventilation/perfusion (V/Q) scan. D-dimer levels often influence the choice of diagnostic test to confirm PE or DVT, although each differs drastically in cost. This study investigates the relationship of levels of D-Dimer to a diagnosis of PE or DVT as established by these three tests.

METHODS USED: In this retrospective cohort study, we reviewed patients who presented in a large urban emergency department (ED) with suspected PE or DVT from 2011 to 2014 who had positive D-dimer values (≥0.5 in our laboratory). Hemodynamically unstable patients were excluded. A total of 394 patients (N=394) were identified. D-dimer levels were grouped into five ranges (0.5-1, 1.01-2, 2.01-5, 5.01-20, >20). Each patient had a CTA, V/Q scan, venous duplex, or a combination thereof. The positive predictive values were calculated using the under the receiver operating curve was calculated for the entire sample and for different age groups.
(PPV) for each D-dimer range were calculated using the results of each imaging study as the gold standard.

Summary of Results: In the 394 patients meeting study criteria, the mean D-dimer value was 9.10 ± 9.88. The PPV for D-dimer based on CTA (256 patients) for the five ranges were, respectively, 50.0%, 58.1%, 72.6%, 81.3%, and 42.9%. The PPV for D-dimer based on venous duplex (322 patients) were 44.4%, 48.6%, 59.3%, 65.1%, and 73.0%, respectively. The PPV for D-dimer based on V/Q scan (102 patients) were 42.9%, 46.7%, 70.0%, 69.0%, and 37.5%, respectively, 84 (21%) patients had both CTA and venous duplex, 23 (5.8%) had V/Q scan and venous duplex, 19 (4.8%) had CTA and V/Q scan, and 5 (1.2%) had CTA, V/Q scan, and venous duplex.

Conclusions: D-dimers of 5 and above yielded the highest PPV in the setting of a venous duplex to confirm a thromboembolic event. Venous duplex is the cheapest test of the three, and the management would be the same in these patients, thus precluding the need for multiple imaging studies.

21 HEART FAILURE DISCHARGE EDUCATION: HOW WELL ARE WE EDUCATING OUR PATIENTS? A PATIENT QUALITY AND SAFETY INITIATIVE
Bryan Doherty2, Tarak Rambhatla1, Evan Levine2, Neil Coplan2

Purpose of Study: Management of heart failure (HF) encompasses a complex treatment course requiring strict medication compliance and lifestyle modifications. A pivotal element in outpatient HF management and readmission prevention is patient education. Studies have identified formal education at hospital discharge as an important element in the management of readmission prevention is patient education. Studies have identified formal education in the setting of HF as the gold standard.

Methods Used:

Management of heart failure (HF) encompasses a complex treatment course requiring strict medication compliance and lifestyle modifications. A pivotal element in outpatient HF management and readmission prevention is patient education. Studies have identified formal education in the setting of HF as the gold standard.

Conclusions: D-dimers of 5 and above yielded the highest PPV in the setting of a venous duplex to confirm a thromboembolic event. Venous duplex is the cheapest test of the three, and the management would be the same in these patients, thus precluding the need for multiple imaging studies.

22 DOES AN UPRIGHT T WAVE IN LEAD V1 PREDICT LEFT ANTERIOR DESCENDING ARTERY LESION AND/OR A LEFT CIRCUMFLEX ARTERY LESION ON CARDIAC CATHETERIZATION?
Naveen Sablani1, Drew Murray2, Praveen Chatani2, Young Lee2, Bonnie Simmonpl, Solehia Talebi2, Roger Chiurugi3, George Fernaine1, Getaw W. Hassen1,3

Purpose of Study: An upright T wave (UTW) in V1 may be a normal variant in some cases, but it is considered abnormal especially if it is very tall and new. Few studies have investigated the significance of a UTW on V1 in predicting the presence of significant coronary artery disease (CAD). We investigated whether an UTW in lead V1 was associated with a left anterior descending (LAD) lesion in addition to association with left circumflex artery disease (LCFx), RCA or multi-vein lesions.

Methods Used: We conducted a retrospective chart review of patients who presented with symptoms of acute coronary syndrome (ACS), or had positive stress test and underwent cardiac catheterization (cath). We evaluated patients with a significant UTW in V1 (≥0.15 mv) in their pre-cath electrocardiogram (EKG) and compared it to their post-cath ECG. We sought to determine if there was a relationship between UTW in V1 and location of coronary lesion.

Summary of Results: Out of 263 patients studied 53 (20.2%) patients had a significant UTW in V1, 29 (55%) had lesions in the LAD, and 102 (34%) had proximal LAD lesion. Post intervention 21 (39%) of 53 patients had normalized their T wave in V1. Nine (42%) out of 21 patients had involvement of the LCFx and another artery. Eleven (52%) patients had involvement of the LAD and another vessel. Only 5/21 (24%) patients had some involvement of the RCA. Of the 20 patients who did not have a change in T wave polarity, 13 (65%) patients had a lesion in the RCA.

Conclusions: A significant UTW in V1 may signify a lesion in the LAD, another artery, or both. In the appropriate clinical setting the presence of a significant CAD should be suspected. Our study was limited by a small sample size. A large scale study in patients undergoing cardiac cath may elucidate the relationship between a UTW and the presence of significant CAD, specifically whether LAD is involved in ACS or as a preceding ominous sign for Wellens Syndrome.

23 COMPARATIVE EFFECT OF USTEKINUMAB AND ADAлимUMAB ON EXPRESSION OF LEPTIN AND LEPTIN RECEPTOR IN THP-1 HUMAN MACROPHAGES
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Purpose of Study: Leptin, an adipostatic circulating hormone produced in white adipose tissue, may play a role in the development of psoriasis and its associated systemic diseases. Patients with psoriasis have abnormal serum leptin levels compared to controls. Here we investigate the effect of two commonly used anti-psoriatic biologics, adalimumab and ustekinumab, on leptin and leptin receptor expression in THP-1 macrophages.

Methods Used: THP-1 differentiated macrophages (PMA 100nM, 24h) were cultured for 18h under 4 conditions: 1) untreated control; 2) adalimumab 50 µg/mL; 3) ustekinumab 1 µg/mL; 4) ustekinumab 5 µg/mL. Expression of leptin and leptin receptor were measured using RT-PCR and immunoblotting techniques.

Summary of Results: The presence of either adalimumab or ustekinumab in growth medium significantly upregulated leptin receptor expression in THP-1 macrophages to 1.979±0.47 and 2.087±0.24 (n=3, P<0.01) respectively, versus 1.12±0.19 for untreated cells. However, only ustekinumab at a concentration of 5 µg/mL augmented expression of leptin to 1.99±0.56 (n=3, P<0.01) versus untreated cells (Fig 1).

Conclusions: These findings shed light on the possible role of leptin in immune-mediated systemic diseases such as psoriasis. This study suggests that one mechanism by which biologics may function in the treatment of
psoriasis and its extra-cutaneous manifestations is by upregulating the leptin receptor. Ustekinumab may have the additional benefit of increasing leptin expression. Further studies identifying its exact mechanism of action could allow for more specific treatment modalities to prevent systemic disease manifestations and ultimately decrease morbidity and mortality.

FIGURE 1. Gene expression of leptin and leptin receptor in THP-1 macrophages exposed to adalimumab and ustekinumab.

TABLE 1. Gene expression of leptin and leptin receptor in THP-1 macrophages exposed to adalimumab and ustekinumab.

Results are presented as means ± SEM of 3 independent experiments. **P < 0.01 vs. control.
regions V3 and V4 of the prokaryotic 16S rRNA were amplified and dual indexed using Illumina sequencing adapters and index barcodes. Illumina MiSeq using 300 cycle paired end reads for sequencing and MiSeq Reporter Metagenomics used for data processing with Greengenes database as a reference.

Summary of Results: Analysis of gut microbiomes was done on 5 food allergic children ages 2-7 and 5 children with no known food allergy ages 2-9 years. Firmicutes and Bacteroidetes are the two major phyla in the gut microbiome and their ratios have been associated with various diseases. We found the average Firmicutes/Bacteroidetes ratio was 3.2 in 5 food allergic subjects and 2.6 in the control subjects. At the genus level, there was a 10% difference among the two groups, however the ratio was not significant in the stool samples from children with food allergies (21.4%) vs. controls (31.1%). There did not appear to be significant differences in the number of operational taxonomic units (OTUs) detected in either group of this limited dataset.

Conclusions: Even in our small dataset, variations in the proportion of bacteria were found between food allergic vs control gut microbiomes. It is noteworthy that there did not appear to be a significant change in the diversity of the bacteria present. The collection and analysis of additional samples will be needed to confirm and expand on these findings. Generating comprehensive microbiome profiles on pediatric patients with and without food allergy will provide novel and invaluable data towards understanding the role of the gut microbiome in the development of food allergy which directly affects the quality of life of those affected.

27 VARIABILITY IN ANTIBIOTIC USE IN LOW-ACUITY PEDIATRIC EMERGENCY DEPARTMENT PATIENTS
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Purpose of Study: Antibiotic overuse in the inpatient setting has been associated with increased antimicrobial resistance and increased healthcare costs. We performed this study to examine variation in antibiotic use among providers and provider groups in low-acuity pediatric emergency department [PED] encounters.

Methods Used: We performed a retrospective cross-sectional medical record review of all Emergency Severity Index [ESI] triage level 4 and 5 patients seen in both sites of an urban, academic PED in 2012-2013. Patients over age 21 and patients with eye infections were excluded. We analyzed rates of antibiotic use for providers with >500 encounters over 2 years. Patient demographics, provider characteristics, ED site, triage level, diagnosis, and presence of at least one antibiotic order were obtained from the electronic medical record.

Summary of Results: There were 87 providers with >500 visits, including 39 (44.8%) pediatric emergency medicine [PEM]-trained providers. Individual provider rates of antibiotic ordering ranged from 2-32% (mean 12.7 ± 4.9%) overall and 1-36% (mean 10.1 ± 6.1%) for respiratory encounters. For PEM providers, rates of antibiotic use ranged from 2-23% (11.8 ± 4.1%) overall and 2-22% (8.8 ± 4.3%) for respiratory encounters. PEM providers with >1000 encounters (N=26) ordered antibiotics in 6-23% of encounters (12.8 ± 4.1%). There were 125,579 total encounters, including 56,886 PEM encounters. At least one antibiotic was ordered in 17,226 (13.7%) of encounters. Antibiotics were less likely to be ordered in PEM encounters compared with other physicians (OR 0.83, 95%CI 0.80-0.86). After adjusting for patient age, arrival time, day of week, ED site, triage or physician assistant involvement, and diagnoses of injury or mental health disorders, encounters with PEM providers remained less likely to have antibiotics ordered (adjOR 0.79, 0.77-0.83). There was no significant difference in antibiotic use for physician encounters compared with nurse practitioner encounters.

Conclusions: Overall rates of antibiotic use in low-acuity PED patients are low, with considerable individual variability between providers. Low-acuity patient encounters with PEM-trained providers are less likely to have antibiotics ordered.

28 INSULIN RESISTANCE DETERMINES SEVERITY OF VASCULAR INFLAMMATION BY 18-FLUORODEOXY GLUCOSE PET-CT IN PSORIASIS
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Purpose of Study: Vascular inflammation (VI) in Psoriasis (PSO) is associated with increased cardiovascular disease (CVD) risk. We have previously shown the presence of insulin resistance (IR) in PSO, however how this relates to subclinical vascular disease is unknown. Here, our aim was to determine whether IR relates to VI measured by 18FDG PET-CT in a well-phenotyped PSO cohort (NCT 01778569).

Methods Used: We performed 18FDG PET-CT scans on 86 consecutive patients with PSO (Siemens Biograph). Target-to-background ratio (TBR) was used as the VI measure. Fasting plasma samples were collected and homeostatic model assessment of IR (HOMA-IR) was used to stratify the study group into normal (n=41) vs high (n=45) HOMA-IR groups using an accepted cut-off value (3). Lipid profile and lipoprotein characteristics were also obtained using NMR spectroscopy (Liposcience, USA).

Summary of Results: Our study cohort was middle aged (mean ±13yrs) with mild to moderate PSO [Median PASI (IQR): 5.5 (3-8.5)]. There was increased VI by TBR in this sample (mean 1.8±0.3) as compared to published values for CAD (mean 1.6±0.3). The high HOMA-IR group had greater skin involvement by PSO [Median PASI (IQR): 6.0 (4.7-8.1) vs 4.3 (2.2-6.6), p<0.01], an increased incidence of CVD risk factors (hypertension 47% vs 12%, p<0.001, type 2 diabetes 20% vs 5%, p=0.03, and hyperlipidemia 76% vs 51%, p=0.02) and a more atherogenic lipid profile on NMR spectroscopy (median HDL-c 47.8±15 vs 61.5±17, p<0.001; median HDL-z=0.9±5 vs 9.5±6.0, p=0.01, mean LDL-z=20.3±6 vs 21±4, p=0.001) when compared to the normal HOMA-IR group. There was greater VI in the high HOMA-IR group (Mean 1.91±0.3 vs 1.69±0.2, p=0.001) which was robust to multivariate adjustment for age, gender, CVD risk factors and BMI (beta 0.38, p<0.01). Finally, on likelihood ratio testing, we observed an incremental effect when HOMA-IR was added to a fully adjusted model with BMI as a covariate (chi2 5.65, p=0.02).

Conclusions: Psoriasis increases VI by 18FDG PET-CT, which is strongly related to the presence of IR beyond traditional CVD risk factors and BMI. This suggests that inflammatory IR may have direct impact on the development of vascular inflammation.

29 Unable to be published

P1 PFO CLOSURE REDUCES HIGH HOMOCYSTEINE LEVEL IN STROKE PATIENTS
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Purpose of Study: PFO allow venous clots to bypass pulmonary filtration, leading to strokes. We previously found PFO endovascular closure lowers oxidative stress and homocysteine levels in peripheral venous blood. Here we study changes of homocysteine during endovascular closure to better understand the mechanism of PFO in circulation.

Methods Used: PFO stroke patients were recruited according to IRB approval with plasma sampled from left (LA) and right (RA) atria pre- and post-PFO closure (n=97). Total homocysteine (tHCY) level was measured by selected reaction monitoring using mass spectrometry.

Summary of Results: tHCY level decreased significantly in both RA and LA post PFO closure (Fig.1A, p = 0.0014; RA: reduced by 8.54% Fig. 1B, p = 0.0304; LA: reduced by 9.90% Fig. 1C, p = 0.0470). Notably, tHCY

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reduction was skewed towards patients with higher tHCY levels before PFO closure (Fig. 1D and E, Kolmogorov-Smirnov test, RA: p = 0.0413; LA: p = 0.0010), such that more patients with higher tHCY level had a more significant reduction in tHCY levels compared to those with lower/normal levels. **Conclusions:** We found that PFO closure efficiently reduced tHCY levels in patients with higher tHCY levels compared to those with lower/normal levels.

**Purpose of Study:** Of the many genes associated with Type 2 Diabetes (T2D), three belong to the adrenergic-receptor β family (ADRB1, ADRβ1, and ADRβ3). Each of these genes exists with single nucleotide polymorphisms (SNPs) that are associated with insulin resistance, obesity, and/or T2D: ADRβ1 rs1042712 and rs1042753; ADRβ2 rs1042711, rs1042713, and rs1042714; and ADRβ3 rs4994. The goal of our study is to determine if these SNPs are associated with other T2D risk factors in college-age populations.

**Methods Used:** These SNPs were investigated in two cohorts of healthy, college-aged subjects: the Assessing Inherited Markers of Metabolic Syndrome in the Young cohort (AIMMY) with 566 subjects, and the Muscle and Bone cohort (MB) with 116 subjects. Anthropometric measures, body fat percentage, and physical activity questionnaires were collected. Weekly energy expenditure was calculated using estimated metabolic equivalents (MET) attributed to reported activities. Genotyping was performed using DNA isolated from blood samples. Each SNP was evaluated for association with phenotypes with age as a covariate. Phenotypes tested include BMI, percent body fat, and physical activity (MET minutes/week).

**Summary of Results:** Four significant associations were identified. African American women (AIMMY) homozygous for the A allele of rs1042752 (AA), Caucasian men (AIMMY) homozygous for the C allele of rs1042714 (CC), and Caucasian men (MB) homozygous for the T allele of rs1042711 (TT) reported higher levels of physical activity. Caucasian women (AIMMY) possessing the G allele of rs4994 (AG/GG) were more likely to have a higher BMI.

**Conclusions:** In conclusion, our study found that not only are some T2D associated polymorphisms associated with BMI and physical activity in certain demographics, but also that they are present in young, healthy populations.

**P3 TISSUE MICRORNA PATTERNS RELIABLY DISCRIMINATE FOR PRESENCE OF MALIGNANCY IN MINUTE BREAST TISSUE SAMPLES**

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**Purpose of Study:** Breast cancer is diagnosed at early stage in more than 50% of patients; the small removed tumors make it difficult to detect predictive and prognostic markers that influence outcome and treatment.

We checked for differences in genome wide microRNA expression profiles between normal and breast cancer tissue samples to identify miRNA expression that correlates with clinic-pathologic features of breast cancer patients.

**Methods Used:** We analyzed tissues from 41 breast cancer and 24 normal tissue samples collected between 2004 and 2011 with available survival data. To identify miRNAs whose expression is significantly differentially expressed in normal and breast cancer tissue samples to identify miRNA expression that correlates with clinic-pathologic features of breast cancer patients.

**Summary of Results:** We used very small samples 10 ngrams of total RNA (15 microliters) mixed with 3 microliters of TaqMan OpenArray microRNA runs on plate Applied Biosystems Openarray qRTPCR system for 75 miRNA microarray. TaqMan miRNA assay expressed as threshold cycle (Ct) after normalization to U6RNA; 1 Ct is 2-fold difference. 10 ngams of total RNA (15 microliters) mixed with 3 microliters of TaqMan miRNA assay RT primer for (RT) reactions. Two-sample t-test was used for 2-sample comparison and ANOVA followed by Tukey HSD post-hoc test to compare the miRs mean differences. All tests were 2-tailed and results with a p < 0.05 were considered statistically significant.

**Conclusions:** Using very small samples 10 ngrams of total RNA of tissue we show that miR expression reliably differentiate normal from malignant tissue; 15 miRNAs are differentially expressed in breast cancer tissue versus normal.
benign. These results suggest that aberrant expression of microRNAs is indeed involved in breast cancer and can be used as minimally invasive biomarkers for rapid diagnosis in small samples.

**P4**

**FREQUENT SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN 13 GENES SEEN IN OVARIAN CANCER AS COMPARED TO BENIGN AND CONTROL TISSUES**

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**Purpose of Study:** Over 75% of women diagnosed with ovarian cancer are cured. We analyzed single nucleotide polymorphisms changes in the genomic DNA in carcinogenic, benign and normal ovary tissues. Tissue samples from 82 with high grade serous ovarian cancer; 27 women diagnosed with a benign neoplasm and 32 women with no known disease. All samples were collected between 2004 and 2011 and survival data was known in all cancer patients. There was no significant difference in age, race.

**Methods Used:** All samples were enriched using the Illumina True Sight DNA enrichment kit. Analysis of Exome Sequencing was done using the Illumina MiSeq. We compared the frequency of polymorphisms detected in cancer, benign and normal ovaries.

**Summary of Results:** In the control group, 10 percent had SNPs, or single nucleotide polymorphisms; in the breast cancer group, over 20-46% had SNPs. The results showed that the EXT2 gene had the highest difference at 25.8% and FANC2D genes with 24.8%. The third highest difference is attributed to the PALB2 gene. The PALB2 gene has also been in recent news because it has recently been accredited with high probabilities of inherited breast cancer. Other genes with a high percentage between the control and ovarian subjects include MEN1, MET, FANCA, ERCC4, FANCG, ERCC3, APC, SLX4, PCT1H, RHBD2 and CDK4.

Percentage difference between cancer/benign/control showed that the PALB2 gene had the highest difference at 39.1%. After that came the RHBD2 gene with a percentage difference of 24.1%. Other targeted genes with high differences in this category include EXT2, CEP57, MET, SDHB, FANC C, ERCC4, NF1, FANCD2, BRCA1, CHI K2, WRN, XPA, HNFA1, MEN1 and SLX4.

**Conclusions:** When studying a panel of 94 genes known to be associated with cancer found only 13 to have SNPs more often seen cancer vs benign vs control. These genes may be implicated in pathways conducive to cancer development of in failure of immune system to recognize and eliminate developing cancer cells.

**P5**

**SUSCEPTIBILITY TO OBESITY AND BONE MINERAL DENSITY IN YOUNG AFRICAN AMERICAN POPULATIONS**

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**Purpose of Study:** Given the disparate effects of obesity on Europeans and African Americans, it is crucial to generate a better understanding of the genetic influences on obesity within the AA pediatric population. Monda et al recently published a genome-wide association study identifying six SNPs associated with BMI, which were selected for genotyping in our pediatric AA cohorts to examine the relationship between genetic risk variants for obesity and bone mineral density (BMD).

**Methods Used:** This study includes AA children, ages 5 to 9 years. Participants had an isolated and radiographically demonstrated forearm fracture. DXA scans were obtained. Phenotypes were analyzed using ANOVA/ANCOVA models as appropriate. Summary of Results: Of the obesity-related SNPs, we found a statistically significant association between Lumbar BMD (height adjusted z-score without head) and SNPs rs974417, and rs10261878. In these SNPs, participants showed higher lumbar BMD z-scores. In literature, obesity has been associated with increased bone mass in some, but results and mechanisms are inconclusive. In our BH cohort, we have shown those children with susceptibility to obesity to have already possessed higher lumbar BMD z-scores. This may indicate that increased BMD associated with obesity is more than just the mechanical loading of bone through excess weight, since the risk alleles confer both susceptibility to obesity and increased BMD z-scores.

**Conclusions:** Our study is one of few that have reported genetic studies of BMI determination in young AA populations. It is crucially understand these genetic differences on obesity. This will offer the possibility of better intervention and treatment options in the future.

**P6**

**HEPATITIS C VIRUS WIDEN PERIOD CAUSING A FALSE NEGATIVE SCREENING RESULT**

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**Purpose of Study:** Hepatitis C virus (HCV) is very accurately detected by screening an individual’s blood with a generation three enzyme-linked immunosorbent assay (ELISA). We report a case, in which, a patient had a negative screening test but a positive polymerase chain reaction (PCR).

**Methods Used:** A 45 year old white male with history of poly substance abuse presented with nausea, vomiting, watery diarrhea and right upper quadrant discomfort for 10 days. The patient denied recent drug use, blood transfusions and tattoos. On admission, the patient had a normal liver function tests (LFTs) which trended up within 2 days. HCV screening results were negative. LFTs trended down on day 3 and were normal at discharge. Despite a negative HCV screening test a high suspicion for acute Hepatitis C remained due to fluctuating LFTs. HCV PCR was performed and positive with >20,000,000 IU/ml, confirming the diagnosis of HCV.

**Summary of Results:** Hepatitis C virus (HCV) is a blood transmitted enveloped RNA virus that has infected approximately three percent of the world’s population and is major cause of liver disease. HCV infects liver cells where it undergoes replication, eventually leading to cell necrosis and chronic hepatitis in up to 80% of those infected. It is most commonly transmitted by sharing needles with infected people while engaging in intravenous drug use, blood transfusions and medical procedure errors. HCV is most often diagnosed by screening blood of individuals with risk factors with a generation three ELISA. However, individuals screened within 8 weeks of infection have a higher false negative rate of approximately 6% due to being in a window period, in which, the infected individual has not made antibodies to the HCV. Individuals with risk factors, signs of HCV infection, such as, increased or fluctuating liver function test, nausea, jaundice, right upper quadrant pain and or immunodeficiency should undergo HCV RNA detection with PCR. PCR can detect HCV RNA within one week of exposure and has a sensitivity and specificity approaching 99%.

**Conclusions:** In conclusion, one must consider confirming any negative HCV screening test results with PCR when patients have risk factors for HCV and may be in the window period.

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P7

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P8

FREQUENT SINGLE NUCLEOTIDE POLYMORPHISMS IN GERM LINE DNA OF CDK4, FANCB, FANCC AND MEN1 ARE SEEN IN BREAST CANCER PATIENTS

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Purpose of Study: Over 230,000 women are diagnosed with breast cancer each year, at age 50 years old in 50 women has the disease, by age 80 one in 12 women will be affected. To understand molecular mechanisms of cancer we looked at single nucleotide polymorphisms changes in the genomic DNA of breast cancer patient and compare frequency of detection to age matched women from cancer free controls.

Methods Used: 24 DNA samples were obtained from the Breast and Ovarian Tissue Bank from breast cancer patients. 20 patients had breast cancer without BRCA gene mutation, 4 patients were carriers of BRCA and had breast cancer and 13 individuals were cancer free age-matched controls. For this experiment, we followed the Nextera Rapid Culture Enrichment protocol provided by Illumina. This study investigated 94 genes and more than 1700 coding regions associated with Breast Cancer by using the TruSight Cancer Panel, set custom oligos targeting identified regions of genes associated with common cancers (4,000-80-mer probes, each constructed against the human reference genome).

Summary of Results: In the control group, about 30 percent had SNPs, or single nucleotide polymorphisms; in the breast cancer group, over 70 percent had SNPs. This showed a correlation between an SNP, a simple mutation, in the PALB2 gene and the development of breast cancer. Likewise, I found that the genes CDK4, FANCB, FANCC and MEN1 polymorphisms were 80% of the time present in breast cancer group than in the breast cancer group than in the control group (less than 10%). No SNPs in BRCA1/2 were correlations seen.

Conclusions: Breast cancer affects only a minority of women for unknown reasons. When studying a panel of 94 genes known to be associated with cancer found only 5 to have SNPs more often seen cancer patients versus control. These genes may be implicated in pathways conducive to cancer development of in failure of immune system to recognize and eliminate developing cancer cells.

P9

STUDIES ON MATERIAL BASIS FOR FLAVONOIDS OF SARCANDRA GLABRA PROMOTING THE PROLIFERATION OF BONE MARROW MEGAKARYOCYTES

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Purpose of Study: Sarcandra glabra, as traditional Chinese medicines recorded in Chinese pharmacopoeia (2005 edition), is widely used for the treatment of primary and secondary thrombocytopenic purpura in clinic. However, what kind of composition for Flavonoids of Sarcandra glabra plays the clinical effects is not clear. The objective of this study was to clarify material basis of total flavonoids of Sarcandra glabra promoting the proliferation of bone marrow megakaryocytes.

Methods Used: We used Agilent 6538A quadrupole-time of flight tandem mass spectrometer to detect composition changes on different time points of plasma containing flavonoids of Sarcandra glabra in 0.39, 2.0g/kg. Then, the R package Metabolomics Univariate and Multivariate Analysis (muma) was performed for the metabolomic analysis based on the mathematical separation method.

Summary of Results: We identified seven compounds (A,B,C,D,E,F,G) in flavonoids of Sarcandra glabra. The model of immune thrombocytopenic purpura (ITP) rats on diets indicated the concentrations of 40, 20 mg/kg of the compound A could significantly increase the number of platelets. Megakaryocytes in vivo showed the concentrations of 500 and 250µg/ml of the compounds A and G could promote the proliferation of rat bone marrow megakaryocytes (P<0.01 and P<0.05, respectively). On the cytokines, only at the concentrations of 125, 62.5µg/ml of the compound A could significantly increase TGF-β1 level (P<0.01 and P<0.05, respectively).

Conclusions: The vivo and vitro experiments indicated the compound A is the material basis of Flavonoids of Sarcandra glabra promoting the proliferation of bone marrow megakaryocytes. This study was supported by the National Science Foundation of China (81001662).

P10

VARIATION IN TEST ORDERING FOR LOW ACUITY PATIENTS BY PEDIATRIC EMERGENCY DEPARTMENT PROVIDERS

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Purpose of Study: Determine the variability of laboratory and radiology testing among licensed individual providers (LIPs) treating low acuity patients in the pediatric emergency department (PED).

Methods Used: This was a retrospective review of the electronic health records of patients aged ≤ 21 years with Emergency Severity Index (ESI) triage level 4 or 5 visiting two urban, academic, PEDs between January 2012 and December 2013. Ordering frequencies for complete blood count, aerobic blood culture, urinalysis, and chest radiographs were collected. Bivariable analysis assessed the odds of ordering tests between physicians vs. nurse practitioners (NP); physicians with pediatric emergency medicine training (PEM) vs. without and physicians with ≥ 5 years since residency graduation vs. <5 years. Logistic regression and subgroup sensitivity analyses adjusted for potential confounders, including location and encounter characteristics.

Summary of Results: We included 148,570 encounters. There were 12 NPs and 144 physicians, of whom 61 were PEM and 73 physicians were more experienced. Testing rates per patient encounter ranged from 0.0% to 40.0% for individual LIPs. In bivariable analyses, testing was more likely when the LIP was a physician (OR 1.2 95%CI 1.1-1.2) or PEM (OR 1.2, 1.2-1.3). In multivariable analyses, testing was more likely for PEM (OR 1.2, 1.1-1.3) and more experienced LIPs (OR 1.1, 1.0-1.1). Sensitivity analysis on a subset seen exclusively in PED-based urgent care revealed similar trends with testing being more likely amongst PEM (OR 1.5, 1.4-1.7) and more experienced LIPs (OR 1.3, 1.2-1.4) compared to physicians. These differences were significantly attenuated or eliminated when excluding high volume LIP outliers.

Conclusions: Our study identifies significant variability in ordering practices of LIPs treating low acuity patients, which is associated with training and experience. However, these differences were primarily driven by a few high volume LIPs. Further research should examine interventions to standardize practice across disciplines.

P11

AUTOIMMUNE HEMOLYTIC ANEMIA FOLLOWING TREATMENT WITH BENZAMUSTINE: A CASE SERIES

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Purpose of Study: The alkylating agent benzamustine is a potent chemotherapeutic agent, FDA approved in 2008 for the treatment of chronic lymphocytic leukemia (CLL) and B-cell non Hodgkin lymphoma. The combination of benzamustine and rituximab (BR) has emerged as an alternative initial therapy for patients with CLL unable to tolerate a regimen such as fludarabine, cyclophosphamide, and rituximab (FCR). Benzamustine can cause myelosuppression, however autoimmune hemolytic anemia (AIHA) has rarely been reported. In this single institution case series, we identified 5 patients with CLL who developed significant AIHA following benzamustine exposure.

Methods Used: We conducted a retrospective review of all patients with CLL who received benzamustine from 2008 - 2014 at our high volume CLL Research and Treatment Center. Hemolytic anemia following benzamustine exposure was noted in 5 patients. Patients with active hemolysis prior to dosing, benzamustine therapy duration, or benzamustine conversion to fludarabine were excluded.

Summary of Results: All patients were Caucasian with median age of 63 years (range 56-69 years). Three patients previously received fludarabine...
at least 7 months prior to treatment with bendamustine, one of whom had a history of fludarabine induced AIHA in remission. Other additional patients not previously treated with fludarabine had a history of AIHA also in remission prior to receiving bendamustine. The mean drop in hemoglobin from baseline was 3.7 g/dL. AIHA developed 5-13 weeks after first bendamustine dose (median of 6 weeks). Treatment for AIHA included corticosteroids in all 5 patients, 2 of whom required additional immunosuppression with rituximab with one patient also requiring cyclosporine. Hemolysis persisted for an average of 8 weeks (range 3-18 weeks).

**Conclusions:** AIHA secondary to bendamustine is extremely rare, but can be serious and potentially life threatening if not recognized and treated promptly, thus it is important for clinicians to be aware of this potential complication. The optimal management of AIHA secondary to bendamustine is unknown. Immediate discontinuation of bendamustine is warranted, and in our institutional experience, immunomodulators (glucocorticoids, rituximab, or cyclosporine) appeared to be an effective strategy for the management of hemolysis in these patients.

**Purpose of Study:** To compare the serum concentrations of clusterin in hepatocellular carcinoma patients and healthy people and determine the protein's concentration and mRNA expression in tissues of hepatocellular carcinoma and in cultured hepatocytes, respectively.

**Methods Used:** Serum clusterin levels were determined in 60 participants with hepatocellular carcinoma and in 60 healthy individuals by iTRAQ labeling and LC-MALDI-TOF/TOF MS; multiple reaction monitoring (MRM) was also used to detect serum clusterin. Real-time RT-PCR was used to measure differences in the expression of clusterin mRNA in cultured hepatocellular carcinoma cells versus healthy hepatocytes. Western blotting was used to check the level of clusterin in 30 paired hepatocellular carcinoma and adjacent normal healthy tissues.

**Summary of Results:** The serum level of clusterin was lower in hepatocellular carcinoma patients than in healthy individuals according to mass spectrometry analysis; At the same time, the mRNA level of clusterin in hepatoma tissues was 42 percent of the level in adjacent normal tissues. The OD values were 8.06 and 27.81 in hepatocellular carcinoma cells and normal hepatocytes (P < 0.01), respectively.

**Conclusions:** In conclusion, the present study demonstrates that clusterin is down-regulated in hepatocellular carcinoma cell lines, serum and tissue. Clusterin is likely to play an important role in the development of the occurrence of hepatocellular carcinoma.

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**P14 STUDIES ON THE ANTI-HYPOXIA EFFECTS OF PAECILOMYCES TENUIPES N45 EXTRACTS**

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**Purpose of Study:** The bioactive compounds of Paecilomyces tenuipes are similar to that of Cordyceps sinensis. In our previous research, via nitrosoguanidine treatment, mutant Paecilomyces tenuipes N45 was obtained. The present study is intended to explore the potential anti-hypoxia activities of Paecilomyces tenuipes N45 extracts.

**Methods Used:** We used KunMing mice (6 week; 20-22 g; Equal numbers of male and female; n=80/dosing group) were treated with Paecilomyces tenuipes N45 extracts (WE) at 0.04 g/kg, 0.2 g/kg and 2 g/kg for 14 days via gavage. The control group (n=20) received equal volume of normal saline. The anti-hypoxia effect of Paecilomyces tenuipes N45 was detected in acute cerebral ischemia hypoxia test, normobaric hypoxia test, and sodium nitrite toxicosis test, respectively. Moreover, another 80 mice were divided into 4 groups randomly. The biochemical indicator changes in serum before and after 30-min swimming were detected via enzyme-linked immunosorbent assay.

**Summary of Results:** In acute cerebral ischemia test, the respiratory rate was significantly increased in WE-treated mice compared to non-treated group (P<0.01). Only 0.04 g/kg and 0.2 g/kg WE treatment resulted in an improvement on survival time compared to non-treated mice in normobaric hypoxia test (P<0.01). WE at all chosen doses strongly enhanced survival time in sodium nitrite toxicosis test (P=0.01). In mouse swimming experiment, WE increased the serum concentration of adreno-cortico-tropic hormone (ACTH) and cortisol (CORT) both before and after swimming, especially after 2 g/kg WE treatment (P<0.01).

**Conclusions:** Our present research confirmed the anti-hypoxia effects of Paecilomyces tenuipes N45 extracts in mouse model. This effect may be related to the increment of serum concentration of ACTH and CORT. Paecilomyces tenuipes N45 may be a potential agent against hypoxia. Our study on Paecilomyces tenuipes may also be helpful to alleviate the Cordyceps sinensis resources pressure and sufficient to meet the increasing demand.

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**P15 PEDIATRIC CRITICAL CARE TRANSPORT AS A CONDUIT TO PALLIATIVE CARE: A CASE SERIES AND LITERATURE REVIEW**

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**Purpose:** The traditional approach to endovascular management of carotid blowout syndrome (CBS) has been occlusion of the bleeding pseudo-aneurysm; the use of thrombin in a case of failed stenting is presented.

**Conclusion:** In conclusion, the present study demonstrates that thrombin is an effective strategy for the management of hemolysis in these patients.

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**P12 A NOVEL APPROACH TO THE MANAGEMENT OF CAROTID BLOWOUT SYNDROME: THE USE OF THROMBIN IN A CASE OF FAILED STENTING**

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**Purpose of Study:** Acute hemorrhage or symptoms relating to an expanding pseudoaneurysm are referred to as carotid blowout syndrome (CBS). Traditional endovascular management of CBS has been occlusion of the bleeding vessel. In patients that cannot tolerate sacrifice, the alternative is to use covered stents. We describe a case of continued filling of the pseudo-aneurysm sac (PAS) despite the stepwise use of three covered stents.

**Methods Used:** An 86-year-old male with a PMH significant for hypertension, coronary artery disease, abdominal aortic aneurysm and right carotid endarterectomy presented with dyspnea for 3 days with an expanding and painful pulsatile mass over his right neck. A computerized tomography angiogram of the neck showed a 6.8 x 6.1 x 4.5 cm expanding pseudo-aneurysm at the bulb of the right internal carotid artery (ICA). Two covered stents (Gore® Viabahn®) were placed in the right ICA with a significant decrease in flow to the PAS. Follow-up carotid doppler showed a significant increase in flow into the PAS the next day. A third Viabahn® stent was placed to provide coverage at the site of the leak but filling into the PAS continued. As an alternative approach, thrombin was injected percutaneously into the PAS under fluoroscopy, with simultaneous balloon occlusion of the stent.

**Summary of Results:** Repeat angiography showed complete cessation of flow into the PAS. The patient had no neurological deficits postoperatively and follow-up doppler showed a decrease in hematoma size with no flow in the PAS.

**Conclusions:** To prevent recurrent risk of bleeding in recalcitrant lesions, different approaches to achieving embolization have been described in the literature - cyanoacrylate embolic mixtures, polyvinyl alcohol (PVA) or absolute alcohol. The use of thrombin to achieve thrombosis comes with the risk of systemic spread and formation of a thrombus that can migrate into the cerebral circulation. Thrombin is commonly used in the endovascular management of peripheral vessels; however, its use in the carotid vasculature opens a new avenue for treatment of a serious medical condition. Success can be achieved in difficult cases with the use of thrombin and simultaneous balloon occlusion and should be considered as an alternative approach in the management of CBS.
Purpose of Study: To present a series of three successful pediatric palliative care transports from the Intensive Care Unit (ICU) of a tertiary care facility to home and to provide an overview of the existing literature on both pediatric and adult palliative care transports.

Methods Used: Cases were identified from the Johns Hopkins Hospital Pediatric Transport database and the literature review was based on the National Library of Medicine PubMed search from 1975 to present. All three cases were terminally ill pediatric patients unable to separate from life-sustaining medical devices in the ICU who were transported home for terminal extubation and end of life care according to their families’ wishes. Review of transport and palliative care literature focusing on the end of life transport process from ICU to home was then undertaken. All pediatric and adult studies (case reports, case series and review articles) were included.

Summary of Results: All three cases presented similar logistical challenges due to the patients’ unstable medical condition and urgent need for transport to facilitate the families’ wishes for withdrawal of care and death at home. These included the need to clarify resuscitation status pre-transport and the limited time to organize the transport (mode of transport and team composition), as well as to coordinate home palliative care with the existent resources in the community. The literature review identified a very limited number of case reports (1 in neonates, 2 in children and 8 in the adult aging population) which shared our logistical challenges.

Conclusions: Palliative critical care transports pose a unique set of challenges in both pediatric and adult populations. Limited data exist in the literature surrounding this field. These data in combination with our recent pediatric experience support the need for further research and formal program development for end of life critical care transports.

P16 UPTAKE OF SPINOSIN FROM THE APICAL MEMBRANES OF THE HUMAN ENTERAL CACO-2 CELLS

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Purpose of Study: Spinosin (2''-O-glucopyranosyl oviertin, CsH26O8 SPI) is a triterpenoid found in the Chinese medicinal herb Ziziphi Spinosi. Spinosin has anxiolytic-like effects that may be mediated by the GABAergic and serotonergic systems. While, previous research showed that, as a single component, spinosin was poorly absorbed in rats after oral administration. In this study, we investigated whether the uptake of spinosin across the apical membrane of Caco-2 cells was mediated via P-glycoprotein (P-gp).

Methods Used: The uptake mechanism of SPI was investigated using Caco-2 cell cultures differentiated with pro-inflamatory media and untreated in pH 7.4 and 37°C. Both different concentrations of SPI (15-250 μM) and different exposure times (5 min - 50 min) were tested. At the same time, we investigated whether the SPI uptake across the apical membrane of Caco-2 cells is mediated by P-GP in the way of pretreatment with Verapamil, which is a P-gp inhibitors.

Summary of Results: The uptake of SPI from the apical membranes was fast, and concentration dependent. The uptake of SPI at pH 7.4 decreased rapidly from 30s to 2min then increased slowly, almost reaching a plateau at 2min. The conclusion was that SPI inhibited the uptake of SPI by 45%, which indicated that efflux pump P-glycoprotein (P-gp) might exert some effects on the uptake of SPI, which was in accordance with our former research that SPI was the substrate of P-glycoprotein (P-gp) using single-pass intestinal perfusion. The relationship between the initial uptake of spinosin (2 min) and spinosin concentrations in the medium (15-250 μM) and different exposure times (5 min - 50 min) were tested. At the same time, we investigated whether the SPI uptake across the apical membrane of Caco-2 cells is mediated by P-GP in the way of pretreatment with Verapamil, which is a P-gp inhibitors.

Conclusions: The uptake of spinosin appears to be mediated mainly via nonsaturable process (simple diffusion) at low concentrations and via saturable process (carrier-mediated process) at high concentrations. These results indicated that the uptake of SPI from the apical membrane of Caco-2 cells is mediated via both simple diffusion and carrier-mediated process and also influenced by P-gp. This work was supported by the Foundation of HENAN Traditional Chinese medicine (MP2013-15).

P17 A CASE OF SYSTEMIC SCLEROSIS WITH ASSOCIATED RHINITIS, FOOD, ALLERGY AND ORAL ALLERGY SYNDROME

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Purpose of Study: Systemic sclerosis is characterized by dermal collagen deposition, and mast cells are important in the pathogenesis of the early cutaneous lesions of progressive systemic sclerosis, by promoting fibrosis. Mast cells disorganization that occurs in rhinitis, food and oral allergy syndromes may interact with fibroblasts in the affected tissue. Chronic degranulation might accelerate additional fibrosis.

Methods Used: We present a 42 year old women with systemic sclerosis, previously diagnosed in 2002 with positive anti-Scl-70 antibodies, Raynaud’s syndrome, acid reflux, pleural fibrosis and sclerodactyly referred to allergy clinic from Rheumatology for recent allergic flares. We re-evaluated her past history and she described chronic allergic rhinitis, and symptoms regarding several fruits as pineapple and apple Physical examination revealed normal vital signs, nasal boggy turbinates, normal cardiovascular system, diffuse tight skin and sclerodactyly. She currently only take omeprazole for acid reflux and close follow up with Rheumatology. Radioallergosorbert sIgE tests were performed.

Summary of Results: Specific IgE test results showed multiple specific IgE antibodies to Birch (class III), June grass (class III), Oak (class III), Maple (class II), Timothy grass (class II), Shrimp (class I), and Pineapple (class I). She was instructed on the pollen-food OAS, related use of anti-histamines, limited nasal steroid due to rhinitis and avoidance of affected food and fruits.

Conclusions: We believe this is the first case of systemic sclerosis in a female with allergic rhinitis and associated oral allergy syndrome. Earlier studies performed indicate that disorganization of mast cells in oral allergy syndrome may have a role of dermal collagen deposition in systemic sclerosis. Rheumatologists may not be aware of OAS. Patients with oral allergy syndrome should be tested to confirm the pollen food connection and prevent systemic sclerosis from progression. Mast cell therapies are a therapeutic option.

P18 INHIBITION OF ENDOTOXINS LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION BY Acanthopanax senticosus Harms EXTRACTS IN MICROGLIAL BV-2 CELLS

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Purpose of Study: Microglia are the principal immune effector cells in the central nervous system. Microglia can be activated by bacterial endotoxins such as lipopolysaccharide (LPS) and produce pro-inflammatory mediators such as nitric oxide (NO) which are thought to induce nitrosative stress and contribute to neuronal injuries leading to the progression of neurodegenerative diseases. Botanicals such as Acanthopanax senticosus Harms has been revealed to have various biological activities and gained interests as potential sources for the treatment and prevention of neuroinflammation and neurodegenerative diseases. In this study, experiments were conducted to investigate if Acanthopanax senticosus Harms extracts could reduce NO-induced nitrosative stress and therefore protect nerve cells from inflammatory injuries in microglial BV-2 cells by a gel-based quantitative proteomic approach.

Methods Used: BV-2 cells were exposed to 100 ng/mL LPS for 16 hours in the presence or absence of Acanthopanax senticosus Harms extracts. NO production was measured by Griess Assay, and cell viability was determined by MTT Assay. Cell lysates of the samples (untreated, LPS-treated, LPS+ Acanthopanax senticosus Harms extracts) in biological triplicates were labeled with CyDyes and resolved by two dimensional difference in-gel electrophoresis (2D-DIGE). The subsequent gels were visualized by Etan DIGE Imager and analyzed with the SameSpot software.

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Summary of Results: Our results showed Acanthopanax senticosus Harms extracts inhibited LPS-induced NO production, while no significant toxicity appeared in the cells as determined by MTT assay. Using SameSpot software, we detected a total of 980 protein spots on the gels. Compared to LPS-treated conditions, 15 protein spots showed significant protein level changes (fold changes >1.5, p < 0.05) after treatment with Acanthopanax senticosus Harms.

Conclusions: Our results revealed the ability of Acanthopanax senticosus Harms extracts to attenuate LPS-induced neuroinflammatory response in microglial cells, and provided insights into the molecular events underlying the treatment of Acanthopanax senticosus Harms extracts.

P19
A RARE CORONARY ARTERY ANOMALY
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Purpose of Study: A single coronary artery occurring in isolation in a structurally normal heart is rare. Most anomalies are benign and asymptomatic, however arrhythmias, syncope, myocardial infarction, and sudden death can occur.

Methods: A 69-year-old woman with history of hypertension and atrial fibrillation presented with recurrent episodes of chest pain. Cardiologist stress test was normal. Echocardiogram revealed normal LV systolic function, moderate to severe mitral and tricuspid regurgitation and mild pulmonary hypertension.

Diagnostic cardiac catheterization for evaluation of valvular disease showed non-obstructive coronary artery disease and anomalous coronary origin, with no visualized vessel arising from the left coronary cusp. The left anterior descending (LAD) and left circumflex (LCx) arteries were seen arising from a common trunk off the right sinus of valsalva, following a retroaortic/benign course. The septal perforator also arose from a common trunk off the right sinus, coursing in an interarterial position between the aorta and right ventricular outflow tract to the interventricular septum. The mid LAD showed moderate luminal narrowing by calcified plaque, and the distal LAD was found as a diminutive vessel not reaching the cardiac apex. The right coronary artery arose from a common trunk off the right sinus and coursed in a normal anatomic fashion with mild calcified plaque in its proximal portion. The posterior descending artery was opacified and the posterior left ventricular branch not seen. There was no evidence of regional hyperperfusion of the left ventricular myocardium or wall motion abnormalities.

Summary of Results: Isolated coronary artery arising from the aortic trunk by a single coronary ostium and supplying the entire heart is a rare congenital anomaly.

Conclusions: It is important to recognize the location and course of anomalous arteries and their role as risk factors for adverse cardiovascular events. Our patient depicted a unique presentation of a benign coronary anomaly with the arteries and their role as risk factors for adverse cardiovascular events. Our study shows that patients with these anomalies may have normal echocardiograms and catheterization studies may be needed to delineate the anatomic abnormality.

P20
HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH): THE MIMICKER
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Purpose of Study: Case Report

Methods Used: HLH, a rare but potentially fatal disease, is characterized by excessive immune activation & cytokine release which stimulates bone marrow (BM) macrophages to engulf hematopoietic cells. HLH is typically seen in patients with immune dysregulation such as immunodeficiencies, hematological malignancies & autoimmune diseases. We present an AIDS patient with HLH who presented with prolonged fever and no significant improvement, despite antibiotics.

Summary of Results: A 45 yr old lady with AIDS (diagnosed at 32, on HAART, CD4 nadir: 170. Latest CD4- 218, viral load <20c/ml) presented with extreme fatigue, fever/chills of 2 weeks duration. Vitals: T 102.8 HR 125/min BP 97/65mmHg. Hb: 8.9g/dl, WBC: 1.4K/uL, platelet: 126,000/uL, lactate: 2.67, ferritin: 16,926, LDH: 564, AST/ALT: 148/24, ALP: 238. She was rehydrated and given empiric antibiotics. Serial cultures remained negative. She however continued to spike fevers. PPd, histoplasma, cryptococcal, Parvovirus B19, EBV, malaria & babesia testing were negative. G6PD activity was normal. CT-scan showed splenomegaly & retroperitoneal lymphadenopathy. Given the lack of response to therapy, she had a BM biopsy which revealed scattered histiocytes containing erythroid & myeloid elements & high iron storage with no evidence of malignancy, consistent with HLH. Treated with etoposide, cyclosporine & dexamethasone, she responded after 2 weeks with fall in ferritin to 5057 and after initial leucopenia & thrombocytopenia (Ndadr: 0.2k/uL, 10,000/uL respectively) had resolution to 2.8K & 61,000/uL respectively. She improved, became febrile, was discharged to complete chemotherapy as outpatient. Her condition continues to improve.

Conclusions: Cytotoxic T-cell activation with hypercytokinemia which is protective in HIV/AIDS & hinders viral replication is responsible for macrophage activation & pancytopenia in HLH. Consequently, patients with HIV/AIDS & HLH share various non-specific symptoms, such as fever, acute liver failure, & splenomegaly. Identification of HLH as the cause of fever in a HIV patient could therefore pose a diagnostic challenge. HLH should be considered as a possible cause of fever in AIDS patients since early suspicion & diagnosis is critical to prompt therapy & improved mortality.